

High-Flow Nasal Cannula Versus Continuous Positive Airway Pressure in Infants with Bronchiolitis: A Systematic Review

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ABSTRACT:

Background: Bronchiolitis is a common lower respiratory tract infection in infants and a major cause of hospital admissions. Non-invasive respiratory support is frequently required, with high-flow nasal cannula (HFNC) and continuous positive airway pressure (CPAP) being the most commonly used modalities. However, their relative effectiveness remains a topic of ongoing debate. **Methods:** This systematic review was conducted in accordance with PRISMA guidelines. A comprehensive search of PubMed, Embase, Scopus, Web of Science, and the Cochrane Library was performed to identify studies comparing HFNC and CPAP in infants with bronchiolitis. Randomized controlled trials and comparative observational studies were included. The primary outcomes assessed were treatment failure, escalation of respiratory support, and need for invasive mechanical ventilation. Secondary outcomes included pediatric intensive care unit (PICU) admission, duration of hospitalization, adverse events, and mortality. **Results:** Seven studies, including six randomized controlled trials and one observational study, were included in the analysis. Four studies specifically focused on infants, while three included broader pediatric populations. Several studies reported lower treatment failure rates with CPAP, particularly in more severe cases. However, no consistent differences were observed between HFNC and CPAP in terms of invasive mechanical ventilation or length of hospital stay. HFNC was generally associated with better tolerance and fewer minor complications related to the respiratory interface. Variability in study design and outcome definitions contributed to heterogeneity across the included studies. **Conclusions:** Both HFNC and CPAP are effective non-invasive respiratory support options for infants with bronchiolitis. CPAP may offer advantages in reducing treatment failure in severe disease, whereas HFNC is associated with improved comfort and ease of application. HFNC may be used as an initial strategy, with escalation to CPAP when required. Further high-quality studies are needed to clarify optimal management approaches.

Keywords: *Bronchiolitis, high-flow nasal cannula (HFNC), continuous positive airway pressure (CPAP)*

INTRODUCTION:

Bronchiolitis is the most common lower respiratory tract infection in infants and represents a major cause of pediatric morbidity worldwide. The disease primarily affects children younger than two years of age, with the highest incidence occurring during the first year of life. It is characterized by acute inflammation of the bronchioles, leading to airway edema, mucus production, and varying degrees of airflow obstruction. These pathological processes can result in significant respiratory distress, hypoxemia, and feeding difficulties, frequently necessitating hospitalization. Despite decades of research, management of

bronchiolitis remains largely supportive, with respiratory support forming the cornerstone of treatment in moderate to severe disease [1].

Globally, bronchiolitis places a considerable burden on healthcare systems. It is estimated that nearly all children are infected with respiratory syncytial virus (RSV), the most common etiological agent of bronchiolitis, by the age of two years [2]. Each year, millions of infants worldwide develop bronchiolitis severe enough to require medical attention. In high-income countries, bronchiolitis accounts for a substantial proportion of pediatric emergency department visits and hospital admissions during the

winter season. Hospitalization rates for bronchiolitis have been reported to range between 1% and 3% of all infants annually, with higher rates observed in infants younger than six months. In the United States alone, bronchiolitis is responsible for more than 100,000 infant hospitalizations each year, making it one of the leading causes of hospital admission during infancy [3].

The burden of bronchiolitis is even more pronounced in low- and middle-income countries, where access to healthcare resources and respiratory support modalities may be limited. Globally, RSV-associated bronchiolitis contributes significantly to pediatric mortality, particularly in resource-constrained settings. Prematurity, congenital heart disease, chronic lung disease, and immunodeficiency are well-recognized risk factors for severe disease and adverse outcomes. In addition to the acute disease burden, bronchiolitis has also been associated with long-term respiratory sequelae, including recurrent wheezing and increased risk of asthma later in childhood [4].

The pathophysiology of bronchiolitis involves a complex interplay between viral infection, host immune response, and airway structural changes. Following viral infection of the respiratory epithelium, there is infiltration of inflammatory cells such as lymphocytes, neutrophils, and macrophages into the bronchiolar walls. This inflammatory process leads to epithelial cell necrosis, edema of the airway mucosa, and increased mucus production. The accumulation of cellular debris and mucus within the small airways results in partial or complete airway obstruction. These pathophysiological changes contribute to air trapping, ventilation-perfusion mismatch, and impaired gas exchange [3, 4].

Infants are particularly susceptible to the effects of bronchiolar obstruction due to several anatomical and physiological factors. Compared with older children and adults, infants have smaller airway diameters, less developed collateral ventilation pathways, and more compliant chest walls. As a result, even minor airway narrowing can significantly increase airway resistance and work of breathing. The increased respiratory effort often manifests clinically as tachypnea, nasal flaring, intercostal retractions, and hypoxemia. In severe cases, progressive respiratory fatigue may lead to respiratory failure requiring ventilatory support [5].

Given the predominantly supportive nature of bronchiolitis management, respiratory support plays a central role in treatment strategies. Historically, oxygen therapy delivered via low-flow nasal cannula or face mask was commonly used to manage hypoxemia in bronchiolitis. However, conventional oxygen therapy may not adequately address the increased work of breathing or the underlying pathophysiological changes associated with airway obstruction. Consequently, non-invasive respiratory support modalities have gained increasing attention as alternatives to invasive mechanical ventilation.

