High Flow Nasal Cannula for primary respiratory support in premature infants > 28 weeks

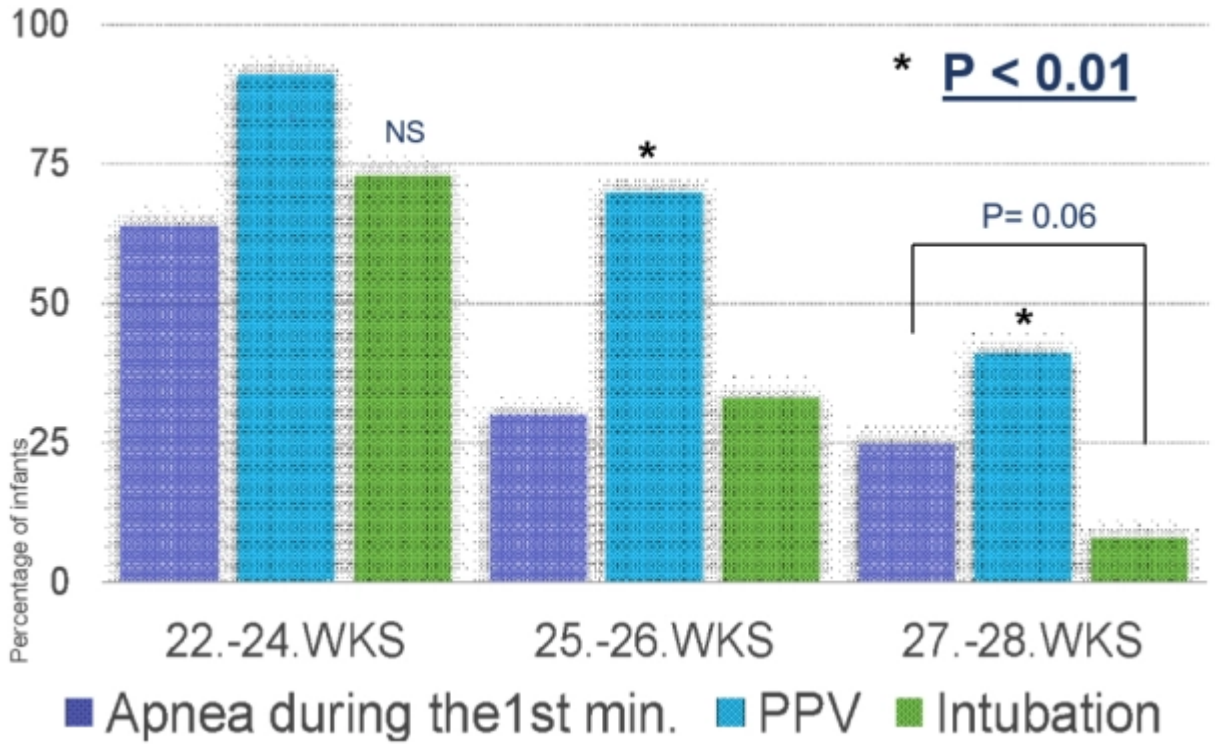
High Flow Nasal Cannula
for primary respiratory support in premature infants > 28 weeks

Richard Plavka, MD., Ph.D., Professor

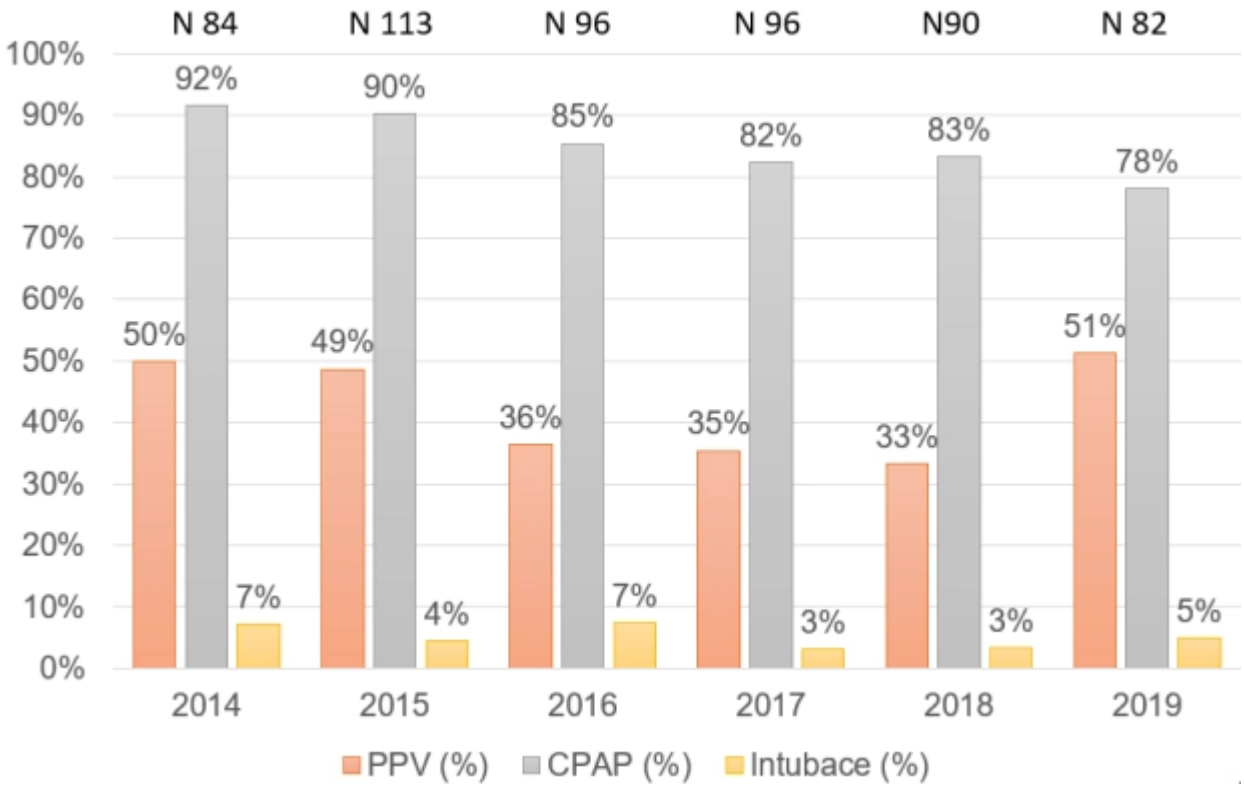
Thesis of care taking of prematures
Evidence basedclinicalpractice

