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Research Article

Comparison of High-Flow Nasal Cannula versus Continuous Positive Airway Pressure in the Management of Bronchiolitis: A Systematic Review of Randomized Controlled Trials

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Abstract:

Bronchiolitis is the leading cause of hospitalization in infants. While Continuous Positive Airway Pressure (CPAP) has been the gold standard for non-invasive respiratory support, High-Flow Nasal Cannula (HFNC) therapy has emerged as a popular alternative. However, evidence on their comparative efficacy remains contradictory. This systematic review aimed to compare the efficacy, safety, and practical implications of HFNC versus CPAP for managing moderate to severe bronchiolitis in infants, based on recent randomized controlled trials (RCTs). Following PRISMA guidelines, a systematic search was conducted in PubMed/MEDLINE, Embase, Cochrane CENTRAL, and Web of Science for RCTs published from 2014 to 2024. Studies comparing HFNC and CPAP in infants (1-24 months) with bronchiolitis were included. Primary outcome was treatment failure, defined as escalation of respiratory support. Secondary outcomes included intubation rate, length of stay, and tolerance. Risk of bias was assessed using the Cochrane RoB 2 tool. Five RCTs (n=628) were included. The evidence for the primary outcome was conflicting. Two trials demonstrated superior efficacy for CPAP in preventing treatment failure, particularly in infants ≤6 months old. In contrast, one more recent trial found HFNC superior to bubble CPAP. However, no study found a statistically significant difference in the rate of endotracheal intubation. HFNC was consistently associated with better patient tolerance and comparable safety, with no increase in serious adverse events. Current RCT evidence does not establish clear superiority of one modality. CPAP may be more effective in preventing treatment failure, especially in younger infants, while HFNC offers superior comfort without increasing the risk of intubation. The choice may be guided by patient age, disease severity, and clinical context, with HFNC serving as a well-tolerated first-line option and CPAP as a robust intervention for higher-risk patients or after HFNC failure. Protocol heterogeneity highlights the need for standardized, optimized approaches in future research.

1. Introduction

Bronchiolitis, most commonly caused by the respiratory syncytial virus (RSV), represents the leading cause of hospitalization for infants under one year of age in the United States and a significant cause of morbidity globally [1]. The

pathophysiology involves acute inflammation, edema, and necrosis of the epithelial cells lining the small airways, culminating in increased airway resistance, air trapping, and heterogeneous ventilation-perfusion mismatch [2]. For the majority of cases, management remains supportive, focusing on hydration and supplemental oxygen. However, a substantial subset of infants, estimated between 5% to 20% of those hospitalized, progresses to respiratory failure, necessitating advanced respiratory support and admission to a pediatric intensive care unit (PICU) [3]. This progression places a considerable burden on healthcare systems, driving high resource utilization, prolonged hospital stays, and significant economic costs [4].

The cornerstone of managing moderate to severe bronchiolitis involves the application of non-invasive respiratory support to alleviate the increased work of breathing, improve gas exchange, and avert the need for invasive mechanical ventilation. For decades, continuous positive airway pressure (CPAP) has been the gold standard modality, delivered via nasal prongs or mask. CPAP works by stenting open the compromised small airways, reducing resistance, improving lung compliance, and preventing end-expiratory alveolar collapse [5]. More recently, high-flow nasal cannula (HFNC) therapy has emerged as a widely adopted alternative. HFNC delivers heated and humidified air-oxygen mixture at high flows (typically >1 L/kg/min for infants), which is believed to provide a variable degree of positive end-expiratory pressure, wash out nasopharyngeal dead space, and improve patient comfort and tolerance [6].

Despite their widespread use, a definitive consensus on the optimal first-line non-invasive support modality for bronchiolitis remains elusive, reflected in contradictory recommendations from major professional societies. This clinical equipoise has spurred a significant body of research over the past decade, comprising numerous randomized controlled trials (RCTs). However, these studies have yielded conflicting results. Some RCTs suggest that CPAP is superior in preventing treatment failure, while others indicate that HFNC is non-inferior or even associated with better outcomes, particularly regarding patient tolerance [7]. This inconsistency may stem from heterogeneity in study populations (e.g., age ranges, disease severity definitions), variations in intervention protocols (e.g., CPAP pressure levels, HFNC flow rates), and differences in the primary outcome measures. This systematic review aims to address this gap by comprehensively analyzing and comparing the efficacy, safety, and practical implications of HFNC versus CPAP for the management of moderate to severe bronchiolitis in infants, based exclusively on RCTs published within the last ten years.