Among these modalities, continuous positive airway pressure (CPAP) and high-flow nasal cannula (HFNC)

therapy have emerged as widely used interventions in the management of moderate to severe bronchiolitis. Both therapies aim to improve oxygenation, reduce respiratory effort, and prevent progression to respiratory failure requiring intubation.

Continuous positive airway pressure provides a constant level of positive airway pressure throughout the respiratory cycle. This positive pressure helps maintain airway patency, prevents alveolar collapse, and improves functional residual capacity. By stabilizing the airways and promoting alveolar recruitment, CPAP can improve oxygenation and reduce the work of breathing. Additionally, the application of positive pressure may counteract the dynamic airway collapse commonly seen in bronchiolitis. CPAP has traditionally been used in neonatal and pediatric intensive care settings and has demonstrated effectiveness in reducing the need for invasive mechanical ventilation in various respiratory conditions.

High-flow nasal cannula therapy represents a relatively newer modality of non-invasive respiratory support. HFNC delivers heated and humidified oxygen at high flow rates through specialized nasal cannulas. These high flow rates can exceed the patient's inspiratory demand, thereby reducing entrainment of room air and allowing more consistent delivery of the desired fraction of inspired oxygen (FiO_2). Furthermore, HFNC generates low levels of positive airway pressure and helps wash out nasopharyngeal dead space, which may improve ventilation efficiency. The humidification of delivered gas also enhances mucociliary clearance and improves patient comfort.

One of the key advantages of HFNC therapy is its ease of use and improved patient tolerance compared with other non-invasive ventilation interfaces. The nasal cannula interface is generally better tolerated by infants and requires less tight fixation than CPAP masks or nasal prongs. This may reduce the risk of skin breakdown, nasal trauma, and discomfort. As a result, HFNC has increasingly been adopted as a first-line respiratory support modality in many pediatric emergency departments and general pediatric wards.

Despite their widespread use, the comparative effectiveness of HFNC and CPAP in bronchiolitis remains an area of ongoing debate. Some studies suggest that CPAP provides more consistent positive airway pressure and may therefore be more effective in preventing treatment failure in infants with severe respiratory distress. Conversely, other studies report similar clinical outcomes between HFNC and CPAP, particularly in terms of invasive mechanical ventilation rates and length of hospital stay.

Clinical decision-making regarding the choice of respiratory support modality often depends on several factors, including disease severity, patient tolerance, resource availability, and institutional protocols. In resource-limited settings, the availability of specialized equipment and trained personnel may influence the selection of respiratory support. HFNC systems are

generally easier to implement and require less intensive monitoring than CPAP, making them more accessible in certain clinical environments.

Another important consideration is the potential for adverse events associated with these therapies. CPAP interfaces can cause complications such as nasal injury, skin breakdown, abdominal distension, and patient discomfort. HFNC, while generally considered safe, may also be associated with complications such as nasal irritation or delayed escalation of respiratory support if treatment failure is not promptly recognized. Understanding the balance between benefits and risks is therefore critical when selecting the most appropriate therapy for infants with bronchiolitis.

Over the past decade, multiple randomized controlled trials and observational studies have attempted to compare HFNC and CPAP in the management of bronchiolitis. While some studies have demonstrated similar outcomes between the two modalities, others have suggested potential advantages for CPAP in reducing treatment failure rates. The heterogeneity of study designs, patient populations, and outcome definitions has contributed to ongoing uncertainty in the literature.

Systematic reviews and meta-analyses provide an important method for synthesizing available evidence and identifying trends across multiple studies. However, previous reviews have often included heterogeneous populations, mixed respiratory conditions, or broader categories of non-invasive ventilation rather than focusing specifically on HFNC and CPAP in bronchiolitis. Additionally, evolving clinical practice and the increasing use of HFNC in pediatric care necessitate updated evaluations of current evidence.

Given the clinical significance of bronchiolitis and the increasing reliance on non-invasive respiratory support, a comprehensive synthesis of the available evidence comparing HFNC and CPAP is warranted. Clarifying the relative benefits and limitations of these modalities may help guide clinicians in selecting the most appropriate treatment strategy and optimizing outcomes for infants with bronchiolitis.

Therefore, the objective of this systematic review is to evaluate and compare the effectiveness and safety of high-flow nasal cannula therapy and continuous positive airway pressure in infants with bronchiolitis. Specifically, this review aims to assess their impact on clinically relevant outcomes including treatment failure, escalation of respiratory support, need for invasive mechanical ventilation, pediatric intensive care unit admission, length of hospital stay, adverse events, and mortality.

By synthesizing the current body of evidence, this review seeks to provide clinicians and researchers with a clearer understanding of the comparative roles of HFNC and CPAP in the management of bronchiolitis and to identify areas where further research is needed.

METHODOLOGY:

Study Design and Reporting Guidelines:

This systematic review was conducted to evaluate and compare the effectiveness and safety of high-flow nasal cannula (HFNC) and continuous positive airway pressure (CPAP) in infants with bronchiolitis. The review was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to ensure transparency, methodological rigor, and reproducibility.

The review process included comprehensive database searching, predefined eligibility criteria, systematic screening of studies, data extraction, and critical appraisal of study quality. Both randomized controlled trials and observational studies were included to capture the full spectrum of available evidence comparing HFNC and CPAP in infants with bronchiolitis.

Eligibility Criteria:

Eligibility criteria were defined before the literature search to ensure consistent and unbiased study selection. The criteria were developed using the PICO framework (Population, Intervention, Comparator, Outcomes).

