NON INVASIVE VENTILATION

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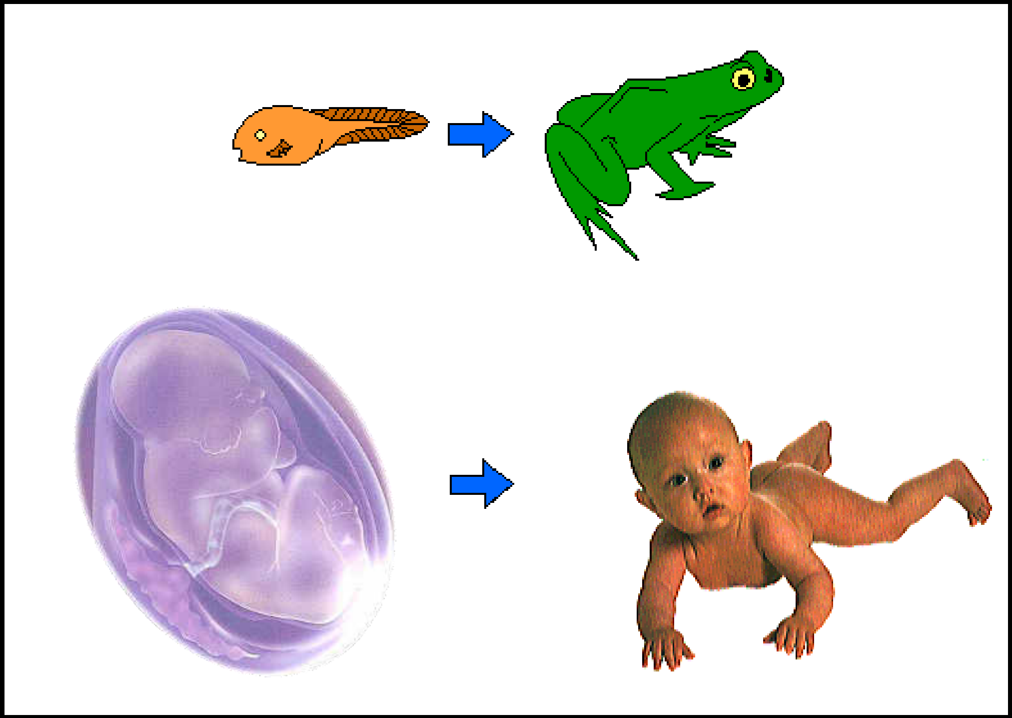
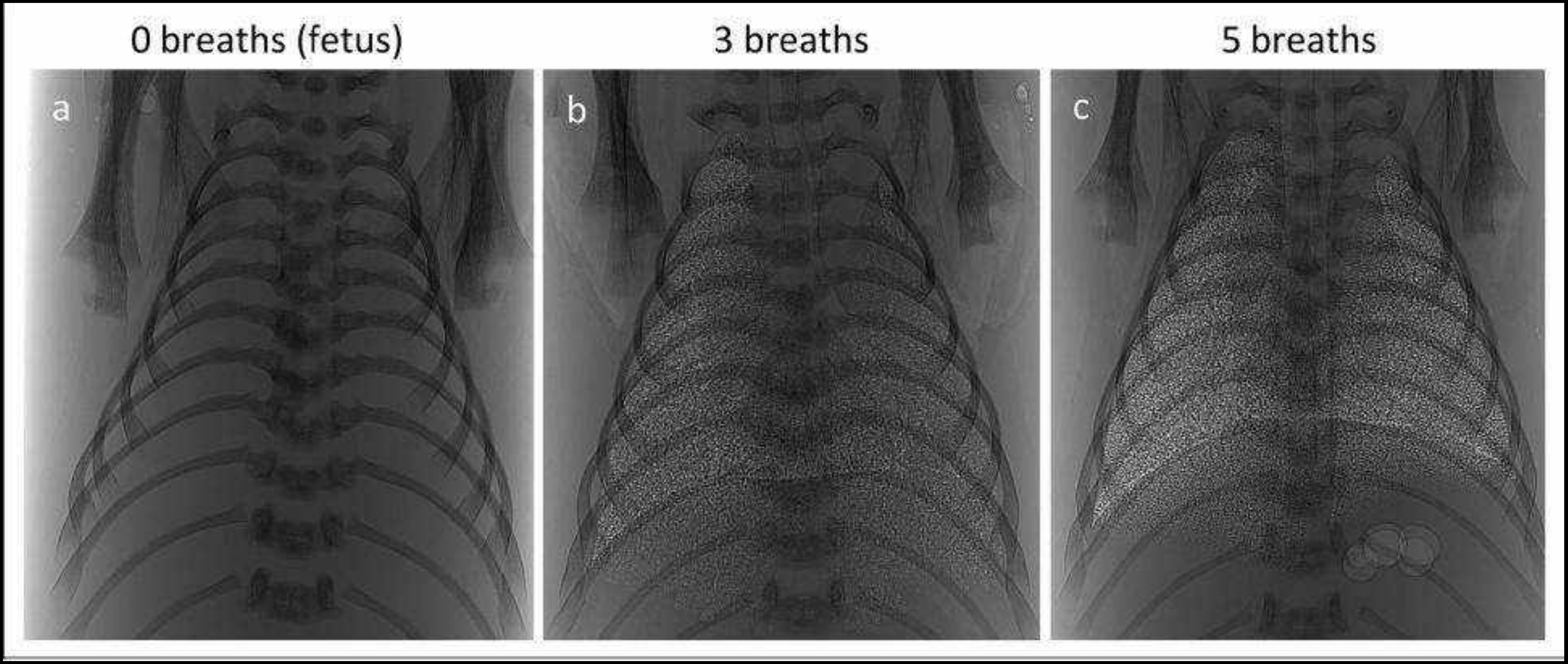
AHMEDABAD

Mammalian Birth is Similar to Amphibian Metamorphosis

- Transition from an aquatic existence to an obligate air breathing state
- Profound functional and structural adjustments in all organ systems
- Top of Mount Everest to sea level in a second



