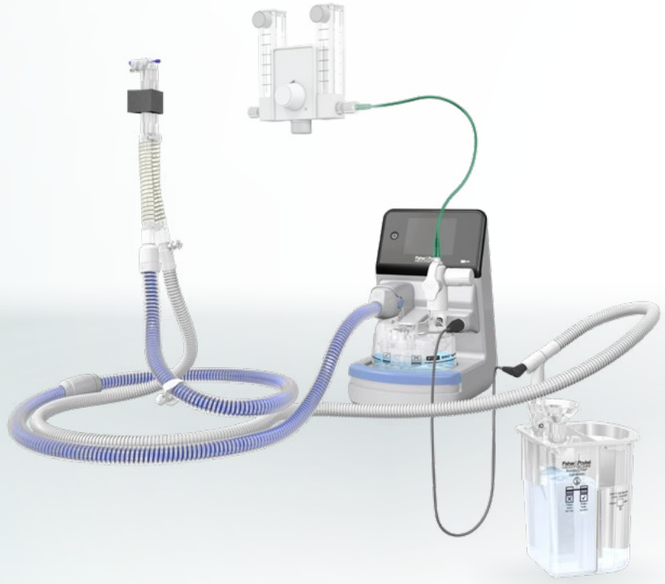
Noninvasive respiratory support in neonatal intensive care

An overview of current neonatal literature and practices globally

Continuous positive airway pressure (CPAP)

CPAP is a mode of noninvasive respiratory support that provides continuous distending pressure throughout the respiratory cycle to spontaneously breathing patients.

CPAP requires a closed system and is typically delivered using a circuit and a pressure generator (either a bubble generator or a ventilator).



Key characteristics of a CPAP interface:

- Intended to deliver prescribed pressure
- Interface designed to seal and maintain prescribed pressure
- Larger tubes lower resistance to flow

Nasal high flow (NHF)

NHF is a mode of noninvasive respiratory support that provides high flows of heated and humidified blended air and oxygen through an unsealed interface.

NHF requires an open system and is typically delivered using a single-limb circuit. The flow range is dependent on the flow driver/ platform used.

Key characteristics of an NHF interface:

- Deliveres prescribed flow
- Interface designed to be unsealed
- Narrower tubes (compared to CPAP) increase resistance to flow

Choosing CPAP

While there is an overlap in the key mechanisms delivered by pressure-based and flow-based therapies, the primary mechanism of each therapy is different. This is important to consider when deciding the choice of therapy.

Primary mechanisms of CPAP

- ✓ Establishes functional residual capacity[1]
- ↓ Reduces work of breathing[1]
- ✓ Promotes gas exchange[2]

Choose CPAP when you want to:

- ✓ Set and control pressure
- ✓ Stent open lungs and airway
- ↓ Reduce the need for mechanical ventilation[3]
- ↓ Reduce the incidence of brochnopulmonary dysplasia[4]

1. Dysart KC. Clin Perinatol. 43(4), 621–631 (2016).
2. Lee KS. et al. Biol Neonate. 73(2), 69–75 (1998).
3. Tapia JL. et al. J Pediatr. 161(1), 75–80 (2012).
4. Subramaniam P et al. Cochrane Database Syst Rev. 14(6), CD001243 (2016).
5. Dysart K et al. Respiratory Medicine. 103(10), 1400–1405 (2009).
6. Bressan S et a. Eur J Pediatr. 172(12), 1649–1656 (2013).
7. Osman M et al. J Perinatol. 35, 263–267 (2015).
8. Spentzas T et al. J. Intensive Care Med. 24, 323–328 (2009).
9. Yoder B et al. Pediatrics. 131, e1482–1490 (2013).

Choosing NHF

Primary mechanisms of NHF

- ✓ Washes anatomical dead space[5]
- ↓ Reduces work of breathing and improves oxygenation[5,6]
- ✓ Improves patient comfort and tolerance to therapy[7,8]

Choose NHF when you want to:

- ✓ Set and control the flow rate
- ✓ Generate a low level of pressure
- ↓ Reduce nasal trauma[9]
- ↓ Reduce re-breathed CO_2

Evidence-based guidelines

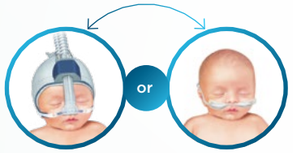
Clinical evidence supports the use of CPAP and NHF in neonates.