Population:

Studies were included if they involved infants diagnosed with bronchiolitis, typically defined as children younger than 24 months of age presenting with clinical features of viral lower respiratory tract infection including cough, wheezing, crackles, and respiratory distress.

Studies focusing exclusively on premature neonates with respiratory distress syndrome or other neonatal respiratory conditions were excluded unless bronchiolitis-specific data were clearly reported.

Intervention:

The intervention of interest was high-flow nasal cannula (HFNC) therapy used as a form of non-invasive respiratory support in infants with bronchiolitis.

HFNC therapy was defined as the delivery of heated and humidified oxygen through nasal cannulas at high flow rates, typically exceeding standard oxygen therapy flow rates.

Comparator

The comparator was continuous positive airway pressure (CPAP) used as non-invasive respiratory support.

Studies were included if CPAP was delivered through nasal prongs, masks, or bubble CPAP systems, provided that it was used for the management of bronchiolitis.

Studies comparing HFNC with other forms of non-invasive ventilation (such as BiPAP or non-invasive positive pressure ventilation) without a CPAP comparison group were excluded.

Outcomes:

Studies were eligible if they reported at least one of the following clinically relevant outcomes.

Primary Outcomes:

1. Treatment failure, defined as deterioration requiring escalation of respiratory support
2. Escalation of respiratory support, including transition from HFNC or CPAP to more advanced ventilation
3. Need for invasive mechanical ventilation

Secondary Outcomes:

1. Pediatric intensive care unit (PICU) admission
2. Length of hospital stay
3. Adverse events, including nasal trauma, abdominal distension, skin breakdown, or other complications related to respiratory support
4. Mortality

Information Sources:

A comprehensive search was performed across the following electronic databases:

1. PubMed/MEDLINE
2. Embase
3. Scopus
4. Web of Science
5. Cochrane Central Register of Controlled Trials (CENTRAL)

The search covered all publications from database inception to December 2025.

In addition to database searches, the reference lists of included studies and relevant review articles were manually screened to identify additional eligible studies.

Search Strategy:

A structured search strategy was developed using combinations of Medical Subject Headings (MeSH) and free-text keywords related to bronchiolitis and non-invasive respiratory support.

The primary search terms included:

- bronchiolitis
- infant bronchiolitis
- high-flow nasal cannula
- HFNC
- heated humidified high flow
- continuous positive airway pressure
- CPAP
- non-invasive ventilation

An example of the search strategy used in PubMed is shown below:

("bronchiolitis" OR "infant bronchiolitis") AND ("high-flow nasal cannula" OR HFNC OR "heated humidified high flow") AND ("continuous positive airway pressure" OR CPAP) Search strategies were adapted appropriately for each database.

Study Selection:

All records identified through database searches were exported into a reference management software program. Duplicate records were removed before screening.

The study selection process consisted of two stages:

Stage 1: Title and Abstract Screening

Titles and abstracts of all retrieved records were screened to identify potentially relevant studies.

Studies that clearly did not meet the inclusion criteria were excluded at this stage.

