Summary

- NHF therapy at 2 L/kg/min is well established in pediatric care areas across the hospital, including the PICU, ED and other general care areas.1–14
- In the ED, the use of NHF as a primary treatment for infants with bronchiolitis resulted in a significantly lower rate of therapy failure compared with standard oxygen therapy.1
- In the PICU, the use of NHF as a primary treatment for acutely-ill children was non-inferior to CPAP, and resulted in lower use of sedation, nasal trauma and shorter durations of PICU and hospital stay.14

Review of the literature

A systematic search of the available literature shows there are over 220 peer-reviewed papers investigating the use of nasal high flow (NHF) therapy in infants and children. These figures exclude papers investigating the use of NHF in the neonatal population. Of these, 30 are randomized controlled trials (RCTs) – 16 of which compared NHF with standard oxygen therapy, 10 with continuous positive airway pressure (CPAP) and four with alternative treatments. A further 12 are in the form of systematic reviews.

220+
NHF papers in infants and children

16 compare NHF vs. standard oxygen therapy
10 compare NHF vs. CPAP
4 compare NHF vs. alternative therapies
12 systematic reviews
These studies represent application of NHF therapy in infants and children in a range of respiratory conditions in the pediatric intensive care unit (PICU), emergency department (ED) and other general care areas in the hospital.

The systematic review conducted showed that 24 out of 30 RCTs (80%) used an F&P Optiflow system.

Of the 4,398 total participants on NHF in RCTs, 3,957 participants (90%) were treated using an F&P Optiflow system.

The body of literature helps to define the role of NHF in pediatric respiratory care and supports:

- the use of NHF early in the course of respiratory distress, which is associated with improved physiological outcomes compared with standard oxygen therapy, including:
  - improved breathing patterns and rapid unloading of the respiratory muscles
  - significant reduction in the work of breathing
  - rapid improvement to respiratory distress
  - improved mucosal function and secretion clearance through the delivery of heated and humidified gas

- the early use of NHF outside of the PICU can lead to reduced intubation rates and PICU admissions.

Use of F&P Optiflow™ systems in RCTs

The weight of evidence is from studies which used an F&P Optiflow™ system, including an F&P Optiflow Junior interface and an F&P humidity delivery system.
Landmark Study: The PARIS Trial

The largest NHF RCT was conducted by Franklin et al. This multi-center RCT supports the use of NHF in the ED and general care areas in young infants with bronchiolitis, and used the F&P Airvo™ with an Optiflow Junior interface.

The primary outcome of the study was that the use of NHF at 2 L/kg/min as a primary treatment in the ED and general care areas resulted in a significantly lower rate of therapy failure compared with standard oxygen therapy (12 vs. 23%, p < 0.001). Therapy failure was defined as an escalation of therapy or PICU admission.

There were no significant differences between the secondary outcomes (PICU admissions, intubation rates and adverse events). It is important to note that the study design allowed patients on standard oxygen therapy who met the therapy failure criteria to escalate to NHF; 61% of the patients who failed on standard oxygen therapy were rescued by NHF and avoided PICU admission.

1,472 patients (< 12 months) with bronchiolitis

17 Emergency Departments and Wards

Therapy failure (%) in patients who received NHF at 2 L/kg/min vs. those who received standard oxygen therapy

Therapy failure p < 0.001
Rescue NHF therapy failure p = 0.08
PICU admission p = 0.08
Intubation p = 0.39

1 in 9 patients experienced therapy failure on NHF 2 L/kg/min

1 in 4 patients experienced therapy failure on standard O₂ < 2 L/min

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The FIRST-ABC Trial

First-line Support for Assistance in Breathing in Children (FIRST-ABC) was designed as a master protocol of two pragmatic noninferiority RCTs by Ramnarayan et al.13 These RCTs investigated the safety and efficacy of NHF and CPAP when used as:

- Post-extubation support in critically ill children (Step down)
- First-line support in acutely ill children (Step up)

### Treatment Algorithm

A standardized treatment protocol was used to ensure the consistency of treatment across the multiple centers involved in the study.

1. CPAP (7 – 8 cmH₂O) or NHF starting at 2 L/kg/min
2. Weaning therapy
3. Stopping therapy
4. Success: ≥ 48 hours free from respiratory support

Primary Outcome: Time to liberation from respiratory support

### Key Findings

**Step down**

Patients in PICU transition to CPAP or NHF post-extubation. 
553 participants (0 – 15 years, median age: 3 months). 
22/28 PICUs in the UK.