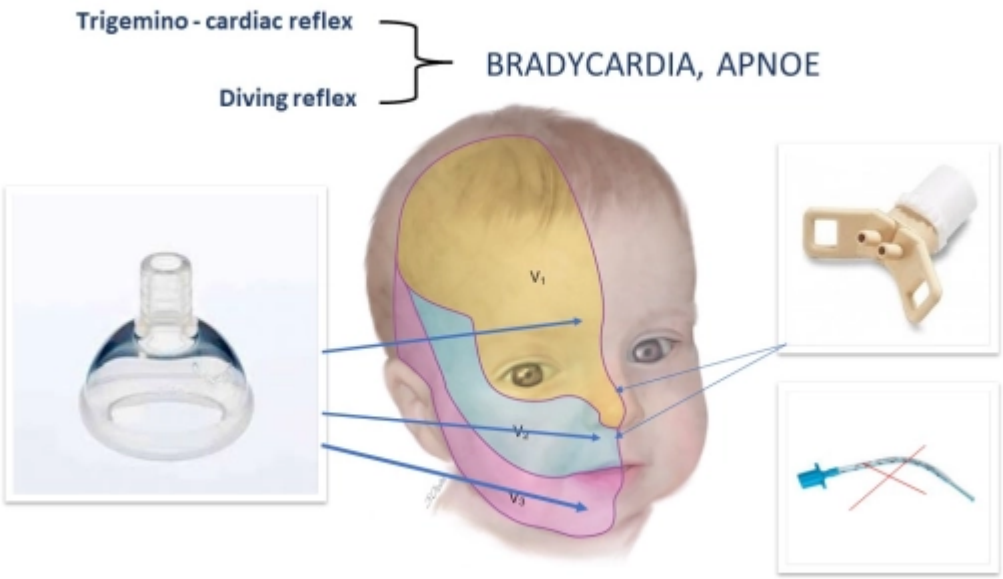
- Prematures are the most heterogenic cohort of infant patients
- Individualized care
- References of minimally invasive procedures
- Comfort for patients together with parents

PPV and intubation in the delivery room



Respiratory support and intubation in the delivery roomGT 28+0 – 31+6 weeks





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Clinical paper

The effect of a face mask for respiratory support on breathing in preterm infants at birth

Kristel L.A.M. Kuypers[a,], Tereza Lamberska[b], Tessa Martherus[a], Janneke Dekker[a], Stefan Böhringer[c], Stuart B. Hooper[d,e], Richard Plavka[b], Arjan B. te Pas[a]*

Table 1 – Characteristics of the patients.

Patients' characteristics	All infants N = 429
Gestational age in weeks, median (IQR)	28[+6] (27[+1] – 30[+4])
Birth weight in grams, mean ± SD	1176 ± 377
Males, n (%)	229 (53)
Antenatal corticosteroids, n (%)	226 (53)
Caesarean delivery, n (%)	257 (60)
General anaesthesia, n (%)	52 (12)
Placental transfusion, n (%)	104 (59)*
Apgar score 1 min, median (IQR)	6 (3–7)
Apgar score 5 min, median (IQR)	8 (7–9)
Umbilical cord blood pH, mean ± SD	7.27 ± 0.12[b]

Table 2 – Breathing before and after face mask application.

Outcome	Signs of breathing before face mask (n = 368)	No signs of breathing before face mask (n = 61)	p-Value
Thorax excursions after face mask, n (%)			<0.001*
• Visible (continued breathing)	171 (46)	0 (0)	
• Not visible (stopped breathing[a])	197 (54)	61 (100)	
PPV is given, n (%)	183 (50)	57 (93)	<0.001*