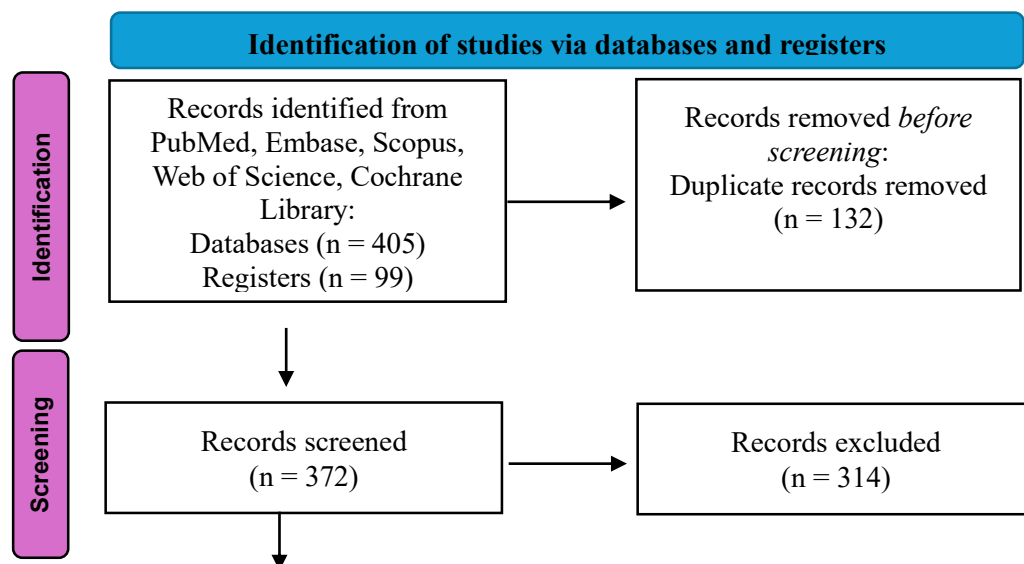
Stage 2: Full-Text Review

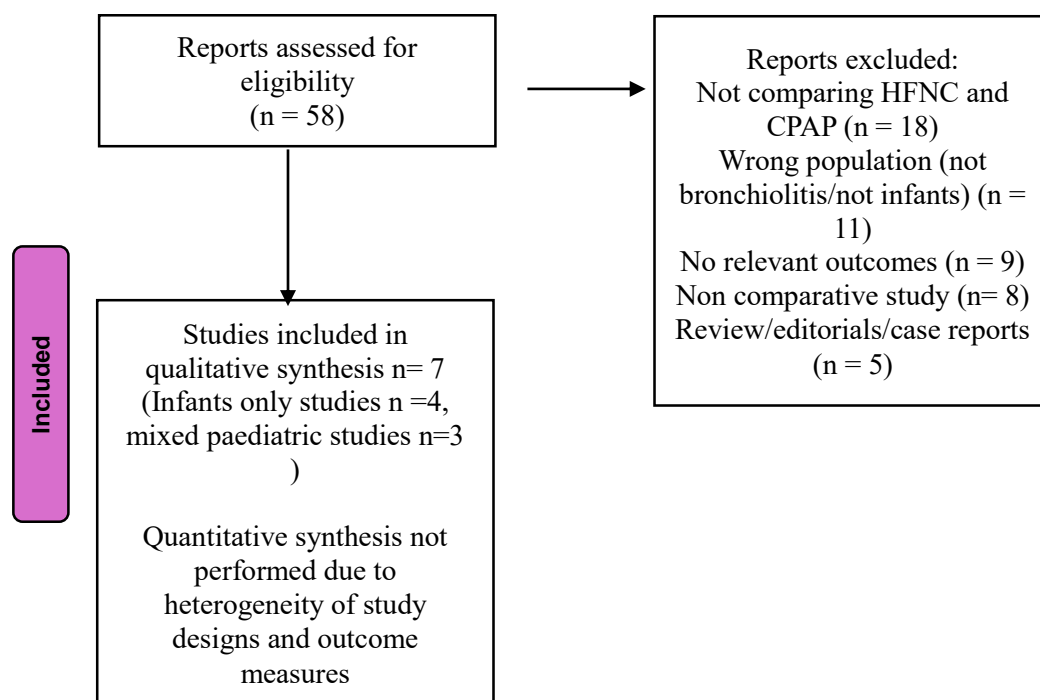
Full texts of potentially eligible studies were retrieved and evaluated against the predefined eligibility criteria. Studies that met all inclusion criteria were included in the final analysis.

Any discrepancies during the selection process were resolved through discussion and consensus.

The study selection process was documented using a PRISMA flow diagram. Figure 1

Figure 1. PRISMA flowchart – Study Selection Process





Data Extraction:

Data were extracted from the included studies using a standardized data extraction form.

The following information was collected:

- Author and year of publication
- Country and study setting
- Study design
- Sample size
- Patient age range
- Intervention characteristics (HFNC settings)
- Comparator characteristics (CPAP settings)
- Outcome measures reported
- Key findings related to clinical outcomes

Data extraction was conducted carefully to ensure accuracy and consistency across studies.

Risk of Bias Assessment:

The methodological quality and risk of bias of the included studies were evaluated using validated assessment tools.

Randomized Controlled Trials:

Randomized controlled trials were assessed using the Cochrane Risk of Bias 2 (RoB 2) tool, which evaluates the following domains:

- Randomization process
- Deviations from intended interventions
- Missing outcome data
- Measurement of outcomes
- Selection of reported results

Observational Studies:

Observational studies were assessed using the Risk Of Bias In Non-randomized Studies of Interventions (ROBINS-I) tool, which evaluates potential bias in domains such as:

- Confounding

- Participant selection
- Classification of interventions
- Deviations from intended interventions
- Missing data
- Outcome measurement
- Reporting bias

Each study was categorized as having low, moderate, serious, or critical risk of bias.

Data Synthesis:

A qualitative synthesis of the included studies was performed to summarize the findings related to HFNC and CPAP in bronchiolitis.

Clinical outcomes including treatment failure, need for invasive ventilation, escalation of respiratory support, PICU admission, length of hospital stay, adverse events, and mortality were compared across studies.

Due to heterogeneity in study design, patient populations, and outcome definitions, a narrative synthesis approach was used to describe trends and patterns in the data.

Where available, findings from randomized controlled trials were emphasized to provide higher-quality evidence.

RESULTS:

Study Selection:

The initial literature search across electronic databases identified a number of potentially relevant studies investigating non-invasive respiratory support in bronchiolitis. After removal of duplicate records and screening of titles and abstracts, full-text articles were assessed for eligibility based on predefined inclusion criteria. Studies were included if they compared high-flow nasal cannula (HFNC) with continuous positive airway pressure (CPAP) in infants with bronchiolitis and reported relevant clinical outcomes.

A total of seven comparative studies met the inclusion criteria for the final synthesis. These consisted of six randomized controlled trials and one retrospective comparative study. Four studies enrolled infants exclusively, while three studies included broader

pediatric populations with ages extending up to 24 months, although the reported median ages remained within infancy. The study selection process is summarized according to PRISMA guidelines.

Study Characteristics:

The characteristics of the included studies are summarized in Table 1.