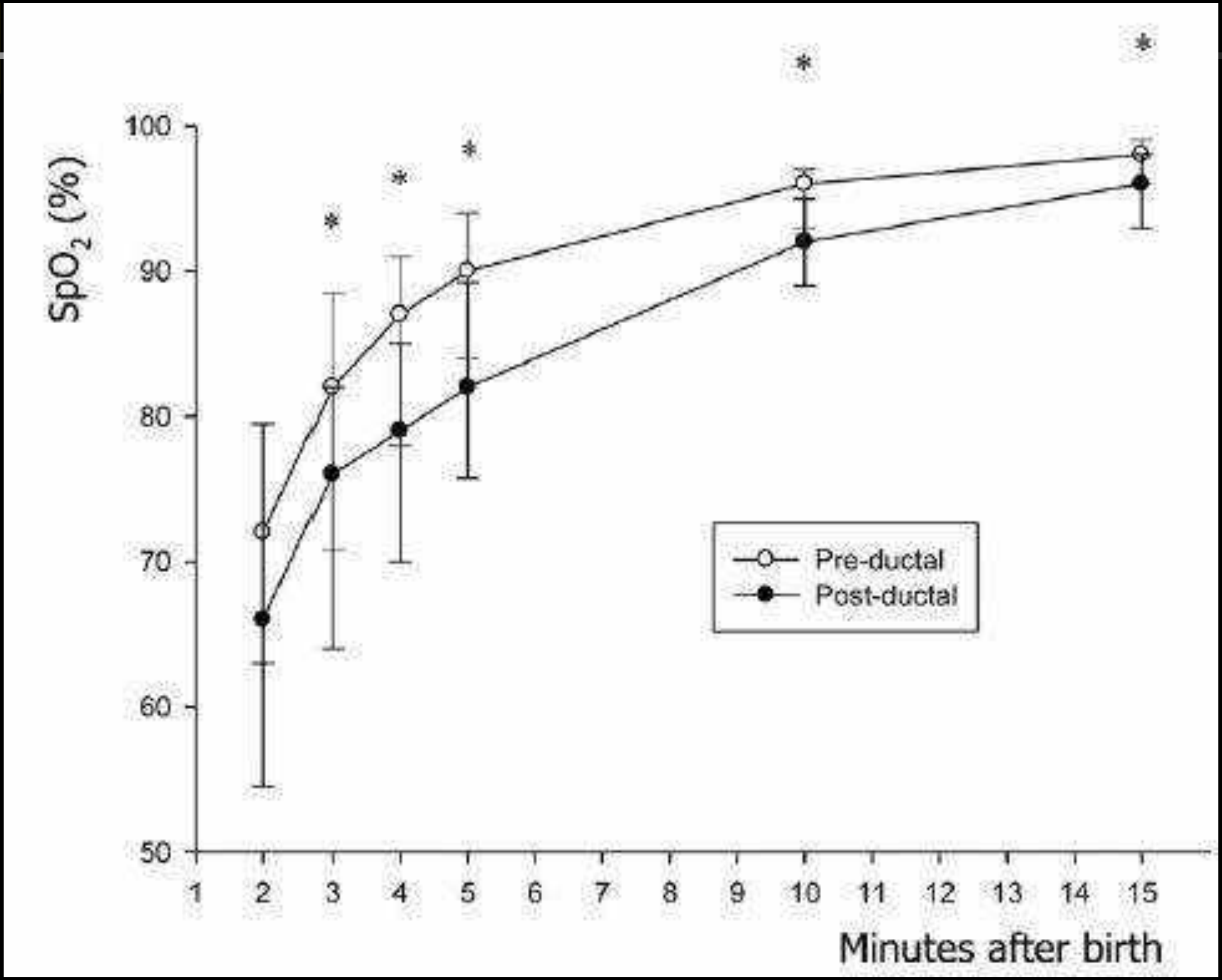
Functional Residual Capacity



Hooper SB et al, NeoReviews, 2010

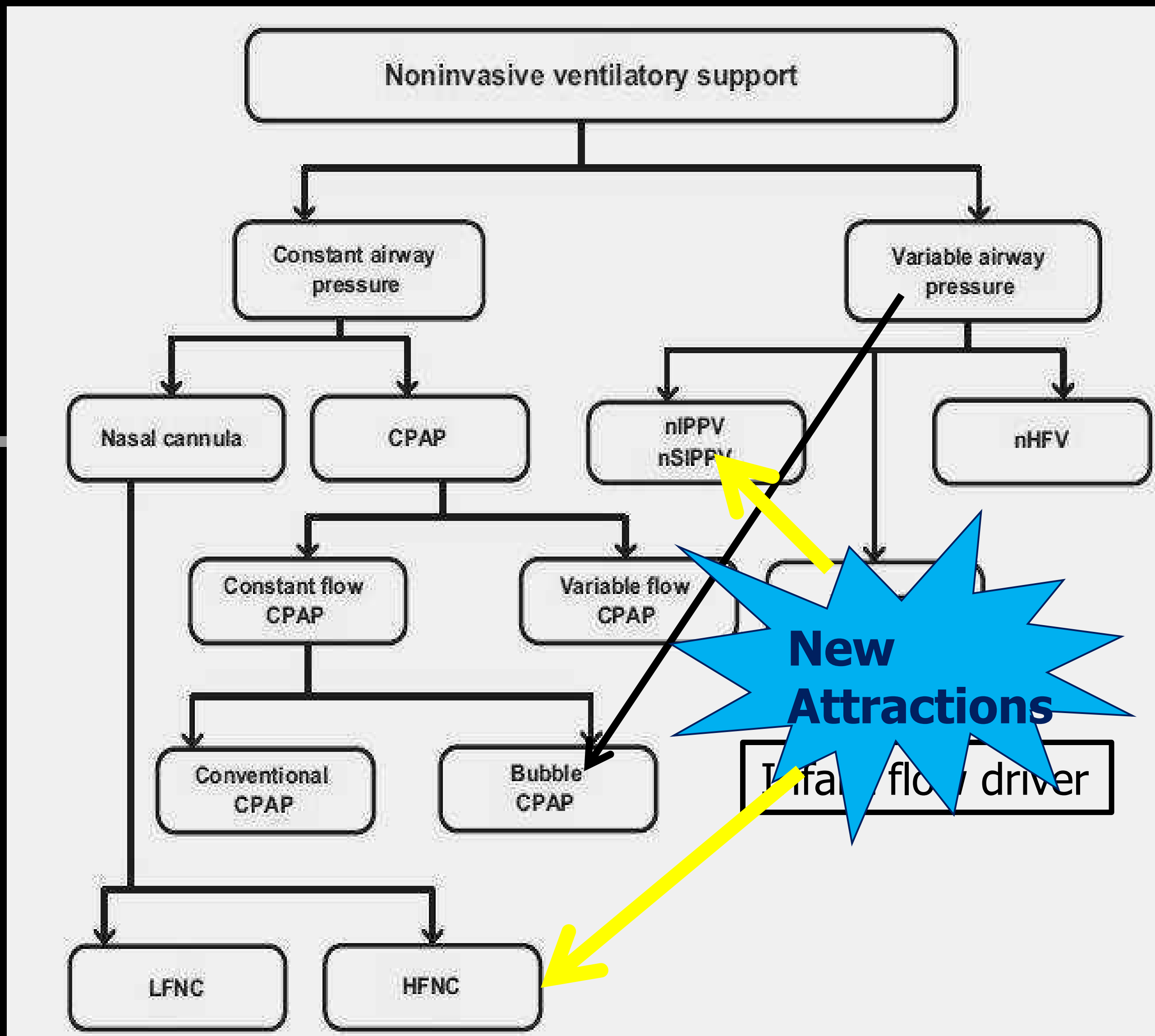
Oxygen saturation in healthy term infants