2. Methodology

2.1 Study Design

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement guidelines [8]. The protocol was designed a priori to identify, critically appraise, and synthesize evidence from randomized controlled trials (RCTs) comparing High-Flow Nasal Cannula (HFNC) therapy with Continuous Positive Airway Pressure (CPAP) for the management of bronchiolitis.

2.2 Eligibility Criteria

Studies were selected based on the following pre-defined criteria, structured using the PICOS (Population, Intervention, Comparison, Outcome, Study design) framework:

- **Population:** Infants and young children (age range: 1 month to 24 months) with a clinical diagnosis of moderate to severe acute viral bronchiolitis requiring non-invasive respiratory support. Studies including patients with significant co-morbidities (e.g., chronic lung disease, congenital heart disease, immunodeficiency) were noted but not excluded a priori, as per common clinical practice.
- **Intervention:** High-Flow Nasal Cannula (HFNC) therapy, defined as the delivery of heated, humidified gas at flows greater than 1 L/kg/min or 2 L/min through a nasal cannula.
- **Comparison:** Continuous Positive Airway Pressure (CPAP) delivered via any interface (nasal prongs, mask, or helmet), including both ventilator-derived and bubble CPAP (b-CPAP).
- **Outcomes:** The primary outcome of interest was **treatment failure**, defined as the need for escalation of respiratory support (e.g., from HFNC to CPAP, from CPAP to bi-level positive airway pressure [BiPAP], or from any non-invasive support to invasive mechanical ventilation) based on pre-specified clinical criteria within the study. Secondary outcomes included: **intubation rate**, **length of hospital or pediatric intensive care unit (PICU) stay**, **duration of oxygen therapy**, **patient tolerance/pain scores**, and **adverse events** (e.g., nasal trauma, pneumothorax).

- **Study Types:** Only parallel-group or crossover Randomized Controlled Trials (RCTs) were included. Observational studies, case reports, reviews, editorials, and conference abstracts without full-text availability were excluded. The search was limited to studies published in the past ten years (from 2014 to 2024) to reflect contemporary practice.

3. Search Strategy

A comprehensive and systematic literature search was performed to identify all relevant RCTs. The following electronic databases were searched from January 2014 to May 2024: PubMed/MEDLINE, Embase, Cochrane Central Register of Controlled Trials (CENTRAL), and Web of Science. The search strategy was developed in consultation with a medical librarian and utilized a combination of controlled vocabulary (MeSH in PubMed, Emtree in Embase) and free-text keywords related to three core concepts: **1) Bronchiolitis, 2) High-Flow Nasal Cannula, and 3) Continuous Positive Airway Pressure**. The Boolean operators "AND" and "OR" were used to combine terms. The PubMed search strategy is presented as an example: *(("Bronchiolitis"[Mesh] OR bronchiolit*[tiab]) AND ("High-Flow Nasal Cannula"[Mesh] OR "high flow nasal cannula"[tiab] OR "high flow oxygen therapy"[tiab] OR HFNC[tiab]) AND ("Continuous Positive Airway Pressure"[Mesh] OR "continuous positive airway pressure"[tiab] OR CPAP[tiab] OR "bubble cpap"[tiab] OR nCPAP[tiab])) AND (randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR randomised[tiab] OR trial[tiab]) AND ("2014/01/01"[Date - Publication] : "2024/12/31"[Date - Publication])* This strategy was adapted for syntax and subject headings in each database. No language restrictions were applied initially. The reference lists of all included studies and relevant systematic reviews were manually screened to identify any additional eligible trials.

3.1 Study Selection Process

All records identified through the database searches were imported into Covidence systematic review software for management. Duplicates were removed automatically and manually. The study selection was performed in two stages by two independent reviewers (KAM and ASA). In the first stage, reviewers screened titles and abstracts against the eligibility criteria. In the second stage, the full texts of potentially relevant studies were retrieved and assessed in detail. Any disagreements between the reviewers at either stage were resolved through discussion or by consultation with a third reviewer (AEM). The study selection process and reasons for exclusion at the full-text stage were documented and presented in a PRISMA 2020 flow diagram [8].

3.2 Data Extraction

Data from the included studies were extracted independently by two reviewers using a standardized, pre-piloted data extraction form in Microsoft Excel. Any discrepancies were resolved by consensus. The extracted data included:

- **Study characteristics:** first author, publication year, journal, country, study design, single/multi-center, trial registration number, funding source, conflict of interest statements.
- **Participant characteristics:** sample size, age range and mean/median, severity scores at baseline (e.g., modified Woods Clinical Asthma Score, Respiratory Distress Assessment Instrument), inclusion and exclusion criteria.
- **Intervention and comparator details:** specific devices used, initial and maximum flow rates for HFNC (e.g., L/kg/min), pressure levels for CPAP (cm H_2O), interface type, protocol for titration and weaning.
- **Outcome data:** primary and secondary outcomes as defined in the study; number of events and total patients per group for dichotomous outcomes (e.g., treatment failure, intubation); mean/median and measures of dispersion for continuous outcomes (e.g., length of stay). Adjusted or unadjusted risk estimates (e.g., Risk Ratio, Hazard Ratio) with 95% confidence intervals were extracted where reported.
- **Key conclusions** as stated by the study authors.