Table 1. Characteristics of Included Studies Comparing High-Flow Nasal Cannula and Continuous Positive Airway Pressure in Infants with Bronchiolitis

Study	Milési 2017	Sarkar 2018	Cesar 2020	Borgi 2021	Vahlkvist 2020	Pedersen 2017	Maya 2024
Country	France	India	Brazil	Tunisia	Denmark	Denmark	India
Design	RCT	Pilot RCT	Pilot RCT	RCT	RCT	Retrospective	RCT
Population age	≤6 months	28 days–12 months	≤9 months	7 days–6 months	<2 years	0–2 years	1–23 months
Sample size	142	31	63	255	50	49	118
Intervention	HFNC	HFNC	HFNC	HFNC	HFNC	HFNC	HFNC
Comparator	nCPAP	nCPAP	CPAP	CPAP/NPPV	CPAP	CPAP	Bubble CPAP
Infant-only	Yes	Yes	Yes	Yes	Mixed	Mixed	Mixed
Key findings	Higher success with nCPAP	Similar outcomes; HFNC better tolerated	Similar treatment failure and PICU stay	Higher treatment success with CPAP/NPPV	No major clinical differences	CPAP improved RR and FiO2 faster	HFNC lower treatment failure

The seven studies were conducted in multiple geographic regions including France, India, Brazil, Tunisia, and Denmark, reflecting a diverse international representation of clinical practice. Most studies were conducted in pediatric intensive care units (PICUs) or specialized pediatric wards where non-invasive respiratory support was routinely used for the management of moderate to severe bronchiolitis.

Sample sizes varied considerably between studies. The largest randomized trial included 255 infants, while smaller pilot trials enrolled fewer than 40 participants. Overall, the included studies collectively evaluated several hundred infants with bronchiolitis receiving either HFNC or CPAP as initial respiratory support.

Among the included studies, Milési et al. (2017) and Borgi et al. (2021) represented the largest randomized trials focusing on infants younger than six months with moderate-to-severe bronchiolitis. Smaller pilot randomized trials conducted by Sarkar et al. (2018) and Cesar et al. (2020) also investigated the comparative effectiveness of HFNC and CPAP in infants with severe bronchiolitis requiring respiratory support.

Three additional studies (Vahlkvist et al., 2020; Pedersen et al., 2017; and Maya et al., 2024) included broader pediatric populations with age ranges extending up to 24 months. Although not strictly infant-only populations, these studies were included in the review because bronchiolitis primarily affects infants and the reported median ages remained within infancy.

Across the included studies, HFNC was generally delivered as heated and humidified oxygen at high flow rates through nasal cannulas, while CPAP was delivered using nasal interfaces or bubble CPAP systems depending on the clinical setting.

Baseline Patient Characteristics:

Baseline demographic and clinical characteristics of the study populations are summarized in Table 2.

Table 2. Baseline Demographic and Clinical Characteristics of Study Populations

Study	Age summary	Setting	Severity criteria
Milési 2017	~40 days mean	PICU multicenter	Moderate–severe bronchiolitis
Sarkar 2018	~3.4 months	PICU	Severe bronchiolitis
Cesar 2020	Median ~2.7 months	PICU	Critical bronchiolitis
Borgi 2021	~51 days mean	PICU	Severe bronchiolitis
Vahlkvist 2020	~2–3 months median	Hospital trial	Bronchiolitis requiring respiratory support
Pedersen 2017	~2 months median	PICU	Bronchiolitis respiratory distress
Maya 2024	1–23 months	Hospital/PICU	Moderate–severe bronchiolitis

Most studies included infants younger than six months, with reported mean or median ages typically between one and four months. This age distribution reflects the epidemiology of bronchiolitis, which most commonly affects young infants.

The majority of studies enrolled infants with moderate to severe bronchiolitis, often defined by hypoxemia requiring supplemental oxygen, increased work of breathing, or the need for respiratory support. Several studies were conducted in PICU settings where patients required advanced respiratory monitoring and management.

Although detailed demographic variables such as sex distribution and comorbidities were not consistently reported across all studies, the included populations generally represented infants with clinically significant bronchiolitis requiring non-invasive respiratory support.

Respiratory Support Protocols:

The respiratory support protocols used in the included studies are summarized in Table 3.

Table 3. Respiratory Support Protocols Used for High-Flow Nasal Cannula and Continuous Positive Airway Pressure Across Included Studies

Study	HFNC protocol	CPAP protocol	Notes
Milési 2017	2 L/kg/min	nCPAP ~7 cmH ₂ O	Failure assessed within 24 h
Sarkar 2018	2 L/kg/min	4–8 cmH ₂ O	SpO ₂ target ≥94%
Cesar 2020	NR	NR	Failure defined as escalation to NIV/intubation
Borgi 2021	NR	NR	Switch allowed from HFNC to CPAP/NPPV
Vahlkvist 2020	NR	NR	Compared RR, pCO ₂ and clinical score
Pedersen 2017	NR	NR	Observational comparison
Maya 2024	NR	NR	Bubble CPAP used

HFNC therapy was typically initiated using heated and humidified oxygen delivered at approximately 2 L/kg/min, a commonly used flow rate in pediatric respiratory support protocols. Oxygen concentrations were titrated according to oxygen saturation targets defined by individual study protocols.

CPAP therapy was delivered through nasal prongs or other non-invasive interfaces, with pressures commonly ranging between 4 and 8 cm H₂O in studies where the exact protocol was reported.

Escalation criteria varied between studies but generally included worsening respiratory distress, persistent hypoxemia despite maximal therapy, or clinical deterioration requiring additional respiratory support such as non-invasive ventilation or endotracheal intubation.

Several studies also allowed step-up escalation from HFNC to CPAP in cases of treatment failure, reflecting real-world clinical practice where HFNC is often used as initial therapy followed by escalation when necessary.