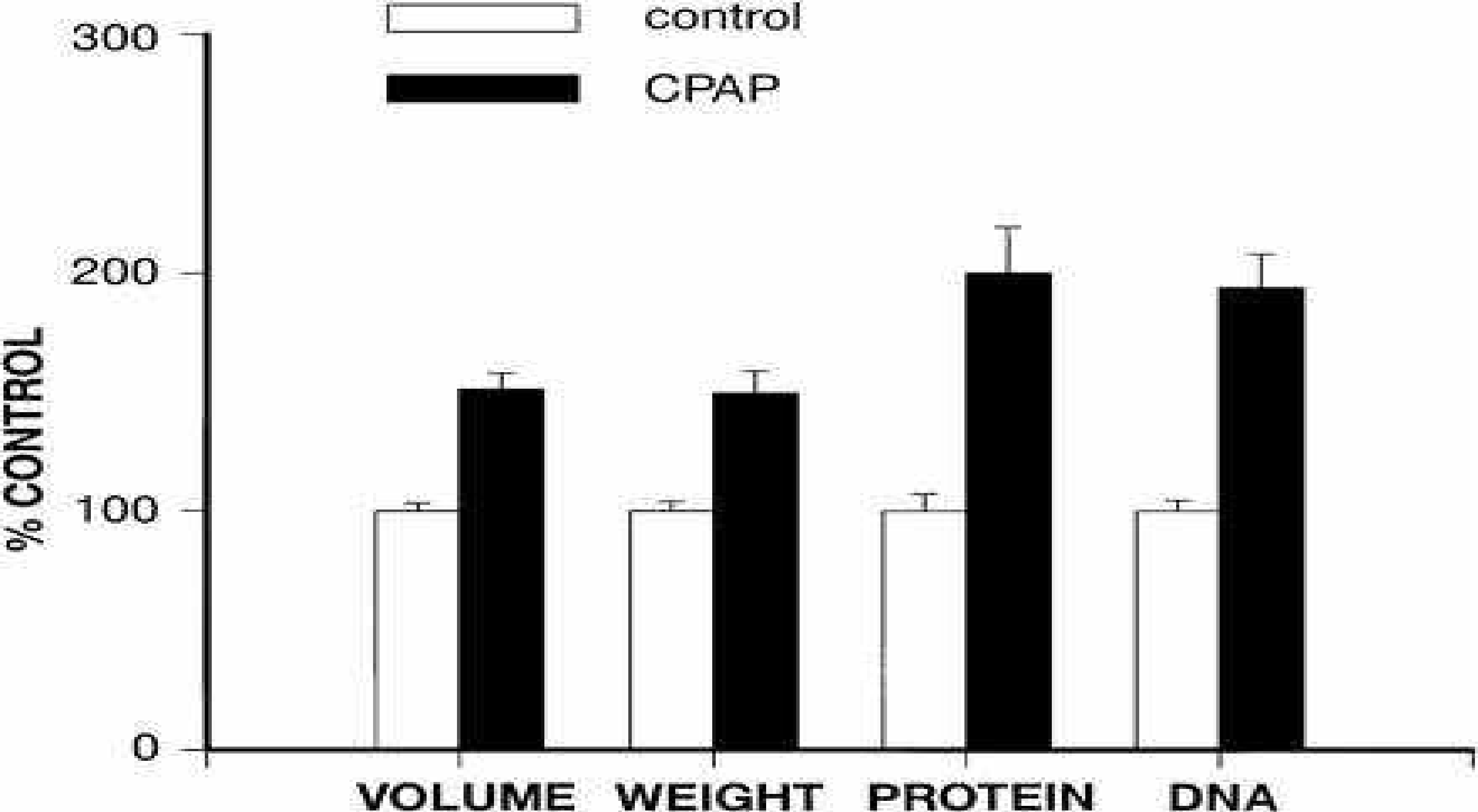
Mariani G et al, J of Peds, 2007



Respiratory support for preterm babies
Aim: open the lung and keep it open!

Traditional Classification of Non Invasive Ventilation



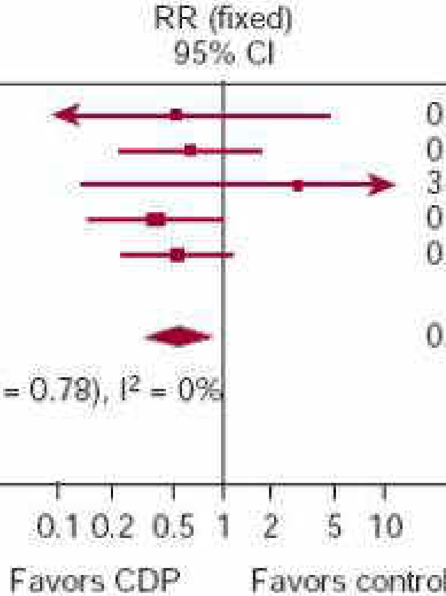


Lung volume, lung weight, and protein and DNA contents at end of study were higher in CPAP-exposed than in control animals (all *P* < 0.01). Strain-induced growth of the immature lung. Zhang S. et al. J. Appl Physiol 1996;81:1471-6

Does CPAP work in RDS ?

Study	CDP n/N	Control n/N	RR (fixed) 95% CI
Durbin 1976 (46)	1/12	2/12	0.50 [0.05, 4.81]
Fanaroff 1973 (43)	4/15	6/14	0.62 [0.22, 1.75]
Samuels 1996 (44)	1/26	0/26	3.00 [0.13, 70.42]
Belenky 1976 (45)	4/22	14/29	0.38 [0.14, 0.99]
Rhodes 1973 (8)	6/22	10/19	0.52 [0.23, 1.16]
Pooled analysis (95% CI)			0.52 [0.32, 0.87]

Test for heterogeneity: $Chi^2 = 1.73$, df = 4 (P = 0.78), $I^2 = 0\%$
Test for overall effect: Z = 2.51 (P = 0.01)



- ✓ Decreased need for assisted ventilation
- ✓ Reduces the duration of MV
- ✓ Significant reduction in mortality

Continuous distending pressure:

- Maintains upper airway patency
- Distends lower airways
- Maintains functional residual capacity (FRC)
- Preserves surfactant
- Increases pulmonary compliance
- Improves gas exchange
- Regulates breathing pattern