CPAP continues to be the gold standard of care in neonates less than 28 weeks gestational age (GA). However, there are several pathways of care in which CPAP and NHF may be used.

Postextubation support

Wilkinson et al. 2016[1]
Cochrane Review

Primary respiratory support



Bruet et al. 2021[2]
Systematic Review

Alternative to prolonged CPAP

Roehr et al. 2016[3], **Yoder et al. 2017**[4]
Consensus

23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40

Less than 28 weeks GA
CPAP first

for neonates with compromised lung development and a higher need for respiratory support.

From 28 weeks GA
NHF first with rescue CPAP

for neonates who are stable or require lower acuity of care. This approach may be considered as it provides two noninvasive options before needing to consider mechanical ventilation.

Clinical judgement is necessary to assess the appropriate treatment for an individual patient. The use of NHF therapy is not typically supported for infants with extreme prematurity, severe respiratory distress syndrome, or untreated surfactant deficiency.

1. Wilkinson D et al. Cochrane Database Syst Rev. 2, CD006405 (2016).
2. Bruet S et al. Arch Dis Child. Fetal Neonatal Ed. 107(1), 59–166 (2021).
3. Roehr CC et al. Clin Perinatol. 43, 693–705 (2016).
4. Yoder B et al. J Perinatol. 37, 809–813 (2017).

Clinical evidence: Postextubation

Wilkinson et al. 2016. Cochrane Review[1]

Data from six postextubation RCTs was analyzed to assess the efficacy and safety of NHF compared with CPAP:

6 RCTs
1,248 participants

Preterm infants ≥ 28 weeks GA with respiratory distress syndrome

CPAP: 2-8 cmH_2O
NHF: 2-8 L/min

No statistically significant difference in rate of treatment failure

No statistically significant difference in rate of reintubation

No statistically significant difference in adverse outcomes i.e. pneumothorax

With NHF, significant reduction in rates of nasal trauma.

Clinical evidence: Primary respiratory support

Bruet et al. 2021[1]
Arch Dis Child Fetal Neonatal Ed

A recent systematic review analyzed 10 RCTs to assess the efficacy and safety of NHF compared with CPAP when used as primary respiratory support:

10 RCTs
1,830 participants

Preterm infants < 37 weeks GA with respiratory distress syndrome

CPAP: 2-8 cmH_2O
NHF: 2-8 L/min

Treatment failure was higher using NHF compared with CPAP

No difference in intubation rates

With NHF, lower rate of nasal trauma

There were no influences of GA, birth weight, flow rates used, type of CPAP or surfactant use on the rate of treatment failure.

1. Bruet S et al. Arch Dis Child Fetal Neonatal Ed. 107(1), 59–6 (2021).
2. Roehr C. C. et al. Clin Perinatol. 43, 693-705 (2016).
3. Yoder B. et al. J Perinatol. 37, 809-813 (2017).

Clinical evidence: Alternative to prolonged CPAP

CONSENSUS:
Roehr et al. 2016 Clin Perinatol[2]

Evidence support and guidelines for using heated, humidified, high-flow nasal cannulae in neonatology: Oxford nasal high-flow therapy meeting, 2015

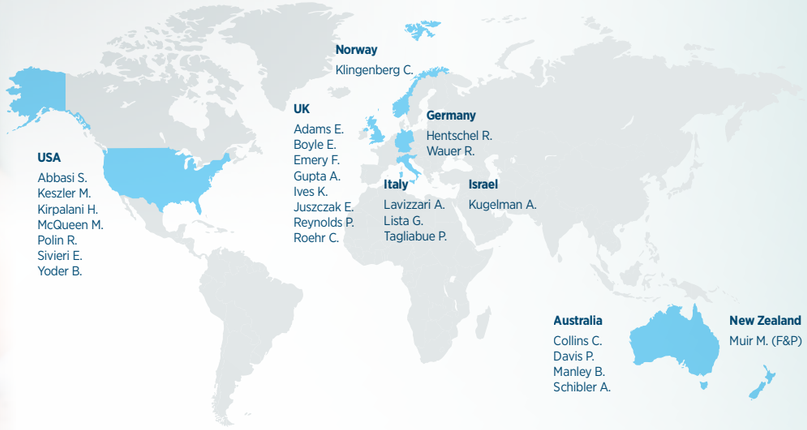
CONSENSUS:
Yoder et al. 2017 J Perinatol[3]

Consensus approach to nasal high-flow therapy in neonates

More than 25 leading NHF researchers have contributed to two consensus publications. These publications provide guidance on how to use NHF therapy in the NICU.