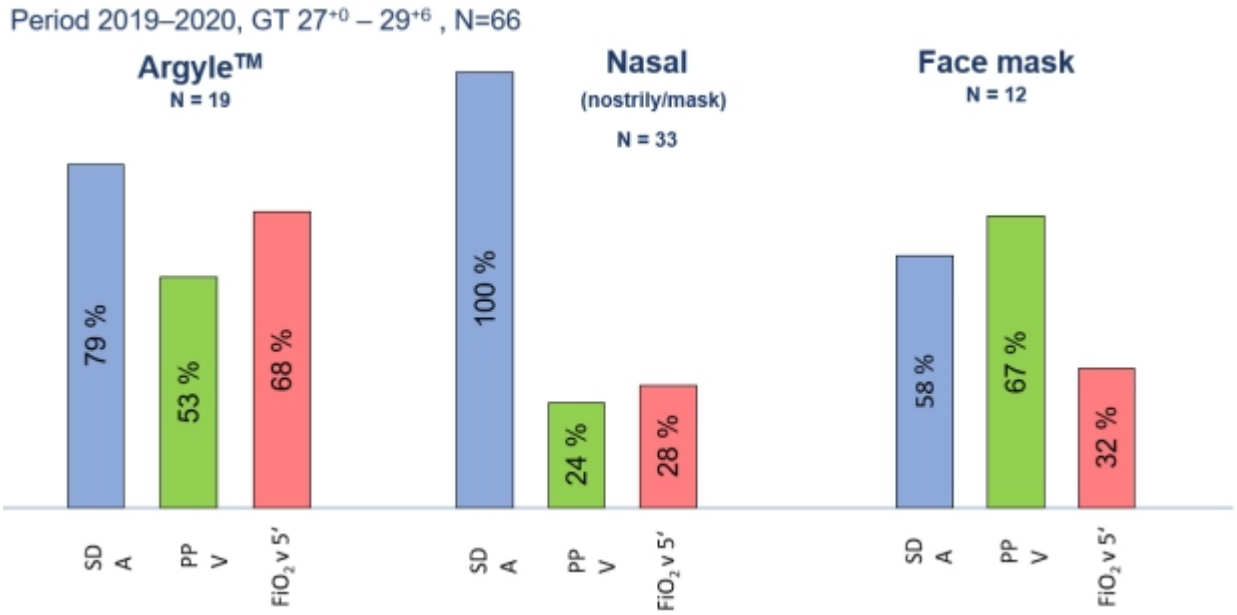
PPV – positive pressure ventilation.

Table 4 – Logistic regression analyse of infants who were initially breathing.

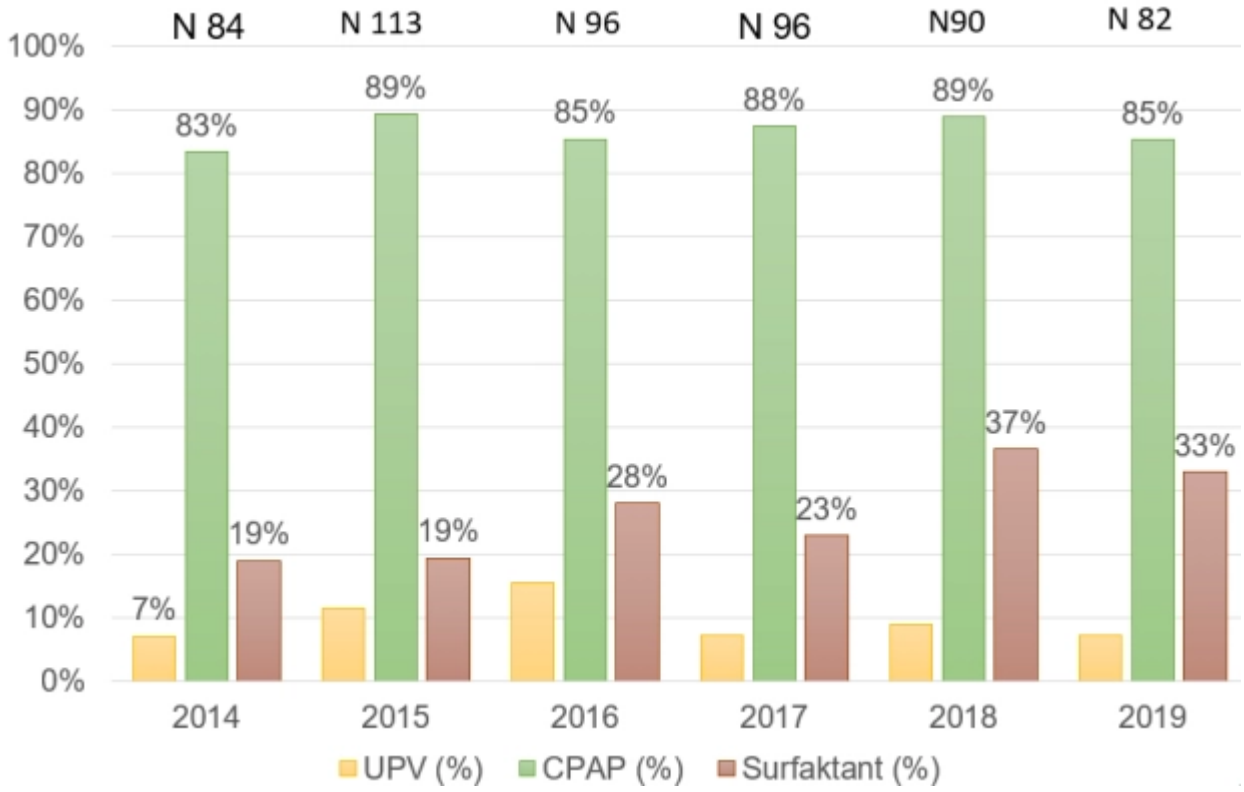
	Odds ratio	95% CI odds ratio lower	upper	p-Value
Gestational age in weeks	1.424	1.281	1.583	<0.001
Males	0.709	0.468	1.075	0.11
General anaesthesia	0.587	0.293	1.175	0.13

Note: $\chi 2(3) = 58.936$, $p < 0.05$, R^2 (Nagelkerke):0.174, correctly classified in 65.3% of the infants.