Morley CJ. ADC 2003

Success Rate with CPAP

Gest-ational Age (wks)	CPAP success rate (no mech vent until 3-7d)	N	Study	Ref
23-25	31%	87	Columbia Univ.	Ammari et al., J. Pediatr 147:341:2005
26-28	78%	106	Columbia Univ.	Ammari et al., J. Pediatr 147:341:2005
29-31	93%	54	Columbia Univ.	Ammari et al., J. Pediatr 147:341:2005
25-28	54%	307	COIN trial	Morely et al N Engl J Med 2008;358:700-8.
24-28	55%	663	SUPPORT trial	Finer et al N Engl J Med 2010;362:1970-9.
25-28	66%	103	CURPAP study	Sandri et al *Pediatrics* 2010;125:e1402–e1409
27-31	61%	138	RCT of Insure technique (Colombia)	Rojas et al *Pediatrics 2009;123:137–142*

CPAP and Surfactant

- Less need of MV
- Lesser duration of MV
- Decreased oxygen days
- Reduce CPAP failure rate
- Less airleak
- Lesser incidence of CLD
- Safe

DR CPAP vs Early Surfactant

Study	N	Design	Comments
COIN (NEJM 2008)	610	25-28 weeks, randomized at 5 minutes, CPAP 8, FiO2>60%	No difference in death or BPD, CPAP arm had more PTX and fewer days on MV. Subgroup analysis at 8 weeks showed CPAP arm had improved lung mechanics and decreased WOB
SUPPORT (NEJM 2010)	1316	24-27 weeks, randomized at birth, CPAP 5, FiO2>50%	No difference in death or BPD, CPAP arm required less intubation, fewer days on MV and less postnatal steroids. Decreased death in the CPAP arm among infants 24-25 weeks
CURPAP (Pediatrics 2010)	208	25-28 weeks, PSX vs Early CPAP CPAP 6, FiO2>40%	No difference in death or morbidities, conclude that >50% will only need CPAP
VON (Pediatrics 2011)	648	26-29 weeks, PS vs IS vs nCPAP, CPAP 5, FiO2 40-60%	No difference in mortality or BPD amongst the 3 groups. nCPAP arm had ~50% reduction in intubation rates and need for surfactant

Non-invasive versus invasive respiratory support in preterm infants at birth: systematic review and meta-analysis

Georg M Schmölzer *consultant*[1 2 3], Manoj Kumar *consultant*[1 2], Gerhard Pichler *consultant*[1 2 3], Khalid Aziz *professor*[1 2], Megan O'Reilly *postdoctoral fellow*[1 2], Po-Yin Cheung *professor*[1 2]

Table 1| Characteristics of included randomised controlled studies. Values are means (standard deviations) unless stated otherwise

Conclusions

Nasal CPAP initiated in the delivery room compared with intubation reduces death or bronchopulmonary dysplasia in very preterm babies. One additional infant could survive to 36 weeks without bronchopulmonary dysplasia for every 25 babies treated with nasal CPAP in the delivery room rather than being intubated and mechanically ventilated.

Stratification (weeks)	$25^{0/7}$-$26^{6/7}$ and $27^{0/7}$-$28^{6/7}$	$24^{0/7}$-$25^{6/7}$ and $26^{0/7}$-$27^{6/7}$	$25^{0/7}$-$26^{6/7}$ and $27^{0/7}$-$28^{6/7}$	$26^{0/7}$-$27^{6/7}$ and $28^{0/7}$-$29^{6/7}$

BMJ

BMJ 2013;347:f5980 doi: 10.1136/bmj.f5980 (Published 17 October 2013)

AAP recommendation…

- Using CPAP immediately after birth with subsequent selective surfactant administration may be considered as an alternative to routine intubation with prophylactic or early surfactant administration in preterm infants.

RA Polin, WA Carlo , AAP Pediatrics 2014

Level of evidence 1 : strong recommendation

AAP recommendation…

- IF respiratory support with a ventilator will be needed….
  - Early administration of surfactant followed by
  - Rapid extubation is preferable to prolonged ventilation…

RA Polin, WA Carlo , AAP Pediatrics 2014

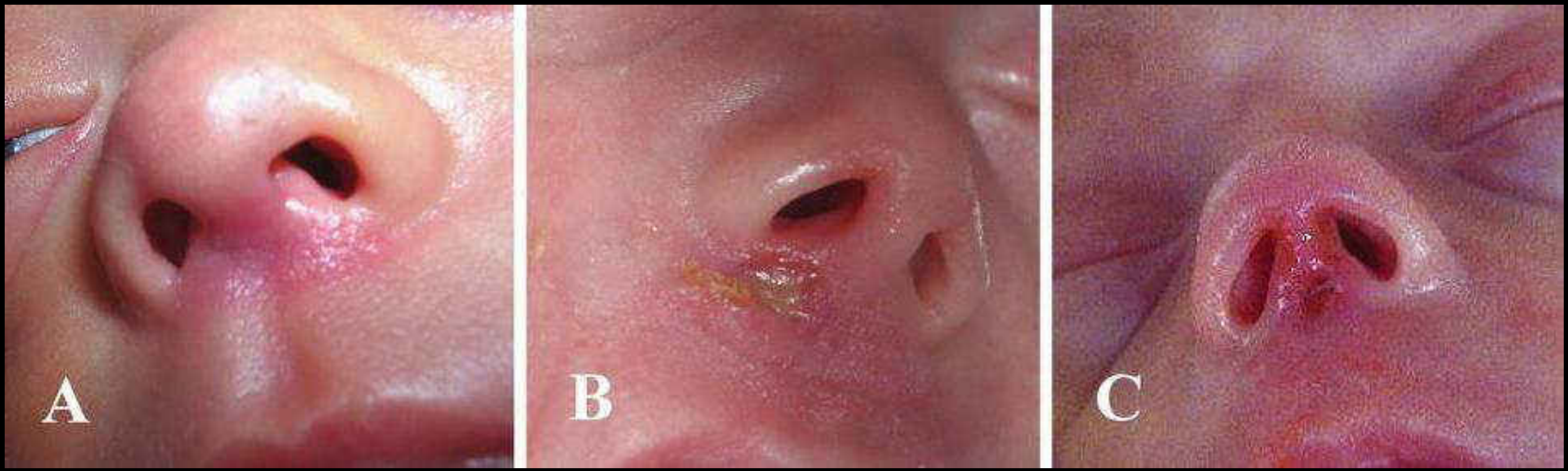
Level of evidence 1 : strong recommendation

Doing CPAP well isn't all that easy!