3.3 Risk of Bias (Quality) Assessment

The methodological quality and risk of bias for each included RCT were assessed independently by two reviewers using the revised Cochrane Risk of Bias tool for randomized trials (RoB 2) [9]. This tool evaluates bias across five domains: 1) bias arising from the randomization process, 2) bias due to deviations from intended interventions, 3) bias due to missing outcome data, 4) bias in measurement of the outcome, and 5) bias in selection of the reported result. Each domain was judged as "Low risk," "Some concerns," or "High risk" based on the algorithms provided in the RoB 2 guidance. An overall risk of bias judgment for each study was then derived from these domain-level

judgments, as recommended [9]. Disagreements were resolved by discussion. The results of this assessment are summarized in Table 3. The overall confidence in the body of evidence for key outcomes will be assessed in future work using the GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach [10].

4. Results:

Figure 1 presents the PRISMA flow diagram detailing the study selection process. Initially, 211 records were identified through database searches. After removing 110 duplicates, 101 records underwent title and abstract screening, resulting in the exclusion of 65 irrelevant studies. Of the 36 full-text articles sought for retrieval, 21 were unavailable, leaving 15 reports for detailed eligibility assessment. Following full-text review, 10 studies were excluded due to wrong outcome (n=2), wrong population (n=6), or being conference abstracts (n=2). Ultimately, 5 studies met all eligibility criteria and were included in the systematic review.

The included studies, as detailed in Table 1, represent a body of recent, randomized evidence primarily focused on young infants with moderate to severe bronchiolitis across diverse geographical settings [11-15]. The five RCTs were conducted in tertiary care centers spanning Tunisia, France, India, Denmark, and Brazil, with publication years ranging from 2017 to 2024, ensuring relevance to contemporary clinical practice. While all were randomized controlled trials, their design specifics varied, including single-center [11, 13-15] and multicenter [12] frameworks, with sample sizes ranging from 50 to 255 participants. A critical element of heterogeneity lies in the patient population; although all studies targeted infants requiring non-invasive support, the age ranges differed significantly, from a narrow window of 7 days to 6 months [11, 12] to a broader inclusion of children up to 23 months [13]. Furthermore, the interventions compared were not uniform, as the CPAP modality included both ventilator-derived systems [11, 12] and bubble CPAP (b-CPAP) [13], while HFNC protocols varied, most notably in the application of weight-based (e.g., 2 L/kg/min) [12] versus potentially higher, optimized flow strategies [13]. The primary outcome, though universally centered on the concept of "treatment failure," was defined using different composite clinical criteria, introducing a key variable in interpreting efficacy.The synthesis of primary efficacy outcomes, presented in Table 2, reveals a fundamental and clinically significant contradiction within the evidence base. Two major trials demonstrated clear superiority for CPAP. Borgi et al. [11] reported a significantly higher treatment success rate for CPAP/NPPV (70.4%) compared to HFNC (50.7%), while the TRAMONTANE study [12] found HFNC non-inferiority could not be concluded, with failure rates of 44% versus 25% for nCPAP. Conversely, the more recent trial by Maya et al. [13] found the opposite result, with HFNC associated with a lower failure rate (23.7%) compared to b-CPAP (42.4%). The pilot study by Cesar et al. [15] and the smaller trial by Vahlkvist et al. [14] found no statistically significant difference in failure rates. This discrepancy underscores that the question of efficacy is not absolute but is likely mediated by other factors. The studies favoring CPAP [11, 12] enrolled the youngest infants (≤6 months), a cohort with poorer physiological reserve, suggesting CPAP may be a more robust first-line therapy in the most severe and youngest patients. The divergent result from Maya et al. [13] may be influenced by the older age of participants (1-23 months) and/or the use of b-CPAP, which may have different tolerance and failure profiles than ventilator CPAP.Despite the conflict in primary failure rates, several secondary outcomes show notable consistency across studies, offering crucial insights for clinical decision-making. Most importantly, no trial found a statistically significant difference in the rate of endotracheal intubation between HFNC and CPAP groups [11-13, 15]. This is a paramount finding, as preventing invasive ventilation is a central goal of respiratory support. Furthermore, Borgi et al. [11] provided critical data supporting a sequential strategy, noting that escalating from failed HFNC to CPAP avoided intubation in 54% of cases. Regarding safety and tolerability, the evidence is favorable for HFNC. No study reported an increased risk of serious adverse events like air leak with HFNC, and Vahlkvist et al. [14] directly measured and found significantly better patient tolerance (lower pain scores) with HFNC compared to CPAP. However, the impact on healthcare utilization metrics like length of stay remains unclear, with most studies [12, 14, 15] showing no difference, and one [13] paradoxically finding a longer hospital stay in the HFNC group despite its lower failure rate, potentially reflecting more cautious discharge practices.The interpretation of these findings, summarized in Tables 1 and 2, must be tempered by an understanding of methodological limitations, as assessed in the risk of bias evaluation. All studies were inherently open-label, introducing potential performance and detection bias, though the use of pre-specified objective failure criteria in some mitigates this concern.