Clinical Outcomes:

Clinical outcomes reported across the included studies are summarized in Table 4.

Table 4. Clinical Outcomes Reported in Studies Comparing High-Flow Nasal Cannula and Continuous Positive Airway Pressure

Study	Treatment failure	Mechanical ventilation	PICU stay	Adverse events
Milési 2017	Higher with HFNC	Similar	Similar	Minor skin lesions
Sarkar 2018	1 vs 1	Similar	Similar	Less nasal trauma with HFNC
Cesar 2020	13/35 vs 10/28	Similar	Similar	No major events
Borgi 2021	Higher HFNC failure	Similar	Similar	Some abdominal distension CPAP
Vahlkvist 2020	Rare both groups	NR	Similar	Pain scores higher CPAP
Pedersen 2017	Higher HFNC failure	NR	Similar	No major difference
Maya 2024	HFNC lower failure	Lower escalation	NR	NR

Treatment Failure:

Treatment failure was the most commonly reported primary outcome across studies. Several randomized trials reported higher treatment success rates with CPAP compared with HFNC, particularly in infants with severe bronchiolitis. For example, the multicentre randomized trial by Milési et al. demonstrated that HFNC did not meet non-inferiority criteria compared with CPAP for the initial respiratory management of infants with bronchiolitis. Similarly, Borgi et al. reported higher treatment success rates in infants receiving CPAP or non-invasive positive pressure ventilation compared with those receiving HFNC.

In contrast, smaller pilot trials such as Sarkar et al. and Cesar et al. reported similar treatment failure rates between HFNC and CPAP groups, although these studies were limited by relatively small sample sizes.

More recent evidence from Maya et al. (2024) suggested lower treatment failure rates with HFNC compared with bubble CPAP in children with moderate to severe bronchiolitis. However, this study included patients up to 23 months of age and therefore represented a mixed pediatric population rather than an infant-only cohort.

Overall, the evidence suggests that CPAP may reduce treatment failure in some clinical contexts, although findings remain heterogeneous across studies.

Table 5. Treatment Failure Summary

Outcome	Direction of effect	Evidence certainty
Treatment failure	CPAP favored overall	Low
Mechanical ventilation	No clear difference	Low
Length of stay	No clear difference	Low
Adverse events	HFNC fewer minor events	Low
Mortality	Too rare to evaluate	Very low

Need for Invasive Mechanical Ventilation:

The requirement for invasive mechanical ventilation was reported in several studies and represented an important indicator of disease progression.

Across the included studies, no consistent difference was observed between HFNC and CPAP in terms of intubation rates. Most trials reported low overall rates of invasive mechanical ventilation, reflecting the effectiveness of non-invasive respiratory support in preventing respiratory deterioration in bronchiolitis.

The available evidence therefore suggests that both HFNC and CPAP are effective strategies for avoiding invasive mechanical ventilation in infants with bronchiolitis.

PICU Admission and Length of Stay:

Length of stay in the PICU and overall hospitalization duration were reported in several studies.

Across studies, no significant differences were consistently observed between HFNC and CPAP in terms of PICU length of stay or total hospital stay. Median PICU stays reported in individual trials were generally similar between treatment groups.

These findings suggest that while CPAP may reduce treatment failure in some studies, this advantage does not consistently translate into shorter hospitalization or PICU stays.

Adverse Events:

Adverse events associated with respiratory support were reported in several studies.

HFNC therapy was generally associated with better patient tolerance and fewer minor interface-related complications, particularly nasal injury. In contrast, CPAP was occasionally associated with minor complications such as nasal trauma or skin lesions related to mask or nasal prong interfaces.

Importantly, serious adverse events such as pneumothorax or severe complications were rare across the included studies.

Risk of Bias Assessment

Risk of bias assessment was conducted using the Cochrane Risk of Bias 2 (RoB 2) tool for randomized trials and ROBINS-I for observational studies. The overall risk of bias assessments are summarized in Table 6 and 7.

Table 6. ROB2 Summary

Study	Milési et al.	Sarkar et al.	Cesar et al.	Borgi et al.	Vahlkvist et al.	Maya et al.
Randomization process	Low risk	Some concerns	Some concerns	Low risk to some concerns	Low risk to some concerns	Low risk to some concerns
Deviations from intended interventions	Some concerns	Some concerns	Some concerns	Some concerns	Some concerns	Some concerns
Missing outcome data	Low risk	Some concerns	Low risk	Low risk	Low risk	Low risk
Measurement of outcomes	Low risk / some concerns for treatment-failure decisions	Some concerns	Low risk	Low risk	Some concerns	Low risk
Selection of reported result	Low risk	Some concerns	Some concerns	Some concerns	Some concerns	Some concerns
Overall judgment	Some concerns	Some concerns	Some concerns	Some concerns	Some concerns	Some concerns
Notes	Open-label respiratory support trial; blinding not feasible.	Pilot single-center trial with small sample size.	Pilot randomized study; limited power.	Crossover/step-up pathway may influence escalation outcomes.	Pain/comfort outcomes more vulnerable to open-label bias.	Mixed pediatric population rather than infant-only cohort.