Prospective study with decubitus score staging

Swiss NICU with wide experience in CPAP use

CPAP-related Nasal Trauma Nasal occurs in > 40% of VLBWI Neonates



Fischer C et al. Arch Dis Child F&N Ed. 2010;95:F447-451

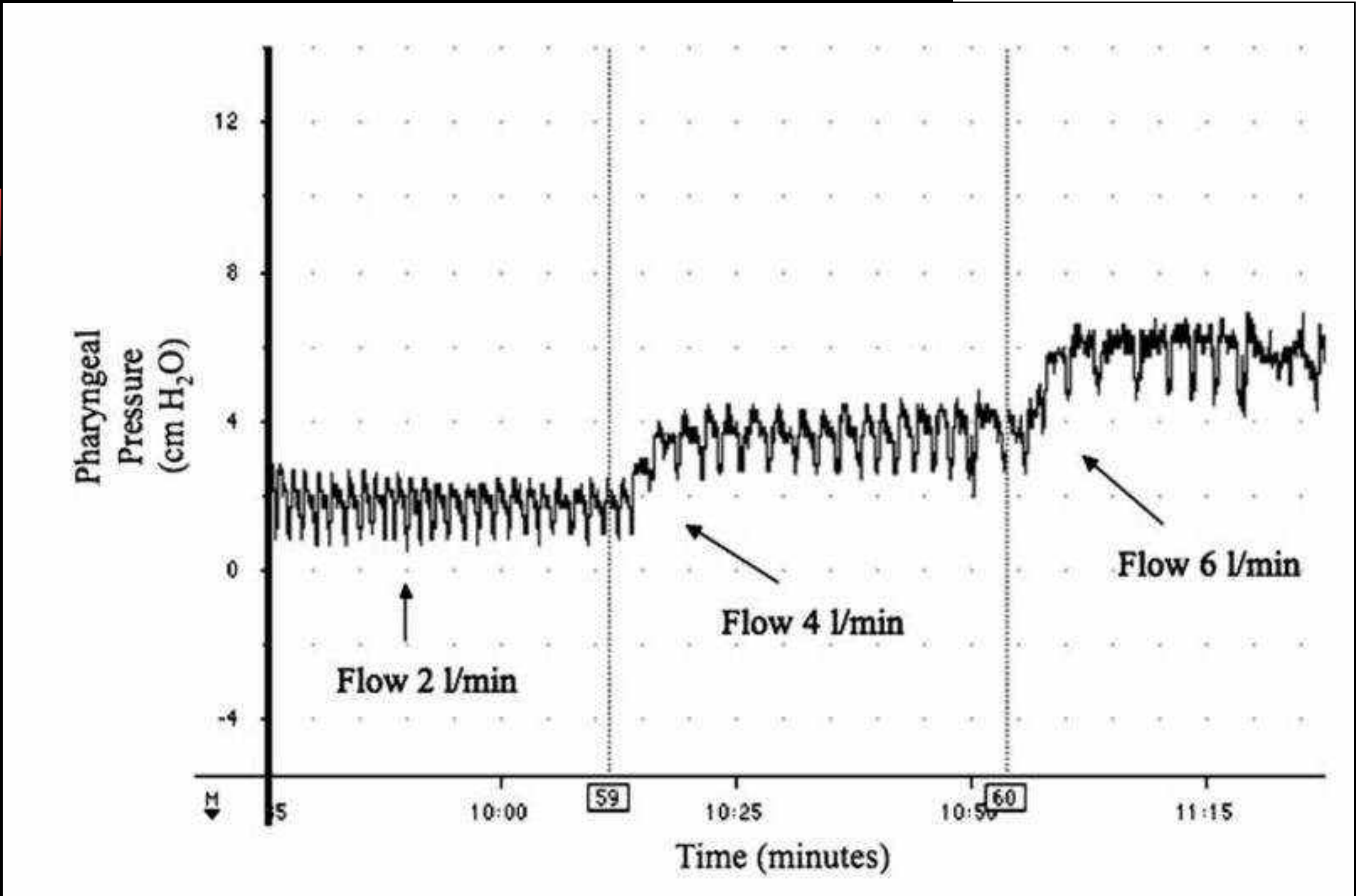
HHHFNC

CPAP

Fundamental difference HHHFNC and CPAP – presence of leak !

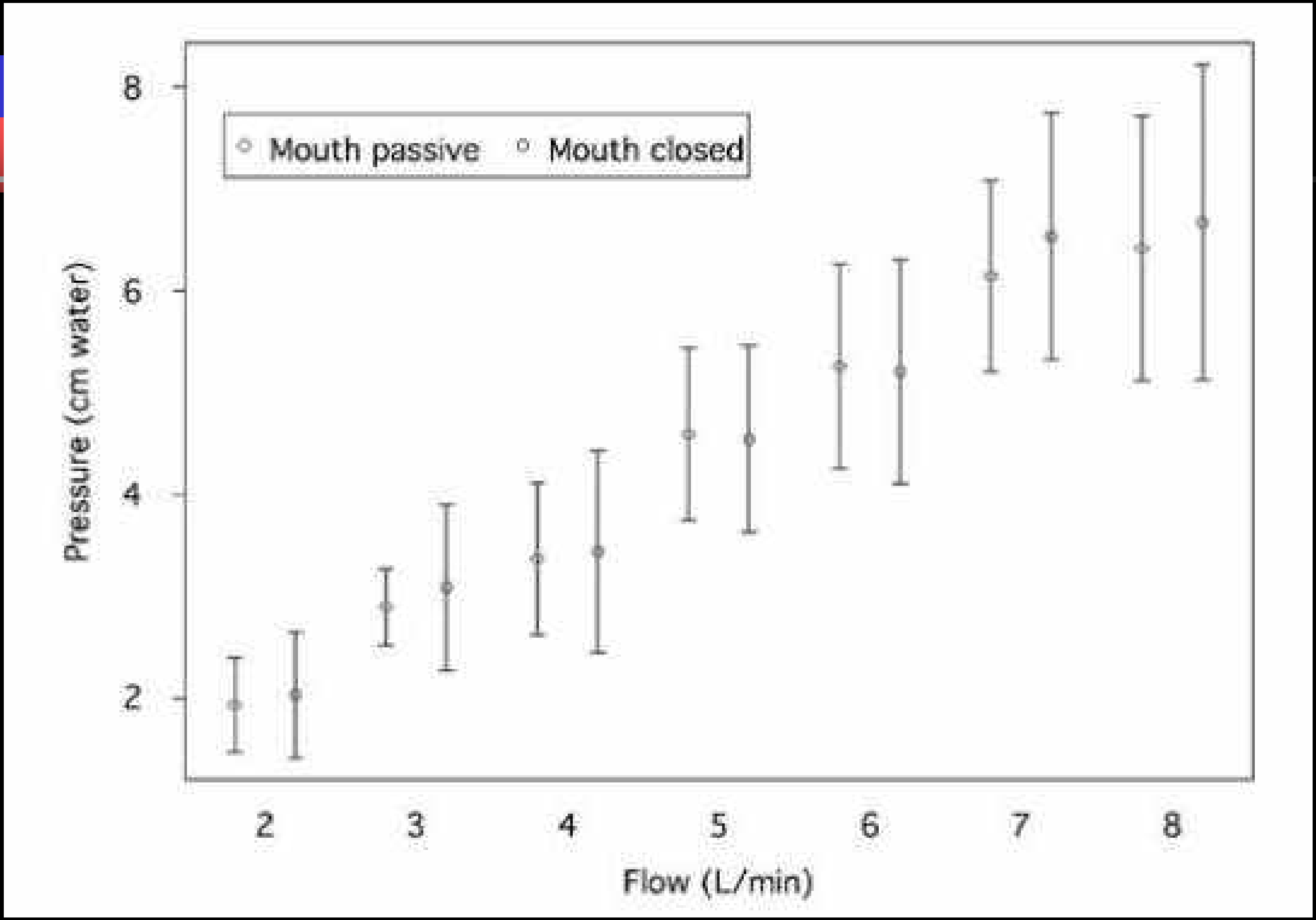
HFNC: Leak between cannula and nares is mandatory! 50-70%

Effective CPAP requires a good seal/minimal leak for pressure transmission!