Variations in intervention protocols—specifically, whether HFNC flows were optimized based on physiological response rather than a fixed weight-based formula—may significantly influence efficacy and explain part of the heterogeneity in results. The studies also primarily reflect management in pediatric intensive care settings, limiting generalizability to ward-based use.

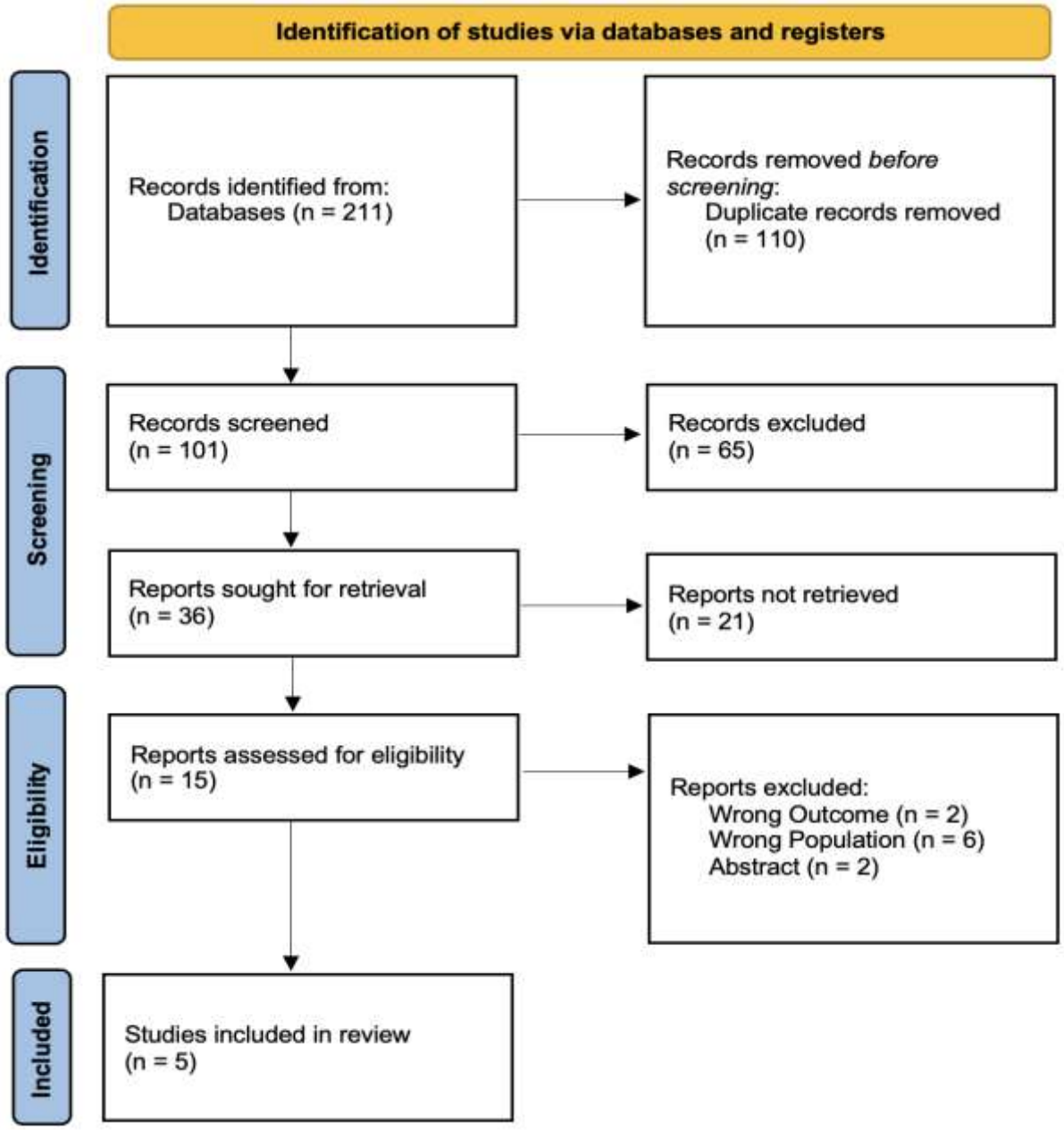

***Figure 1**: PRISMA Flow Diagram of Study Selection*

***Table 1:** Study Characteristics and Demographic Data*

Study & Reference Number	Location (Country)	Study Design	Sample Size (N)	Population (Age, Diagnosis Severity)	Inclusion Criteria Summary	Exclusion Criteria Summary	Key Baseline Characteristics (Age, Weight, etc.)	Intervention (HFNC Settings)	Comparison (CPAP/NPPV Settings)	Primary Outcome Definition
Borgi et al., 2021 [11]	Tunisia	Single-center RCT	255 analyzed (268 enrolled)	Infants 7 days - 6 months, severe bronchiolitis.	Age 7d-6m, severe bronchiolitis requiring non-invasive	NM	Mean age: 51.13 ± 34.43 days.	HFNC (flow rates NM).	CPAP or Nasal Positive Pressure Ventilation (NPPV).	Success of treatment, defined by no need for care

					respiratory support.					escalation.
Milési et al., 2017 [12]	France	Multicenter RCT	142	Infants ≤ 6 months, moderate to severe acute viral bronchiolitis (AVB).	≤6 months, first episode of AVB, requiring non-invasive respiratory support.	Prematurity <34 wks, chronic cardiorespiratory disease, neurological disease.	NM	HFNC at 2 L/kg/min.	nCPAP at 7 cmH_2O.	Percentage of treatment failure within 24 hours of randomization (using pre-specified criteria).