Expert consensus indicates that for neonates who require prolonged periods of noninvasive respiratory support, NHF is a suitable alternative to CPAP, either to:

→ Reduce risk of adverse events such as nasal injury, head molding or air leak issues, or
→ Wean from CPAP therapy.



An overview of key evidence: Flow rates on NHF and pressure settings on CPAP

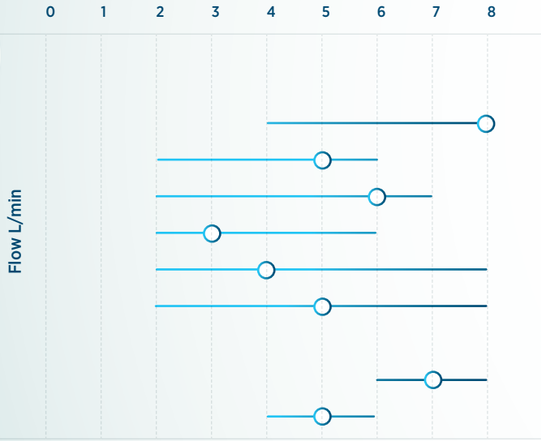
Setting flow (NHF)

Results from the Cochrane Review[1] demonstrate that adequate starting flow rates provide physiological and clinical benefits. Data from RCTs and guidance from leading experts suggest that NHF can be initiated between 4–6 L/min.

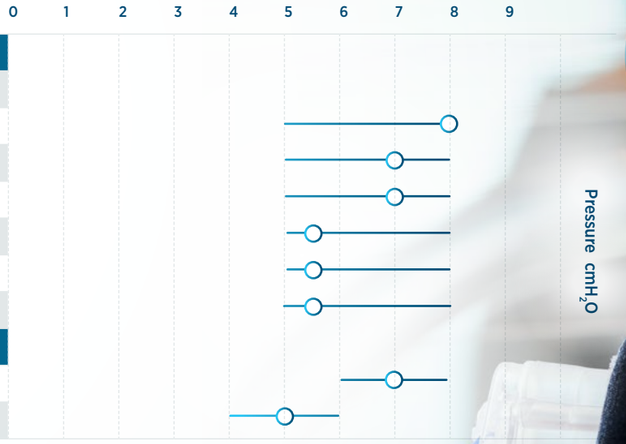
Setting pressure (CPAP)

Results from the Cochrane Review demonstrates that adequate starting pressures provide physiological and clinical outcomes. Data from RCTs demonstrates that CPAP is typically initiated between 5–7 cmH_2O.

RCTs investigating NHF and CPAP: Comparison of flow rates and pressure settings



Postextubation RCTs	
Publication	**Population**
Collins et al. 2013[2]	< 32 weeks GA
Manley et al. 2013[3]	Premature and neonatal cannula
	Infant cannula
Yoder et al. 2013[4]	< 2 kg
	2-3 kg
	> 3 kg
Primary respiratory support RCTs	
Roberts et al. 2016[5]	≥ 28 weeks
Lavizzari et al. 2016[6]	≥ 29 weeks



RCT: Randomized Controlled Trial

1. Wilkinson D. et al. Cochrane Database Syst. Rev. 2, CD006405 (2016).
2. Collins C. L. et al. J Pediatr. 162, 949–54.e1 (2013).
3. Manley B. et al. N Engl J Med. 369, 1425–33 (2013).
4. Yoder B. et al. Pediatrics. 131, e1482-90 (2013).
5. Roberts CT et al. N Eng J Med. 375, 1142-51 (2016).
6. Lavizzari A et al. JAMA Ped. (2016).