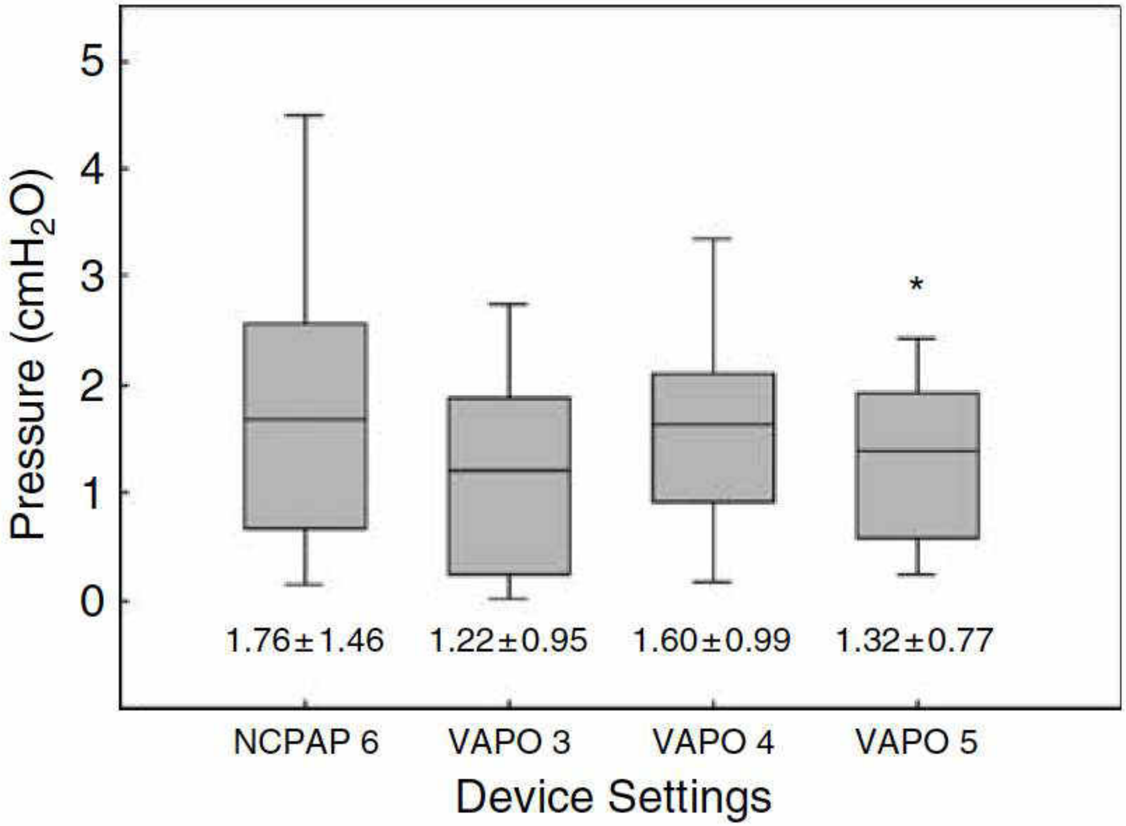


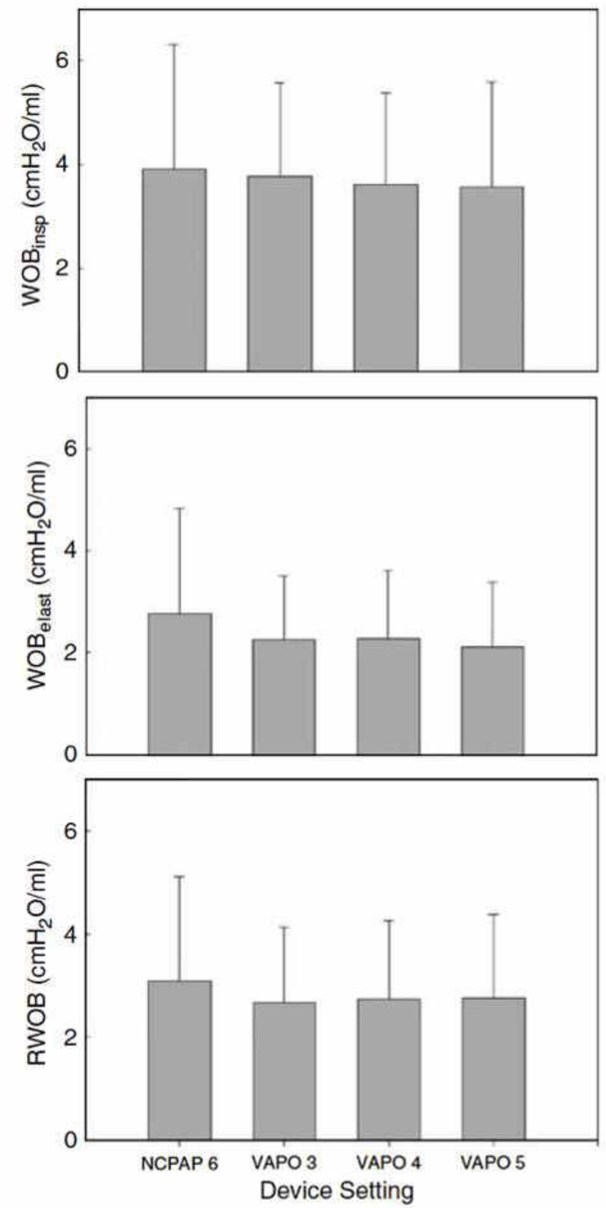
Result: pressure increases with increasing flow ($p<0.003$)

Wilkinson D et al. J Perinatol 2008; 28: 47-49



Wilkinson D et al. J Perinatol 2008; 28: 47-49





Conclusion:

WOB and pharyngeal pressures comparable between nCPAP and HHHFNC.