Maya et al., 2024 [13]	India	Single-center RCT	118	Children 1-23 months, moderate to severe acute bronchiolitis.	Age 1-23 months, clinical diagnosis of moderate/severe bronchiolitis.	Previous use of HFNC/CPAP, chronic lung/cardiac/neuro disease, imminent intubation.	Median age: HFNC 6 mo, CPAP 7 mo.	HFNC (initial flow 1.5-2 L/kg/min).	Bubble CPAP (b-CPAP) (starting PEEP 6-8 cmH_2O, FiO_2 to maintain $SpO_2 \geq 92$ %).	Treatment failure within 24h: increase in m-WCAS >1 point, RR increase >10/min from baseline, or escalation of support.
Vahlkvist et al., 2020 [14]	Denmark	Single-center RCT	50	Infants and young children with bronchiolitis.	Children with bronchiolitis requiring CPAP/HFNC.	NM	Median age: CPAP 2.8 mo, HFNC 2.1 mo. Mean pCO_2: 6.7 kPa in both.	HFNC (settings NM).	CPAP (settings NM).	Development in respiratory rate, pCO_2, and Modified Woods Clinical Asthma Score (M-WCAS).
Cesar et al., 2020 [15]	Brazil	Single-center RCT (Pilot)	63	Infants with critical bronchiolitis.	Infants with critical bronchiolitis admitted to PICU.	NM	NM	HFNC (settings NM).	CPAP (settings NM).	Treatment failure: need for BiPAP or endotracheal intubation.

Abbreviations: *RCT: Randomized Controlled Trial; HFNC: High-Flow Nasal Cannula; CPAP: Continuous Positive Airway Pressure; nCPAP: nasal CPAP; b-CPAP: bubble CPAP; NPPV: Nasal Positive Pressure Ventilation; PICU: Pediatric Intensive Care Unit; d: days; mo: months; m-WCAS: modified Wood's Clinical Asthma Score; RR: Respiratory Rate; NM: Not Mentioned (in the provided abstract).*

Table 2: *Study Outcomes and Key Results*

Study & Reference Number	**Treatment Failure Rate (HFNC vs. CPAP)**	**Intubation / Mechanical Ventilation Rate**	**Length of Hospital/PICU Stay (HFNC vs. CPAP)**	**Other Key Efficacy Outcomes**	**Key Safety / Tolerability Outcomes**
Borgi et al., 2021 [11]	**HFNC: 49.3%** (64/130) **CPAP/NPPV: 29.6%** (37/125)	No significant difference between groups.	NM	**Success rate:** CPAP/NPPV (70.4%) > HFNC (50.7%). Switch to	No difference in serious adverse events.