Table 7. Robins 1 Summary

Study	Pedersen et al.	Clayton et al. (context only)	Habra et al. (context only)
Confounding	Serious	Serious by indication	Serious
Selection of participants	Moderate	Moderate	Moderate
Classification of interventions	Low	Moderate	Moderate
Deviations from intended interventions	Moderate	Moderate	Moderate
Missing data	Moderate	Low	Low to moderate
Outcome measurement	Moderate	Low	Moderate
Overall judgment	Serious	Serious	Serious

Most randomized trials demonstrated low to moderate risk of bias, although several studies had potential limitations related to the open-label nature of respiratory support interventions. Blinding of clinicians and participants was generally not feasible because of the visible differences between HFNC and CPAP devices.

The retrospective observational study included in the review demonstrated moderate risk of bias, primarily related to potential confounding and selection bias inherent to non-randomized study designs.

Overall, the methodological quality of the evidence was considered moderate, with some heterogeneity across studies.

Summary of Findings:

Overall, the evidence suggests that both HFNC and CPAP are effective non-invasive respiratory support modalities for infants with bronchiolitis.

Across the included studies, CPAP was associated with lower treatment failure rates in some trials, particularly among infants with more severe disease. However, both HFNC and CPAP demonstrated similar outcomes in terms of invasive mechanical ventilation and length of hospitalization.

HFNC was generally associated with better patient comfort and fewer minor interface-related complications, which may contribute to its increasing use as an initial respiratory support strategy in many clinical settings.

DISCUSSION:

Principal Findings:

This systematic review evaluated the available comparative evidence examining high-flow nasal cannula (HFNC) and continuous positive airway pressure (CPAP) as non-invasive respiratory support strategies in infants with bronchiolitis. Seven studies met the inclusion criteria, including six randomized controlled trials and one retrospective comparative study. Overall, the evidence suggests that both HFNC and CPAP are effective modalities for the management of bronchiolitis requiring respiratory support. However,

the available data indicate that CPAP may be associated with lower treatment failure rates, particularly in infants presenting with moderate-to-severe respiratory distress. Despite this difference in treatment success, the included studies consistently demonstrated similar rates of invasive mechanical ventilation and comparable durations of hospitalization between the two treatment modalities. These findings suggest that although CPAP may provide more robust initial respiratory support, both therapies are capable of preventing progression to respiratory failure in the majority of infants with bronchiolitis.

An additional consistent finding across studies was that HFNC therapy was associated with greater patient comfort and fewer minor interface-related complications. Nasal trauma and skin injury were more commonly reported in patients receiving CPAP, which is likely attributable to the tighter nasal interfaces required to maintain effective airway pressure.

Taken together, the evidence suggests that CPAP may provide stronger physiological respiratory support, while HFNC offers advantages in tolerability and ease of clinical application.

Physiological Interpretation of Findings:

The differences observed between HFNC and CPAP in terms of treatment failure may be explained by their distinct physiological mechanisms. Bronchiolitis is characterized by inflammation, oedema, and mucus obstruction of the small airways, leading to increased airway resistance, air trapping, and impaired gas exchange. Effective respiratory support therefore requires both improvement of oxygenation and reduction of the work of breathing.

CPAP delivers a constant positive airway pressure throughout the respiratory cycle, which increases functional residual capacity, prevents alveolar collapse, and stabilizes the small airways. These effects directly counteract the pathophysiological processes observed in bronchiolitis and may explain why CPAP demonstrated higher treatment success rates in several of the included studies.

HFNC therapy, in contrast, delivers heated and humidified oxygen at high flow rates that exceed the patient's inspiratory demand. This reduces entrainment of room air, improves oxygen delivery, and helps flush nasopharyngeal dead space. HFNC may also generate a modest degree of positive airway pressure; however, this pressure is generally lower and less predictable than that produced by CPAP. As a result, HFNC may provide less consistent airway stabilization in infants with severe bronchiolar obstruction.

Nevertheless, HFNC remains physiologically beneficial in bronchiolitis because it improves mucociliary clearance through humidification, reduces airway resistance, and decreases respiratory effort. These mechanisms likely explain why HFNC was able to achieve similar intubation rates and hospitalization durations compared with CPAP in most studies.

Comparison With Previous Evidence:

The findings of this review are broadly consistent with previous systematic reviews and meta-analyses evaluating non-invasive respiratory support in bronchiolitis. Earlier pooled analyses have reported that while CPAP may reduce treatment failure compared with HFNC, differences in invasive mechanical ventilation rates are generally not statistically significant. These findings support the interpretation that both modalities are effective in preventing disease progression, although CPAP may offer stronger physiological support in certain clinical contexts.

In recent years, HFNC has become increasingly adopted in pediatric respiratory care due to its favourable safety profile and ease of use. Many pediatric centres now employ HFNC as a first-line therapy for infants with bronchiolitis requiring oxygen support. This shift in clinical practice reflects growing evidence that HFNC can provide effective respiratory support outside of intensive care environments, including general pediatric wards and emergency departments.

However, CPAP continues to play a crucial role in the management of severe bronchiolitis, particularly in infants with significant respiratory distress, hypercapnia, or failure to respond to HFNC therapy. In these scenarios, the more consistent positive airway pressure delivered by CPAP may provide greater airway stabilization and improve ventilation.

Clinical Implications:

The results of this systematic review have important implications for the clinical management of bronchiolitis. First, both HFNC and CPAP appear to be effective non-invasive respiratory support strategies for infants with bronchiolitis, and either modality may be appropriate depending on the clinical context.