Heated, Humidified High-Flow Nasal Cannula Versus Nasal CPAP for Respiratory Support in Neonates

Bradley A. Yoder, Ronald A. Stoddard, Ma Li, Jerald King, Daniel R. Dirnberger and Soraya Abbasi

Pediatrics 2013;131;e1482; originally published online April 22, 2013;

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ORIGINAL ARTICLES

A Randomized Controlled Trial to Compare Heated Humidified High-Flow Nasal Cannulae with Nasal Continuous Positive Airway Pressure Postextubation in Premature Infants

Clare L. Collins, MBChB, FRACP[1], James R. Holberton, MBBS, FRACP[1], Charles Barfield, MBBS, FRACP[1], and Peter G. Davis, MD, FRACP[2]

High-Flow Nasal Cannulae in Very Preterm Infants after Extubation

Brett J. Manley, M.B., B.S., Louise S. Owen, M.D., Lex W. Doyle, M.D.,

N ENGL J MED 369;15 NEJM.ORG OCTOBER 10, 2013

Pediatr Pulmonol. 2015; 50:576–583.

Safety and Efficacy of High-Flow Nasal Cannula Therapy in Preterm Infants: A Meta-analysis

Sarah J. Kotecha, Roshan Adappa, Nakul Gupta, W. John Watkins, Sailesh Kotecha and Mallinath Chakraborty

Pediatrics; originally published online August 17, 2015;

- 1112 neonates
- HHHFNC compared with other modes of NIV when used as primary mode or post extubation

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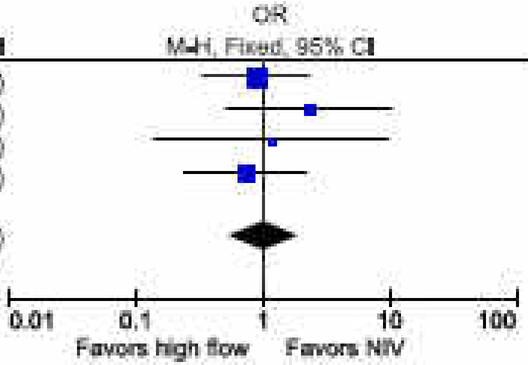
Primary Mode

Study or Subgroup	High Flow Events	High Flow Total	NIV Events	NIV Total	Weight, %	OR M-H, Fixed, 95% CI
Kugelman et al 2015[43]	12	38	13	38	44.0	0.89 (0.34 to 2.31)
Lavizzari et al 2013[44]	5	40	3	52	11.3	2.33 (0.52 to 10.41)
Nair and Kamat 2005[40]	2	13	2	15	7.8	1.18 (0.14 to 9.83)
Yoder et al 2013[38]	6	58	9	67	37.0	0.74 (0.25 to 2.23)
Total (95% CI)		149		172	100.0	1.02 (0.55 to 1.88)
Total events	25		27			

Heterogeneity: $\chi^2 = 1.59$, df = 3 ($P = .66$); $I^2 = 0\%$

Test for overall effect: $Z = .06$ ($P = .95$)

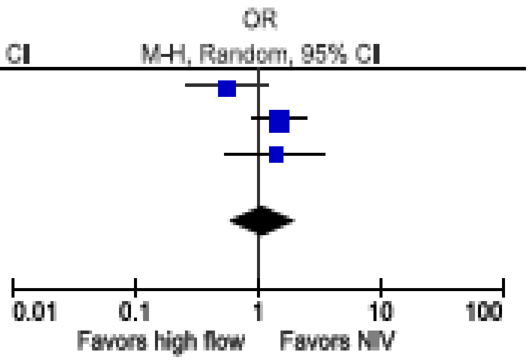


Post Extubation

Study or Subgroup	High Flow Events	High Flow Total	NIV Events	NIV Total	Weight, %	OR M-H, Random, 95% CI
Collins et al 2013[27]	15	67	22	65	31.0	0.56 (0.26 to 1.22)
Manley et al 2013[21]	52	152	39	151	43.2	1.49 (0.91 to 2.45)
Yoder et al 2013[38]	11	107	9	119	25.7	1.40 (0.56 to 3.52)
Total (95% CI)		326		335	100.0	1.09 (0.58 to 2.02)
Total events	78		70			

Heterogeneity: $\tau^2 = 0.17$; $\chi^2 = 4.53$, df = 2 ($P = .10$); $I^2 = 56\%$

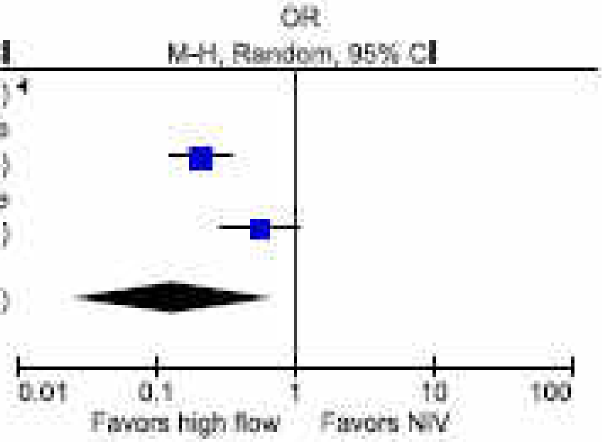
Test for overall effect: $Z = .26$ ($P = .80$)



Study or Subgroup	High Flow Events	High Flow Total	NIV Events	NIV Total	Weight, %	OR M-H, Random, 95% CI
Iranpour et al 2011	0	35	35	35	12.8	0.00 (0.00 to 0.01)
Kugelman et al 2015	0	38	0	38		Not estimable
Manley et al 2013	29	152	80	151	44.2	0.21 (0.12 to 0.35)
Phadtare et al 2009	0	26	0	44		Not estimable
Yoder et al 2013	16	159	30	179	43.1	0.56 (0.29 to 1.06)
Total (95% CI)		410		447	100.0	0.13 (0.02 to 0.69)
Total events	45		145			

Heterogeneity: $\tau^2 = 1.55$; $\chi^2 = 19.94$, df = 2 ($P < .0001$); $I^2 = 90\%$

Test for overall effect: $Z = 2.40$ ($P = .02$)



CONCLUSIONS: High-flow therapy appears to be similar in efficacy and safety to other conventional modes of NIV in preterm infants. It is associated with significantly lower odds of nasal trauma. Caution needs to be exercised in extreme preterm infants because of the paucity of published data.