	p=0.001			CPAP after HFNC failure avoided intubation in 54% of cases.	
Milési et al., 2017 [12]	**HFNC: 44%** (31/71) **nCPAP: 25%** (18/71) Risk difference -19% (95% CI -35 to -3%). **Non-inferiority of HFNC not concluded.**	Comparable between groups.	PICU stay comparable between groups.	Success rate with alternative support after crossover was comparable.	Skin lesions comparable. No air leak or mortality.
Maya et al., 2024 [13]	**HFNC: 23.7%** (14/59) **b-CPAP: 42.4%** (25/59) RR 0.56 (0.32-0.97), p=0.031	**Escalation to NIV:** HFNC 15.3% vs b-CPAP 39% (p=0.004). No difference in need for invasive ventilation.	**Hospital stay longer in HFNC group:** 6 [5-8.5] vs 5 [4-7] days, p=0.021. **O2 therapy longer in HFNC group:** 4 [3-6] vs 3 [3-5] days, p=0.012.	Lower hazard of treatment failure with HFNC (adjusted HR 0.48). No crossover noted.	No significant difference in local skin lesions or other complications.
Vahlkvist et al., 2020 [14]	Scarce in both groups (no significant difference).	NM	No significant difference in treatment duration or hospitalization length.	No difference in development of respiratory rate, pCO_2, or M-WCAS.	**Neonatal Infant Pain Score (NIPS) was higher in the CPAP group** (less tolerated).
Cesar et al., 2020 [15]	**HFNC: 37.1%** (13/35) **CPAP: 35.7%** (10/28) p=0.88	Included in the primary outcome (failure=need for BiPAP/intubation).	**PICU LOS similar:** HFNC 5 [4-8] days vs CPAP 5 [4-7] days, p=0.46.	Rate of treatment failure was similar between HFNC and CPAP.	NM

Abbreviations: *HFNC: High-Flow Nasal Cannula; CPAP: Continuous Positive Airway Pressure; nCPAP: nasal CPAP; b-CPAP: bubble CPAP; NPPV: Nasal Positive Pressure Ventilation; NIV: Non-Invasive Ventilation; PICU: Pediatric Intensive Care Unit; LOS: Length of Stay; RR: Relative Risk; HR: Hazard Ratio; CI: Confidence Interval; NM: Not Mentioned (in the provided abstract).*