The effect of INTERFACE on the respiratory status and support of premature newborns in the delivery room



Respiratory support and surfactant on JIRP GT 28+0 – 31+6 weeks



European Consensus Guidelines on the Management of Respiratory Distress Syndrome - 2019 Update

Recommendations

CPAP should be started from birth in all babies at risk of RDS, such as those <30 weeks' gestation who do not need intubation for stabilisation (A1).

CPAP with early rescue surfactant is considered optimal management for babies with RDS (**A1**).
During weaning, HFNC can be used as an alternative to CPAP for some babies with the advantage of less nasal trauma (**B2**).

Summary - HFNC primary use

- CPAP is superior of HFNC in RDS primary treatment in > 28 week infants
- HFNC fails in 25% (CPAP 15%) without previous surfactant administration (FiO2 ≥ 0.4) *(HIPSTER and HUNTER trial. NEJM 2016, NEJM 2019)*
- The use of 30/30 rule" may reduce the risk of failure. *Manley 2018*
- No difference between CPAP and HFNC in primary use when surfactant is administered before filling of failure criteria. *Systematic review and Meta-analysis Fleeman N 2019, Hong H 2018*
- Pharyngeal pressures fluctuated and are significantly influenced by mouth position, flow and nares/prongs ratio. *Liew Z et al 2019, Mazmanyan P 2020*
- The data about the use of HFNC use in DR are limited. *Reynolds P 2015*

Pall Mall

- The clinical use of HFNC has been increasing. There is a great variety in use of HFNC: indications, flows, cannulas. *Eklund WM 2018*
- Vapotherm HFNC generates higher level of noise (approx.>5-10 dB) than continuous flow CPAP (continuous flow) Konig K 2013
- HFNC is better tolerate by parents and nurse staff. *Klingenberg C 2015*
- Positive effect on GIT has been unclear.

Heated Humidified High-Flow Nasal Cannula for Preterm Infants: An Updated Systematic Review and Meta-analysis

Nigel Fleeman[1], Yenal Dundar[1,2], Prakesh S Shah[3] and Ben NJ Shaw[4]

International Journal of Technology Assessment in Health Care

Table 4. GRADE Ratings for HHHFNC Versus NCPAP (Analysis of Primary Respiratory Support: Preterm Infants with No Prior Mechanical Endotracheal Ventilation)

Certainty assessment a						No. of patients		Effect		Overall certainty of evidence (quality)
Outcome	No. of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	HHHFNC	NCPAP	Relative (95% CI)	Absolute (95% CI)	
Intubation/ critical	6	Not serious	Not serious	Not serious	Serious b	90/704 (12.8%)	81/728 (11.1%)	RR 1.15 (0.87 to 1.52)	17 more per 1,000 (from 14 fewer to 58 more)	⊕⊕⊕◯ Moderate
BPD/ important	6	Not serious	Not serious	Not serious	Serious b	27/348 (7.8%)	24/359 (6.7%)	RR 1.14 (0.75 to 1.75)	9 more per 1,000 (from 17 fewer to 50 more)	⊕⊕⊕◯ Moderate
Death/ critical	7	Not serious	Not serious	Not serious	Serious b	5/717 (0.7%)	5/741 (0.7%)	RR 1.03 (0.32 to 3.33)	0 fewer per 1,000 (from 5 fewer to 16 more)	⊕⊕⊕◯ Moderate
Air leak/ important	6	Not serious	Not serious	Not serious	Serious b	15/702 (2.1%)	18/727 (2.5%)	RR 0.88 (0.46 to 1.67)	3 fewer per 1,000 (from 13 fewer to 17 more)	⊕⊕⊕◯ Moderate
Nasal trauma/ important	6	Not serious	Not serious	Not serious	Serious b	42/578 (7.3%)	85/601 (14.1%)	RR 0.52 (0.37 to 0.74)	68 fewer per 1,000 (from 37 fewer to 89 fewer)	⊕⊕⊕◯ Moderate

Heated Humidified High-Flow Nasal Cannula for Preterm Infants: An Updated Systematic Review and Meta-analysis

Nigel Fleeman[1], Yenal Dundar[1,2], Prakesh S Shah[3] and Ben NJ Shaw[4]