- **When used for post-extubation, NHF did not meet noninferiority criteria compared with CPAP for time on respiratory support.**

- Patients on NHF required an average of 7.6 hours longer of respiratory support (NHF: 50.5 hours vs. CPAP: 42.9 hours; adjusted hazard ratio: 0.83 (95% CI: 0.70 – 0.99))

**Step up**

Patients admitted to PICU receive CPAP or NHF as first-line therapy. 
573 participants (0 – 15 years, median age: 9 months). 
24/28 PICUs in the UK.

- **When used as first-line therapy, NHF met the noninferiority criteria when compared with CPAP for time on respiratory support.**

- Patients on NHF required an average of 5 hours longer of respiratory support (NHF: 52.5 hours vs. CPAP: 47.9 hours; adjusted hazard ratio: 1.03 (95% CI: 0.86 – 1.22))

**Therapy failure occurred more frequently in the CPAP group compared with the NHF group.**

- 31% of patients switched to NHF: Predominantly due to discomfort
- 20% of patients switched to CPAP: Predominantly due to clinical deterioration

**Of the secondary outcomes, the NHF group had significantly:**

- Lower use of sedation: NHF 27.7% vs. CPAP 37.0%
- Fewer occurrences of nasal trauma: NHF 2.0% vs. CPAP 6.5%
- Shorter mean duration of PICU stay: Mean difference -3.1 days
- Shorter mean duration of acute hospital stay: Mean difference -7.6 days

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An evidence-based approach to implementation of NHF in pediatric patients

This information collates data from published guidelines and the body of evidence. It does not overrule expert clinical judgment in individual patient management.

Flows

• **2 L/kg/min for patients up to 12 kg** in weight has been shown to produce a rapid improvement in respiratory distress, and a reduced need for escalation of therapy.
  
  • Flow rates for those over 12 kg have been protocolized by the PARIS\textsuperscript{12} and FIRST-ABC\textsuperscript{15} research groups.

<table>
<thead>
<tr>
<th>Weight (kg)</th>
<th>≤ 12</th>
<th>13–15</th>
<th>16–30</th>
<th>31–50</th>
<th>&gt; 50</th>
</tr>
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<tbody>
<tr>
<td>Starting flow rate</td>
<td>2 L/min/kg</td>
<td>25 – 30 L/min</td>
<td>35 L/min</td>
<td>40 L/min</td>
<td>50 L/min</td>
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Humidity

Heating and humidification of gases during respiratory support (including NHF and standard oxygen therapy):

• enables maintenance of airway defenses and mucociliary transport
• promotes efficient gas exchange
• reduces respiratory effort for the patient
• enables conservation of energy for growth and development.

O\textsubscript{2}

• PARIS 2 Protocol and FIRST-ABC group implemented the titration of FiO\textsubscript{2} to achieve a target SpO\textsubscript{2} of ≥ 92%.

Monitoring

• Non-responders can be identified within the first 60 minutes of NHF initiation, by the monitoring of physiological parameters such as heart rate, respiratory rate, and work of breathing.

Weaning off NHF therapy

ED (PARIS)

• Reduce the FiO\textsubscript{2} to maintain SpO\textsubscript{2} at target levels without reducing flow.
• Once the FiO\textsubscript{2} has been reduced to 21% (room air) and the patient is stable at this concentration, NHF therapy can be stopped.

PICU (FIRST-ABC)

• When FiO\textsubscript{2} < 40% and respiratory distress is not severe, use weaning flow rates
• When FiO\textsubscript{2} < 30% and/or mild respiratory distress, stop NHF

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<th>&gt; 50</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weaning flow rate</td>
<td>1 L/min/kg</td>
<td>13 - 15 L/min</td>
<td>18 L/min</td>
<td>20 L/min</td>
<td>25 L/min</td>
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Nasal high flow (NHF): NHF is a mode of noninvasive respiratory support that delivers high flows of heated and humidified blended air and oxygen through an unsealed nasal interface.

Standard oxygen therapy: A form of oxygen therapy that is delivered through a nasal cannula at low flow rates (< 2 L/min) and is typically unheated and unhumidified. May also be referred to as conventional oxygen therapy.

Systematic search of the available literature: Conducted on July 21, 2022 using predefined search terms on PubMed, Embase & Cochrane Library, with data extraction and screening performed via DistillerSR (Evidence-Based Partners, Ottawa, Ontario) by internal F&P clinical researchers.

For further information, please visit https://www.fphcare.com/hospital/infant-respiratory/nasal-high-flow/ or click on the hyperlinked references below.