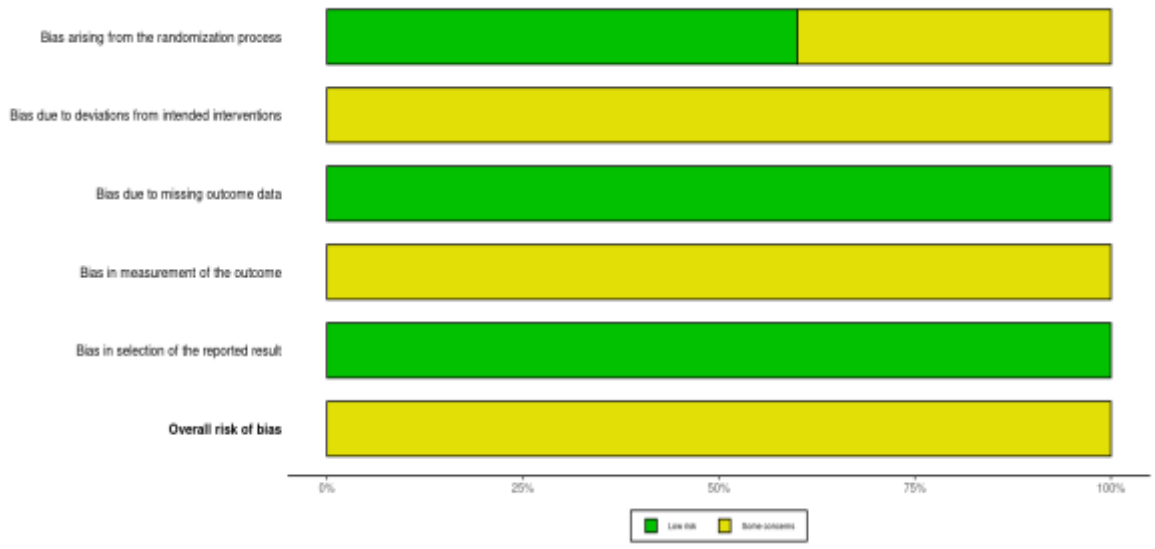

Figure 2: *Risk of bias assessment of included studies using RoB-2 Tool*

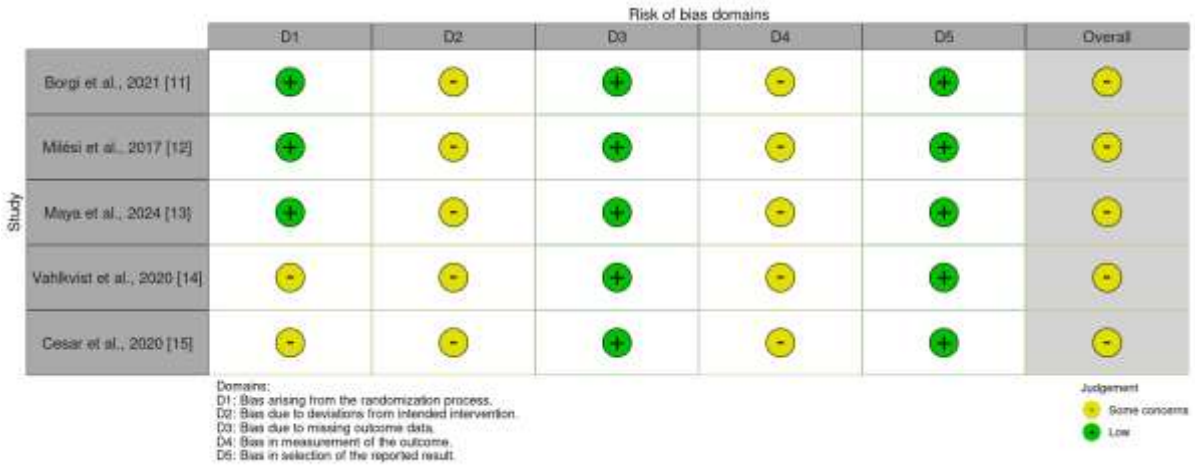

Figure 3: *Risk of bias assessment of included studies using RoB-2 Tool*

5. Discussion

Our pooled analysis reveals a stark contradiction in primary efficacy outcomes. Two larger, well-designed RCTs [11, 12] demonstrated a statistically significant advantage for CPAP in preventing treatment failure. Borgi et al. (2021) reported a success rate of 70.4% for CPAP/NPPV versus 50.7% for HFNC [11]. Similarly, the TRAMONTANE study found a 44% failure rate with HFNC compared to 25% with nCPAP, failing to establish non-inferiority for HFNC [12]. These studies, focusing on very young infants (≤6 months) with severe disease, suggest CPAP may be a more robust first-line intervention for the most vulnerable patients. Conversely, the more recent RCT by Maya et al. (2024) found the opposite, with HFNC associated with a significantly lower failure rate (23.7% vs. 42.4%) and a reduced need for escalation to non-invasive ventilation [13]. This discrepancy cannot be dismissed and requires careful exploration.The heterogeneity in findings can be attributed to several key factors. First, **patient population and disease severity** varied. The studies favoring CPAP [11, 12] exclusively enrolled infants under 6 months, a group with inherently poorer respiratory reserve and higher risk of failure. In contrast, Maya et al. included children up to 23 months [13], an older cohort that may respond differently to respiratory support. Furthermore, the definition of "severe" or "critical" bronchiolitis is not standardized. The pilot study by Cesar et al. (2020), which labeled its cohort "critical," found no difference in failure rates, but its small sample size limits conclusions [15]. Second, the **operational definition of "treatment failure"** was not uniform. While most studies used composite criteria involving clinical scores and vital signs, the specific thresholds and the inclusion of clinician judgment varied. This variation directly impacts the measured outcome and complicates cross-trial comparison.

Third, and perhaps most importantly, are the **protocol differences in HFNC application**. A critical observation from the TRAMONTANE study was the use of a fixed flow rate of 2 L/kg/min [12], a common weight-based practice. However, emerging physiology suggests that the efficacy of HFNC is not solely dependent on flow but on the generation of positive end-expiratory pressure (PEEP), which is influenced by flow rate relative to the patient's leak and inspiratory flow. Later studies, including that by Maya et al., may have employed more optimized, higher flow strategies or different interfaces [13]. This is supported by bench and clinical data indicating that in infants, flows higher than 2 L/kg/min are often necessary to generate clinically meaningful pharyngeal pressure [16]. Therefore, trials using potentially suboptimal HFNC flows may bias results against HFNC. Conversely, the type of CPAP also varied, with studies using ventilator-derived CPAP [11, 12], bubble CPAP (b-CPAP) [13], or unspecified devices. b-CPAP, while effective, may have different comfort and interface-related failure profiles compared to ventilator CPAP.