International Journal of Technology Assessment in Health Care

Primary support

Study	Study design, location	HHHFNC flow rate	Arm (number of preterm infants)	Eligibility criteria	GA, mean (SD), weeks	Birth weight, mean (SD) g
Nair and Karna 2005(31)	Single center: United States	1.8 L/min	HHHNFC (n = 13)[a] NCPAP (n = 15)[a]	GA 27 to 34 weeks	32 (0.5) 31 (0.5)	1,675 (139) 1,493 (64)
Iranpour et al 2011(19)	Single center: Iran	1.5 L/min to 3 L/min	HHHFNC (n = 35) NCPAP (n = 35)	GA 30 to 35 weeks	32.3 (1.6) 33.0 (1.9)	1,824 (410) 2,021 (498)
Yoder et al 2013 (37)	Multicenter: United States	3 L/min to 8 L/min	HHHNFC (n = 58) NCPAP (n = 67)	No limitation on GA[b]	NR[b] NR[b]	NR[b] NR[b]
Klingenberg et al 2014(23)	Single center, cross over: Norway	5 L/min to 6 L/min	HHHNFC / NCPAP (n = 20)[c]	GA <34 weeks	29.3 (1.7)[c]	1,234 (353)[c]
Kugelman et al 2014(24)	Single center: Israel	1 L/min to 5 L/min	HHHFNC (n = 38) NIPPV (n = 38)	GA <35 weeks	31.8 (2.3) 32.0 (2.3)	1,759 (488) 1,835 (530)
Glackin et al 2016(18)	Single center: Ireland	7 L/min	HHHNFC (n = 22) NCPAP (n = 22)	GA <30 weeks	26.9 (1.5) 27.3 (1.5)	868 (160) 891 (202)
Lavizzari et al 2016(25)	Single center non-inferiority: Italy	4 L/min to 6 L/min	HHHNFC (n = 158) NCPAP (n = 158)	GA (29 weeks to 36 weeks	33.1 (1.9) 33.0 (2.1)	1,968 (581) 1,908 (528)
Roberts et al 2016(33)	Multicenter non-inferiority: Australia and Norway	6 L/min to 8 L/min	HHHNFC (n = 278) NCPAP (n = 286)	GA ≥28 weeks	32.0 (2.1) 32.0 (2.2)	1,737 (580) 1,751 (599)
Shin et al 2017 (35)	Single center non-inferiority: South Korea	3 L/min to 7 L/min	HHHNFC (n = 42) NCPAP (n = 43)	GA >30 to <35 weeks	32.5 (1.5) 33.0 (1.2)	2,058 (371) 1,996 (374)
Murki et al 2018 (38)	Two centernon-inferiority: India	5 L/min to 7 L/min	HHHNFC (n = 133) NCPAP (n = 139)	≥28 weeks	31.8 (1.9) 31.6 (2.2)	1,632 (431) 1,642 (437)

Nasal High-Flow Therapy for Primary Respiratory Support in Preterm Infants

Calum T. Roberts, M.B., Ch.B., Louise S. Owen, M.D., Brett J. Manley, Ph.D

N ENGL J MED 375;12 NEJM.ORG SEPTEMBER 22, 2016

HIPSTER Trial: 9 NICUs (Australia+Norway) 5/2013 – 6/2015

ICs and Random: GW ≥ 28+0, CPAP after delivery < 24hrs, no ventilation, no surfaktant
⇒ 1. CPAP 6cmH20, 2. HFNC 6l/min (CPAP after failure)

Failure criteria: **1. FiO2 ≥ 0.4** (>1hr) 2. **pH < 7.2 /pCO2 > 60mmHg** (>1hr) 3. **Apnea >2 with PPV/24h or 6 episodes with any intervention**

Primary Outcome Per-protocol analysis	High-Flow Group (N = 278)	CPAP Group (N = 286)	Risk Difference (95% CI)*	P Value
Treatment failure within 72 hr	64/264 (24.2)	36/279 (12.9)	11.3 (4.8 to 17.8)	<0.001
Intubation within 72 hr	39/264 (14.8)	33/279 (11.8)	2.9 (–2.8 to 8.7)	0.31
Primary intention-to-treat analysis				
Gestational age <32 wk	30/140 (21.4)	24/149 (16.1)	5.3 (–3.7 to 14.3)	0.25
Gestational age ≥32 wk	13/138 (9.4)	9/137 (6.6)	2.9 (–3.5 to 9.3)	0.38

HIPSTER Trial: 9 NICUs (Australia+Norway) 5/2013 – 6/2015

Event	High-Flow Group (N=278)	CPAP Group (N=286)	Risk Difference (95% CI)*	P Value
	no. of infants (%)		*percentage points*	
Death before discharge	1 (0.4)	1 (0.4)	0.0 (−1.0 to 1.0)	0.98
Oxygen supplementation, respiratory support, or both at postmenstrual age of 36 wk†	17 (12.1)	17 (11.4)	0.7 (−6.7 to 8.2)	0.85
Pneumothorax or other air leak syndrome				
During assigned treatment	0	6 (2.1)	−2.1 (−3.8 to −0.4)	0.02
Any time during admission	10 (3.6)	8 (2.8)	0.8 (−2.1 to 3.7)	0.59
Postnatal glucocorticoid treatment for lung disease	1 (0.4)	3 (1.0)	−0.7 (−2.1 to 0.7)	0.33
Nasal trauma	23 (8.3)	53 (18.5)	−10.3 (−15.8 to −4.7)	<0.001
Patent ductus arteriosus treated with medication or surgical ligation	11 (4.0)	6 (2.1)	1.9 (−1.0 to 4.7)	0.20
Confirmed sepsis‡	7 (2.5)	13 (4.5)	−2.0 (−5.1 to 1.0)	0.19
Necrotizing enterocolitis, Bell's stage II or III§	2 (0.7)	0	0.7 (−0.3 to 1.7)	0.15
Isolated intestinal perforation	0	1 (0.3)	−0.3 (−1.0 to 0.3)	0.32
Laser surgery for retinopathy of prematurity†	0	1 (0.7)	−0.7 (−2.0 to 0.6)	0.33
Intraventricular hemorrhage, grade 3 or 4†	4 (2.9)	1 (0.7)	2.2 (−0.9 to 5.2)	0.15
Cystic periventricular leukomalacia†	3 (2.1)	2 (1.3)	0.8 (−2.2 to 3.8)	0.60

Nasal High-Flow Therapy for Newborn Infants in Special Care Nurseries N ENGL J MED 380;21 NEJM.ORG MAY 23, 2019

Brett J. Manley, Ph.D., Gaston R.B. Arnolda, Ph.D., Ian M.R. Wright, M.B., B.S.