Consensus of evidence

- High flow **equivalent** to neonatal CPAP in terms of safety and efficacy
- **Less nasal trauma**
- No clinically significant adverse event
- More acceptable to patient and family
- Simpliflies care for the care giver

Not all infants can be supported with Nasal CPAP/HFNC alone

50-60% of infants fail CPAP as initial form of support ***(Morley, 2008 and SUPPORT TRIAL, 2010)***

25-38% of infants fail nCPAP following InSurE ***(Stefanescu, 2003)***

Respiratory Failure: pH<7.20, PaO_2>50 on FiO_2>0.5, and $PaCO_2$>65; or intractable apnea requiring frequent stimulation or manual resuscitation, <u>and high WOB</u>

NIPPV as Primary mode

Author/Ref	Type	No. of Infants	NIPPV Group[a]	Control Group[a]	Outcomes
Primary mode:					
Manzar et al[48]	Prospective, Obs	16	Details not available.	N/A.	81% (n = 13) avoided intubation
Kugelman et al[38]	RCT	84	NIPPV: Rate: 12–30; PIP: 14–22;	NCPAP: 6–7; Fio_2 adjusted for	NIPPV group had decreased BPD … support
Sai Sunil Kishore et al[39]	RCT	76	NIPPV: Rate: 50; PIP: 15–16; PEEP: 5; Ti: 0.3–0.35 s; Flow: 6–7 L/min; Fio_2 adjusted for Spo_2: 88%–93%	NCPAP: 5; Flow: 6–7 L/min; Fio_2 adjusted for Spo_2: 88%–93%	Less failed extubation with NIPPV at 48 h and 7 d
Meneses et al[40]	RCT	200	NIPPV: Rate: 20–30; PIP: 15–20; PEEP: 4–6; Ti: 0.4–0.35 s; Flow: 8–10 L/min; Fio_2 adjusted for Spo_2: 88%–92%	NCPAP: 5–6; Flow: 8–10 L/min; Fio_2 adjusted for Spo_2: 88%–92%	Less failed extubation with NIPPV at 24–72 h
Ramanathan et al[35]	RCT	110	NIPPV: Rate: 30–40; PIP: 10–15; PEEP: 5; Ti: 0.5 s; Flow: 8–10 L/min; Fio_2 adjusted for Spo_2: 84%–92%	NCPAP: 5–8; Fio_2 adjusted for Spo_2: 84%–92%	Less failed extubation with NIPPV and decreased clinical and physiologic BPD

Less failed extubations , Shorter duration of respiratory support
Decreased clinical and physiological BPD

(S) NIPPV as secondary mode

Secondary mode:					
Friedlich et al[4]	RCT	41	SNIPPV[b]: Rate: 10; PIP: same as pre-extubation; PEEP: 4–6; Ti: 0.6 s; Fio_2 adjusted for Spo_2: 92%–95%	NP-CPAP: clinician discretion; Fio_2 adjusted for Spo_2: 92%–95%	Less failed extubation with SNIPPV at 48 h
Barrington et al[5]	RCT	54	SNIPPV: Rate: 12; PIP: 16 (to deliver at least 12); PEEP: 6;	NCPAP: 6	Less failed extubation with SNIPPV at 72 h
Khalaf et al[6]	RCT	64	SNIPPV: Rate: same as before extubation; PIP: increased by 2–4 over	NCPAP: 4–6; Flow: 8–10 L/min; Fio_2 adjusted for Spo_2: 90%–96%	Less failed extubation with SNIPPV at 72 h and 7 d

Less failed extubations , Shorter duration of respiratory support
Decreased BPD/death, NDI and NDI/Death

			before extubation; PIP: increased by 2–4 over pre-extubation values; PEEP: ≤5; Flow: 8–10 L/min; Fio_2 adjusted for Spo_2: 90%–96%	min; Fio_2 adjusted for Spo_2: 90%–96%	duration of supplemental oxygen, and decreased BPD
Moretti et al[32]	RCT	63	SNIPPV: Rate: same as before extubation; PIP: 10–20; PEEP: 3–5; Flow: 6–10 L/min; Fio_2 adjusted for Spo_2: 90%–94%	NCPAP: 3–5; Flow: 6–10 L/min; Fio_2 adjusted for Spo_2: 90%–94%	Less failed extubation with SNIPPV at 72 h
Gao et al[45]	RCT	50	SNIPPV: Rate: 40; PIP: 20; PEEP: 5; Fio_2 adjusted for Spo_2: 88%–92%	NCPAP: 4–8; Flow: 8–10 L/min; Fio_2 adjusted for Spo_2: 88%–92%	Less failed extubation with SNIPPV
Bhandari et al[46]	Retrospective	469	SNIPPV: Rate: same as before extubation; PIP: increased by 2–4 over pre-extubation values; PEEP: ≤6; Flow: 8–10 L/min; Fio_2 adjusted for Spo_2: 85%–96%	NCPAP: 4–6; Flow: 8–10 L/min; Fio_2 adjusted for Spo_2: 85%–96%	SNIPPV group (BW 500–750 g) had decreased BPD, BPD/death, NDI and NDI/death

Table 2. Primary Outcome.*

Outcome	Nasal IPPV	Nasal CPAP	Odds Ratio	Odds Ratio Adjusted for Strata (95% CI)	P Value	Odds Ratio Adjusted for Strata and Baseline Covariates (95% CI)†
	no./total no. (%)					
Primary outcome: death at <36 wk of postmenstrual age or BPD	191/497 (38.4)	180/490 (36.7)	1.07	1.09 (0.83–1.43)‡	0.56	1.05 (0.80–1.39)
Components of primary outcome						
Death at <36 wk of postmenstrual age	34/504 (6.7)	41/503 (8.2)	0.82	0.81 (0.51–1.31)§	0.39	0.77 (0.48–1.24)
Survival with BPD	157/463 (33.9)	139/449 (31.0)	1.14	1.17 (0.86–1.57)‡	0.32	1.14 (0.84–1.54)
Death at <36 wk of postmenstrual age or BPD according to older NIH criteria in 20 infants	197/504 (39.1)	193/503 (38.4)	1.03	1.03 (0.79–1.35)‡	0.82	1.00 (0.76–1.31)
Subgroup analyses						
Prior intubation						
No	72/241 (29.9)	72/252 (28.6)	1.07	1.08 (0.72–1.62)¶	0.70	1.05 (0.70–1.57)
Yes	119/256 (46.5)	108/238 (45.4)	1.05	1.04 (0.73–1.50)¶	0.81 Interaction 0.85	1.02 (0.70–1.46)
Birth weight						
<750 g	93/161 (57.8)	79/158 (50.0)	1.37	1.35 (0.87–2.10)‖	0.18	1.30 (0.83–2.04)
750–999 g	98/336 (29.2)	101/332 (30.4)	0.94	0.92 (0.66–1.29)‖	0.64 Interaction 0.15	0.90 (0.64–1.26)

ET tube induced complications

- Traumatic and painful
- Hemodynamic instability
- Infection- Sepsis
- ↑ Airway emergencies
- ↑ Resistance/WOB
- ↑ Incidence of air-leak
- Permanent airway lesions

	CPAP	MV
Breathing	[redacted]	[redacted]
Support	[redacted]	[redacted]
Hyperventilation	[redacted]	[redacted]
Need for ABG	[redacted]	[redacted]
Sedation	[redacted]	[redacted]
Paralysing drug	[redacted]	[redacted]
Risk of VILI	[redacted]	[redacted]
Risk for sepsis	[redacted]	[redacted]
Parent support	[redacted]	[redacted]
Expertise	[redacted]	[redacted]
Cost	[redacted]	[redacted]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