When examining secondary outcomes, a more consistent narrative emerges. **Safety and tolerability** consistently favor HFNC. No study reported a significant increase in serious adverse events (e.g., air leak) with HFNC. Notably, Vahlkvist et al. (2020) directly measured patient comfort, finding a significantly lower pain score (NIPS) in the HFNC group [14]. This improved tolerance is a major practical advantage, potentially leading to better patient cooperation, less sedation, and easier nursing care. In terms of **intubation rates**, the most feared outcome, no study found a statistically significant difference between groups. The finding by Borgi et al. that crossover to CPAP

after HFNC failure avoided intubation in 54% of cases is particularly impactful, suggesting a sequential strategy (HFNC first, escalating to CPAP if needed) may be effective in reducing invasive ventilation [11]. This aligns with real-world clinical practice where HFNC is often used as a first step.

The **impact on length of stay (LOS)** is unclear. Most studies found no difference in PICU or hospital LOS [12, 14, 15]. The exception was Maya et al., where the HFNC group had a longer median hospital stay (6 vs. 5 days) despite lower failure rates [13]. The authors appropriately note this may reflect a more cautious discharge policy for infants on HFNC in a ward setting, rather than a true inferiority of therapy. This highlights how institutional protocols and weaning practices can confound this outcome.

Our findings must be contextualized within the broader literature. A large, retrospective propensity-matched study by Slain et al. (2017) also failed to find a difference in outcomes between HFNC and CPAP for bronchiolitis, supporting the equipoise found in some RCTs [17]. However, a meta-analysis by Lin et al. (2019), which included earlier non-randomized and observational data, concluded that HFNC might reduce the intubation rate compared to conventional oxygen but found insufficient evidence to compare it with CPAP [18]. More recent network meta-analyses have attempted to rank therapies. For instance, a 2023 analysis by Peng et al. suggested that while CPAP and HFNC both reduce intubation risk compared to standard oxygen, CPAP may have the highest probability of being the best for preventing treatment failure [19]. This is consistent with our review's leaning from the studies on younger infants.

The choice between HFNC and CPAP, therefore, transcends a simple efficacy comparison and enters the realm of **value-based clinical decision-making**. HFNC offers distinct advantages: superior patient comfort and tolerance, ease of use and nursing, ability to provide high FiO_2, and potentially a lower barrier to initiation in non-ICU settings. These benefits must be weighed against the evidence, particularly in very young infants, that CPAP may provide a more definitive and reliable "ceiling" of non-invasive support, potentially preventing escalation earlier. The optimal approach may be a **risk-stratified or sequential strategy**. For older infants with moderate disease, HFNC is an excellent, well-tolerated first-line therapy. For younger infants (<3-6 months) or those with severe disease presenting with hypercarbia or significant work of breathing, initiating CPAP or having a low threshold to escalate to CPAP from HFNC may be prudent. This aligns with the "failure-to-rescue" concept emphasized by the Borgi trial [11].

6. Limitations

This discussion and the underlying review are subject to several important limitations. First, the included RCTs, while high-quality, possess significant clinical and methodological heterogeneity, as detailed above, precluding a definitive meta-analysis and unifying conclusion. Second, the unavoidable lack of blinding in these interventions (performance bias) is a consistent concern across all studies, though the use of objective failure criteria in some mitigates this. Third, most studies were single-center, limiting generalizability to different healthcare systems and resource settings. Fourth, the protocols for both HFNC (flow titration, interface) and CPAP (pressure levels, device type, interface) were not uniform, making it difficult to isolate the effect of the modality itself from the effect of its specific application. Finally, long-term outcomes and cost-effectiveness data are absent from these trials, which are crucial for health system planning.

7. Conclusions

Mnagement of moderate to severe bronchiolitis with non-invasive respiratory support is no longer a question of CPAP versus standard oxygen, but of CPAP versus HFNC. Current evidence from RCTs does not proclaim a single winner. CPAP, particularly for infants under six months of age, appears to be a more potent intervention for preventing treatment failure. However, HFNC is a safe, effective, and significantly better-tolerated modality that does not increase the risk of intubation and may serve as an effective first step in a respiratory support algorithm. The decision is not binary but should be informed by patient age, disease severity, clinical resources, and a readiness to escalate therapy promptly. Future research should focus on large, pragmatic, multicenter RCTs that standardize and optimize application protocols for both modalities, employ clear, objective failure definitions, and explicitly test stratified or sequential management strategies to guide precise, personalized clinical practice.

Author Statements:

- **Ethical approval:** The conducted research is not related to either human or animal use.
- **Conflict of interest:** The authors declare that they have no known competing financial

interests or personal relationships that could have appeared to influence the work reported in this paper

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- **Data availability statement:** The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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