HUNTER Trial: 9 non-tertiary centers, 4/2015 – 11/2017

IC and Random: GW ≥ 31+0, BW ≥ 1200g; CPAP after delivery < 2hrs ⇒ 1. CPAP 6cmH20, 2. HFNC 6l/min

Failure criteria: **1. FiO2 ≥ 0.4** (>1hr) 2. **pH < 7.2 /pCO2 > 60mmHg** (2 samples) 3**. Apnea >2 with PPV/24h or 6 episodes with any intervention**

RESULTS

Primary Outcome Per-protocol analysis	All Patients	High-Flow Group (N=381)	CPAP Group (N=373)	Univariate Analysis	Adjusted Analysis‡
Treatment failure within 72 hr after randomization	677	49/339 (14.5)	27/338 (8.0)	6.5 (1.7 to 11.2)	5.5 (0.5 to 10.4)
Gestational age <34 wk	129	14/65 (21.5)	10/64 (15.6)	5.9 (−7.5 to 19.3)	6.0 (−8.0 to 19.9)
Gestational age ≥34 wk	548	35/274 (12.8)	17/274 (6.2)	6.6 (1.7 to 11.5)	5.5 (0.2 to 10.7)

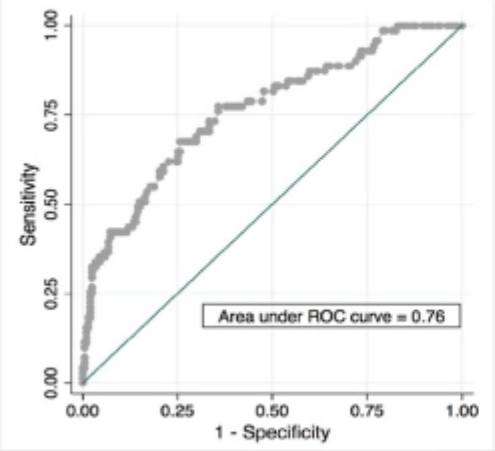
Adjusted for: GW, BW, AN steroids, sex

HUNTER Trial: 9 non-tertiary centers, 4/2015 – 11/2017

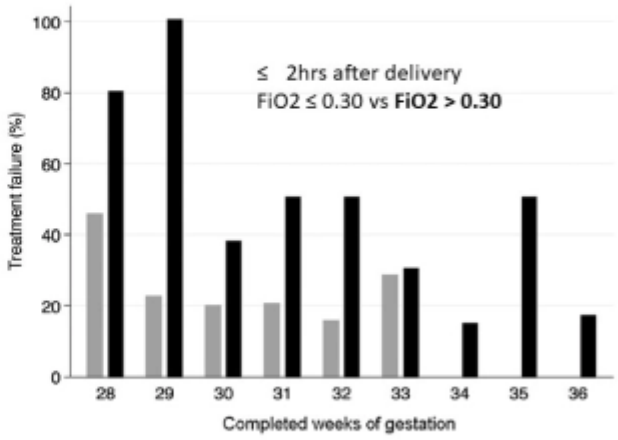
Secondary Outcomes and Adverse Events.

	High-Flow Group (N=381)	≈	CPAP Group (N=373)	
Mechanical ventilation through an endotracheal tube — no. (%)				
<72 hr after randomization	21 (5.5)		22 (5.9)	−0.4 (−3.7 to 2.9)
At any time after randomization	25 (6.6)		22 (5.9)	0.7 (−2.8 to 4.1)
Supplemental oxygen or respiratory support		≈		
At 28 days of life; born ≥32 wk gestational age‡‡	2 (0.5)		0	0.5 (−0.2 to 1.3)
At 36 wk postmenstrual age; born <32 wk gestational age§§	0		0	NC
Drained with needle thoracocentesis or intercostal catheter**	9 (2.4)		18 (4.8)	−2.5 (−5.1 to 0.2)
Nasal trauma after randomization	2 (0.5)		6 (1.6)	−1.1 (−2.6 to 0.4)

ROC model includes A and pre randomization FiO2



HFNC failure depends on pre randomization FiO2



Refining the Use of Nasal High-Flow Therapy as Primary Respiratory Support for Preterm Infants

Brett J. Manley, PhD[1,2,3], Calum T. Roberts, MB, ChB[1,2,4,5], Dag H. Frøisland, PhD[1,6], Lex W. Doyle, MD[2,3,7], Peter G. Davis, MD[1,2,3], and Louise S. Owen, MD[1,2,3]

Results There were 278 preterm infants included, with a mean gestational age (GA) of 32.0 ± 2.1 weeks and a birth weight of 1737 ± 580 g; of these, nHF treatment failed in 71 infants (25.5%). Treatment failure was moderately predicted by a lower GA and higher prerandomization fraction of inspired oxygen (FiO_2): area under a receiver operating characteristic curve of 0.76 (95% CI, 0.70-0.83). Nasal HF treatment success was more likely in infants born at ≥30 weeks GA and with prerandomization FiO_2 <0.30.