Minimum — Starting — Maximum

Bressan S, Balzani M, Krauss B, Pettenazzo A, Zanconato S, Baraldi E. High-flow nasal cannula oxygen for bronchiolitis in a pediatric ward: a pilot study. European Journal of Pediatrics. 2013 Dec 31;172(12):1649–1656.

Bruet S, Butin M, Dutheil F. Systematic review of high-flow nasal cannula versus continuous positive airway pressure for primary support in preterm infants. Archives of Disease in Childhood – Fetal and Neonatal Edition. 2022 Jan;107(1):56–59.

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Dysart K, Miller TL, Wolfson MR, Shaffer TH. Research in high-flow therapy: Mechanisms of action. Respiratory Medicine. 2009 Oct;103(10):1400–1405.

Dysart KC. Physiologic Basis for Nasal Continuous Positive Airway Pressure, Heated and Humidified High-Flow Nasal Cannula, and Nasal Ventilation. Clinics in Perinatology. 2016 Dec;43(4):621–631.

Lavizzari A, Colnaghi M, Ciuffini F, Veneroni C, Musumeci S, Cortinovis I, et al. Heated, Humidified High-Flow Nasal Cannula vs. Nasal Continuous Positive Airway Pressure for Respiratory Distress Syndrome of Prematurity: A Randomized Clinical Noninferiority Trial. JAMA Pediatr. 2016 Aug 8.

Lee KS, Dunn MS, Fenwick M, Shennan AT. A Comparison of Underwater Bubble Continuous Positive Airway Pressure with Ventilator-Derived Continuous Positive Airway Pressure in Premature Neonates Ready for Extubation. Neonatology. 1998;73(2):69–75.

Manley BJ, Owen LS, Doyle LW, Andersen CC, Cartwright DW, Pritchard MA, et al. High-Flow Nasal Cannulae in Very Preterm Infants after Extubation. New England Journal of Medicine. 2013 Oct 10;369(15):1425–1433.

Osman M, Elsharkawy A, Abdel-Hady H. Assessment of pain during application of nasal-continuous positive airway pressure and heated, humidified high-flow nasal cannulae in preterm infants. Journal of Perinatology. 2015 Apr 27;35(4):263–267.

Roberts CT, Owen LS, Manley BJ, Frøisland DH, Donath SM, Dalziel KM, et al. Nasal High-Flow Therapy for Primary Respiratory Support in Preterm Infants. New England Journal of Medicine. 2016 Sep 22;375(12):1142–1151.

Roehr CC, Yoder BA, Davis PG, Ives K. Evidence Support and Guidelines for Using Heated, Humidified, High-Flow Nasal Cannulae in Neonatology. Clinics in Perinatology. 2016 Dec;43(4):693–705.

Spentzas T, Minarik M, Patters AB, Vinson B, Stidham G. Children With Respiratory Distress Treated With High-Flow Nasal Cannula. Journal of Intensive Care Medicine. 2009 Sep 23;24(5):323–328.

Subramaniam P, Ho JJ, Davis PG. Prophylactic nasal continuous positive airway pressure for preventing morbidity and mortality in very preterm infants. Cochrane Database of Systematic Reviews. 2016 Jun 14;(6).

Tapia JL, Urzua S, Bancalari A, Meritano J, Torres G, Fabres J, et al. Randomized Trial of Early Bubble Continuous Positive Airway Pressure for Very Low Birth Weight Infants. The Journal of Pediatrics. 2012 Jul;161(1):75–80.e1.

Wilkinson D, Andersen C, O'Donnell CP, de Paoli AG, Manley BJ. High flow nasal cannula for respiratory support in preterm infants. Cochrane Database of Systematic Reviews. 2016 Feb 22;2016(2).

Yoder BA, Manley B, Collins C, Ives K, Kugelman A, Lavizzari A, et al. Consensus approach to nasal high-flow therapy in neonates. Journal of Perinatology. 2017 Jul 23;37(7):809–813.

Yoder BA, Stoddard RA, Li M, King J, Dirnberger DR, Abbasi S. Heated, Humidified High-Flow Nasal Cannula Versus Nasal CPAP for Respiratory Support in Neonates. Pediatrics. 2013 May 1;131(5):e1482–1490.