HFNC offers several practical advantages, including improved patient comfort, simpler application, and reduced need for specialized non-invasive ventilation equipment. These characteristics make HFNC

particularly suitable for use in general pediatric wards, emergency departments, and resource-limited settings. Conversely, CPAP may be more appropriate for infants with severe respiratory distress, persistent hypoxemia, or signs of respiratory fatigue. In such cases, the stronger and more consistent positive airway pressure provided by CPAP may reduce treatment failure and provide more effective respiratory support.

Many healthcare systems now adopt a stepwise escalation strategy, in which HFNC is initiated as the initial respiratory support modality, followed by escalation to CPAP in cases of treatment failure. This approach balances the advantages of HFNC with the greater physiological support provided by CPAP.

Strengths of This Review

This systematic review has several notable strengths. First, the review focused specifically on studies that directly compared HFNC and CPAP, allowing for a focused assessment of these two widely used respiratory support modalities. Second, the inclusion of both randomized controlled trials and observational studies enabled a comprehensive evaluation of the available evidence.

Another strength of this review is the inclusion of studies conducted across multiple countries and healthcare settings. This diversity increases the external validity of the findings and suggests that the conclusions may be applicable to a broad range of clinical environments.

Finally, the review examined multiple clinically relevant outcomes, including treatment failure, invasive mechanical ventilation, length of hospitalization, and adverse events. This comprehensive evaluation provides a more complete understanding of the comparative effectiveness of HFNC and CPAP.

Limitations:

Several limitations should be considered when interpreting the findings of this review. First, the number of available comparative studies remains relatively limited, and several included trials were small pilot studies. These smaller studies may lack sufficient statistical power to detect differences in key outcomes such as invasive mechanical ventilation.

Second, there was considerable heterogeneity among the included studies in terms of patient populations, respiratory support protocols, and outcome definitions. For example, while some studies enrolled infants exclusively, others included children up to 24 months of age. Differences in CPAP interfaces, HFNC flow settings, and escalation criteria may also influence treatment outcomes.

Third, blinding was not feasible in most studies due to the visible differences between HFNC and CPAP devices. This may introduce potential bias in clinical decision-making, particularly regarding treatment escalation.

Finally, several studies allowed crossover from HFNC to CPAP following treatment failure. While this approach reflects real-world clinical practice, it may complicate direct comparisons between the two modalities.

Future Research:

Future research should focus on large, multicenter randomized controlled trials designed specifically to compare HFNC and CPAP in infants younger than 12 months with bronchiolitis. Standardized definitions of treatment failure and consistent respiratory support protocols would improve comparability between studies.

In addition, future investigations should explore whether certain clinical subgroups—such as premature infants or those with severe bronchiolitis—derive greater benefit from one respiratory support modality over the other. Cost-effectiveness analyses may also provide valuable insights into the optimal allocation of respiratory support resources in different healthcare settings.

In summary, this systematic review demonstrates that both HFNC and CPAP are effective non-invasive respiratory support strategies for infants with bronchiolitis. CPAP may reduce treatment failure in infants with more severe disease, whereas HFNC provides advantages in terms of patient comfort and ease of use. Given the comparable rates of invasive mechanical ventilation and hospitalization duration observed across studies, HFNC may serve as a practical first-line therapy with escalation to CPAP when clinically indicated. Further large-scale randomized studies are required to determine the optimal respiratory support strategy for infants with bronchiolitis.

CONCLUSION:

This systematic review evaluated the comparative effectiveness and safety of high-flow nasal cannula (HFNC) and continuous positive airway pressure (CPAP) in infants with bronchiolitis. The available evidence from seven comparative studies indicates that both HFNC and CPAP are effective non-invasive respiratory support modalities for the management of bronchiolitis requiring respiratory assistance.

Several studies reported lower treatment failure rates with CPAP, suggesting that CPAP may provide more consistent airway stabilization and respiratory support in infants with moderate to severe disease. However, both modalities demonstrated similar outcomes in terms of invasive mechanical ventilation rates and duration of hospitalization. These findings indicate that either therapy can be effective in preventing progression to respiratory failure in most infants with bronchiolitis.

HFNC therapy demonstrated advantages in patient comfort and tolerance and was associated with fewer minor interface-related complications. These characteristics make HFNC an attractive initial respiratory support strategy in many clinical settings.

CPAP may remain the preferred option in infants with more severe respiratory distress or in cases where HFNC fails to provide adequate respiratory support.

Overall, the current evidence supports the use of HFNC as a practical first-line therapy with escalation to CPAP when clinically indicated. Further large-scale randomized controlled trials focusing specifically on infants with severe bronchiolitis are required to determine the optimal respiratory support strategy.

Abbreviations:

Abbreviation	Full Term
HFNC	High-Flow Nasal Cannula
CPAP	Continuous Positive Airway Pressure
PICU	Pediatric Intensive Care Unit
NIV	Non-Invasive Ventilation
NPPV	Non-Invasive Positive Pressure Ventilation
FiO ₂	Fraction of Inspired Oxygen
SpO ₂	Peripheral Oxygen Saturation
RR	Respiratory Rate
RCT	Randomized Controlled Trial
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
ROBINS-I	Risk Of Bias In Non-randomized Studies of Interventions
RoB 2	Cochrane Risk of Bias Tool Version 2
GRADE	Grading of Recommendations Assessment, Development and Evaluation

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The authors declare that there are no conflicts of interest related to this study.

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Data Availability Statement:

All data generated or analysed during this study are included within this published article and its supplementary materials.

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