Conclusions In preterm infants ≥28 weeks' GA enrolled in a randomized, controlled trial, lower GA and higher FiO_2 before randomization predicted early nHF treatment failure. Infants were more likely to be successfully treated with nHF from soon after birth if they were born at ≥30 weeks GA and had a prerandomization FiO_2 <0.30. However, even in this select population, continuous positive airway pressure remains superior to nHF as early respiratory support in preventing treatment failure. *(J Pediatr 2018;196:65-70).*

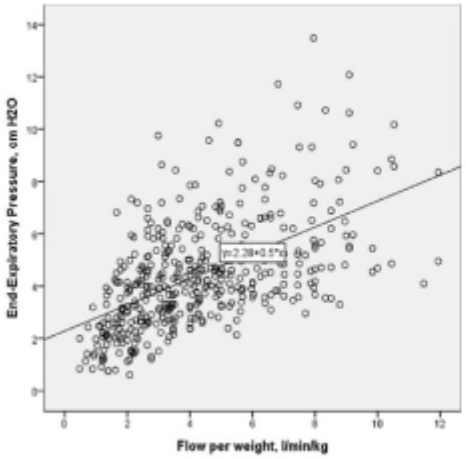
30/30 rule

Further research into how to best select which infants receiving noninvasive respiratory support should receive surfactant treatment is required.

30 rule is applied. Further prospective, RCTs are required to optimize the use of nHF as primary respiratory support for preterm infants. ■

Variables with significant impact on pharyngeal EEP

Flow r= 0.589



SIMPLY & SAFELY

Mouth position r= 0.589
Difference 0.6-2.3cmH2O

Weight r= -0,247 p< 0.001
Δ 0.7 cmH2O/kg

Prongs to nares ratio r= 0,165 p< 0.001
0.7< and > 0.7

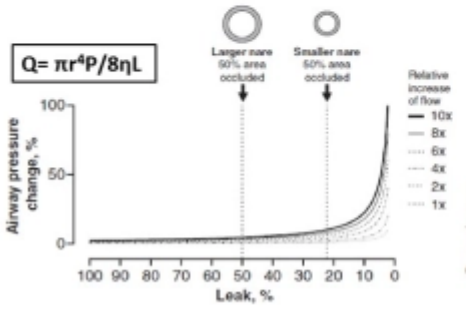
Predicted pEEP = -6.4+0.53 x (-FLOW) +1.45 x (mouth possition 0/1) – 1.86 x (WEIGHT) + 0.31 x (GW wks)

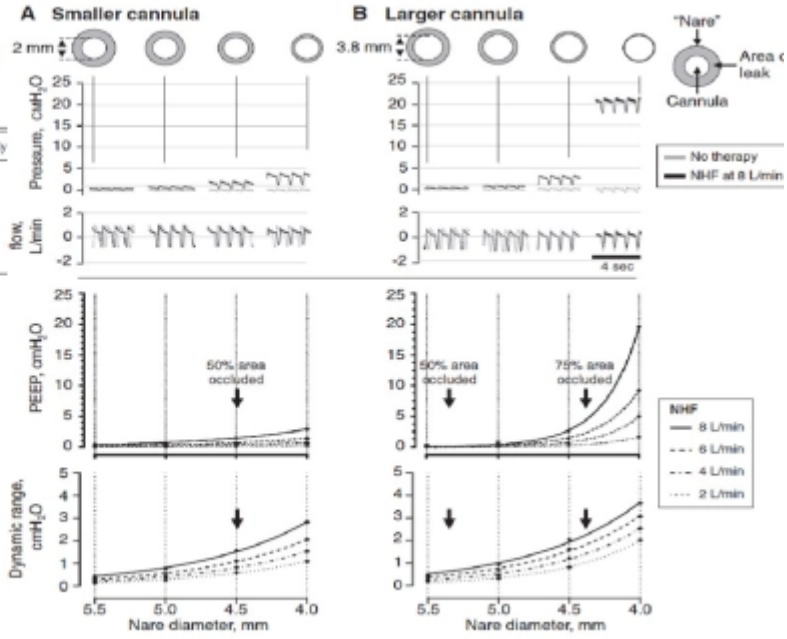
Mechanisms of nasal high flow

Table 1. *Anthropometric data*

	Pressure Study	Ventilation Study
n	9	20
Gestation, wk	37.1 ± 1.4	39.1 ± 1.5
Postnatal age, day	1.1 ± 0.4	1.3 ± 0.5
Birth weight, g	2,573 ± 477	3,090 ± 441
Length, cm	48.4 ± 2.2	50.5 ± 2.1
Male, *n* (%)	5 (56%)	12 (60%)

Data are means ± SD.





J Appl Physiol 128: 822–829, 2020.

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Resuscitation

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EUROPEAN RESUSCITATION COUNCIL

Neonatal Life Support
2020 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations☆

PEEP Versus No PEEP

Oxygen for Preterm Resuscitation

Treatment Recommendations

We suggest using PEEP for the initial ventilation of premature newborn infants during delivery room resuscitation (weak recommendation, low-quality evidence).

We suggest the range of 21% to 30% oxygen because all trials used this for the low oxygen concentration group. Subsequent titration of oxygen concentration using pulse oximetry is advised (weak recommendation, very low-certainty evidence).

Stabilisation of premature infants in the delivery room with nasal high flow

Peter Reynolds, Stamatina Leontiadi, Tracy Lawson, Tosin Otunla, Olayinka Ejiwumi, Nicola Holland

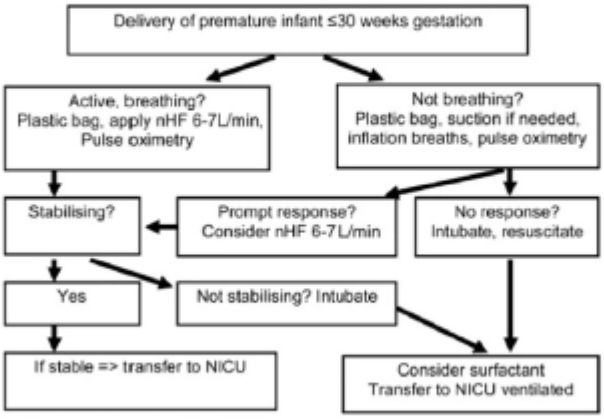


Figure 2 Protocol for stabilisation. nHF, nasal high flow; NICU, neonatal intensive care unit.

Reynolds P, *et al. Arch Dis Child Fetal Neonatal Ed* 2016;**101**:F284–F287

Stabilisation of premature infants in the delivery room with nasal high flow

Peter Reynolds, Stamatina Leontiadi, Tracy Lawson, Tosin Otunla, Olayinka Ejiwumi, Nicola Holland

Ethics Committee (REC). Written parental consent was obtained prior to delivery. The study was terminated after 28 babies had been enrolled in agreement with the R and D department and the REC as feasibility with successful completion of protocol in all cases had been established.

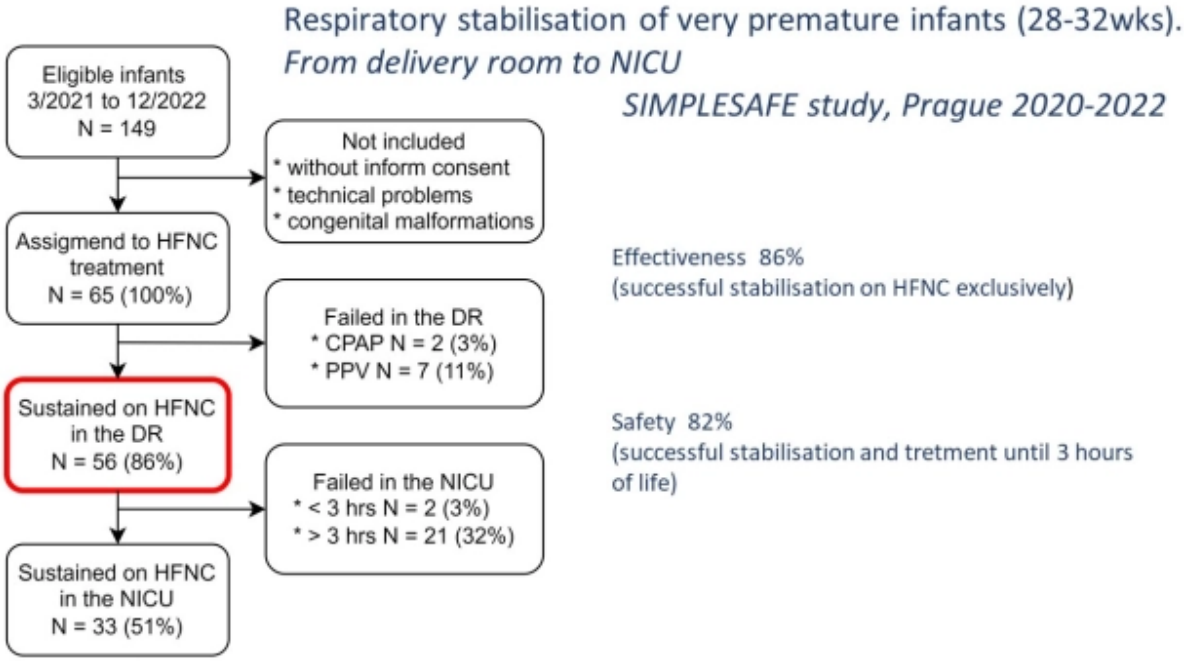
Table 1 Characteristics of study participants (n=28)

GA at delivery	N (% total)	Vaginal/caesarean delivery	PPROM >24 h (%)	Intubated for transfer to NICU	Surfactant in DR
23+0 to 23+6	1 (4)	1/0	0 (0)	1	1
24+0 to 24+6	3 (11)	2/1	1 (33)	2	2
25+0 to 25+6	6 (18.5)	2/4	0 (0)	0	1
26+0 to 26+6	5 (18.5)	2/3	2 (40)	0	0
27+0 to 27+6	5 (18.5)	2/3	0 (0)	0	0
28+0 to 28+6	5 (18.5)	1/4	1 (20)	0	0
29+0 to 29+6	3 (11)	1/2	1 (33)	0	0
Mean GA 26+5	28 (100)	11 (39%)/17 (61%)	5 (18)	3 (11%)	4 (14%)

DR, delivery room; GA, gestational age; NICU, neonatal intensive care unit; PPROM, preterm prelabour rupture of membranes.

Reynolds P, *et al. Arch Dis Child Fetal Neonatal Ed* 2016;**101**:F284–F287

- High VT delivery during mask PPV at birth was associated with brain injury. Strategies to limit VT delivery during mask PPV should be used to prevent high VT delivery. *(Quaasim M 2019)*



Summary: HFNC 2-8l/min

- The clinical use of HFNC has been increasing.
- HFNC can be use as a primary respiratory support of premature infants ≥ 28 weeks suffered from mild-moderate RDS.
- The rule 30/30 can decrease HFNC failure.
- Crossover to CPAP earlier is superior to later (FiO2 >0.35, flow 8l)

- HFNC seems to be safe and effective respiratory support even in the delivery room however further investigation is required.