Annals of Middle Eastern Medicine

ORIGINAL ARTICLE

Nasal continuous positive airway pressure versus high-flow nasal cannula in infants with respiratory distress syndrome: a systematic review

Yara Hamed Abo Sabaah[1,2,3]*, Rasha Ahmed Almumlah[2], Mohammed Hamed Abosabaah[1,2,3], Abdulrahman Sultan Al Qattoumah[4], Ali Ibrahim Almoghassl[5], Hussain Abdullah Alqahtani[5], Hams Oudah Aljadani[2], Amal Saleh Alzahrani[2], Sulaiman Al Queflie[6]

ABSTRACT

Background: Respiratory distress syndrome (RDS) is a leading cause of respiratory failure in preterm infants, primarily resulting from surfactant deficiency and alveolar collapse. Approximately 15%–20% of affected children require respiratory support. Despite advances in antenatal care and non-invasive ventilation that have reduced mortality and complications, the optimal mode of respiratory support remains uncertain. Nasal continuous positive airway pressure (NCPAP) and high-flow nasal cannula (HFNC) are among the most widely used non-invasive methods for managing RDS—NCPAP enhances lung expansion and oxygenation, while HFNC offers greater comfort and ease of application. Given the ongoing debate over their relative efficacy and safety, this study aimed to systematically review and compare HFNC and NCPAP as initial respiratory support strategies in preterm infants with RDS.

Methods: This systematic review was conducted in accordance with PRISMA guidelines. A comprehensive literature search of PubMed, Web of Science, and Scopus was performed to identify studies published between 2015 and 2025 comparing NCPAP with HFNC in preterm or term infants diagnosed with respiratory distress syndrome. Randomized controlled trials and eligible observational studies reporting at least one relevant clinical outcome were considered. Following duplicate removal, titles and abstracts were screened, and potentially relevant articles were assessed for full-text eligibility. Of 565 records identified, 336 were screened, and 12 studies met the inclusion criteria and were included in the final qualitative synthesis.

Results: Twelve published studies, conducted between 2017 and 2022, with a total of 1,242 patients, were included. The studies, including preterm infants with respiratory distress, were analyzed. HFNC demonstrated comparable efficacy to NCPAP in terms of respiratory outcomes, including respiratory distress syndrome, bronchopulmonary dysplasia, need for invasive mechanical ventilation, and treatment failure. HFNC was associated with reduced nasal trauma and, in some studies, faster achievement of full enteral feeding. Trends toward shorter non-invasive ventilation duration and hospital stay were observed, but were not consistently statistically significant.

Conclusion: HFNC is a safe and generally effective alternative to NCPAP for preterm infants with respiratory distress, particularly those over 28 weeks' gestation. HFNC offers advantages in comfort, ease of use, and reduced nasal injury, with similar respiratory outcomes and complication rates compared to NCPAP. Evidence is less clear for extremely low-birth-weight infants, highlighting the need for larger trials to guide optimal use.

Introduction

Bronchiolitis is the leading cause of respiratory distress in infants under 1 year old who are admitted to the hospital. Previous research indicated that bronchiolitis accounts for 17.1% of all urgent admissions to pediatric intensive care units and is a major cause of mortality and morbidity in preterm neonates, placing a significant strain on

Correspondence to: Yara Abo Sabaah
*College of Medicine, King Saud bin Abdulaziz University for Health Sciences, Ministry of National Guard Health Affairs, Riyadh, Saudi Arabia.
Email: yara.hamed071@gmail.com
Full list of author information is available at the end of the article.
Received: 01 February 2026 | **Accepted:** 09 February 2026

healthcare resources [1,2]. As well, about 15% to 20% of children who are affected need respiratory assistance and intensive care because they quickly develop breathing difficulties [3].

The latest recommendations for treating infants with bronchiolitis or other forms of respiratory distress in hospital settings highlight the critical role of oxygen therapy, respiratory assistance, and ensuring proper hydration in cases of hypoxia [4]. Managing patients, especially infants, experiencing respiratory distress, presents a significant challenge for pediatricians in primary care [5]. Timely and effective management is essential to prevent fatalities, minimize the risk of long-term disabilities, and reduce healthcare costs. Once respiratory distress has been identified, treatment should focus first on ensuring proper oxygenation, followed by diagnosing the root causes and any potential complications [1].

In preterm infants, the lungs are immature, and the system responsible for surfactant production is underdeveloped. Respiratory distress syndrome (RDS) mainly results from insufficient surfactant production, leading to difficulty in exchanging oxygen and carbon dioxide by alveoli [6]. Primarily, this difficulty could lead to alveolar collapse, impaired gas exchange, and respiratory failure. Surfactant is a complex mixture of phospholipids and proteins produced by type II alveolar cells. The resulting alveolar collapse due to insufficient surfactant production causes leakage of plasma proteins into alveoli, forming a hyaline membrane that reduces oxygen diffusion. This dysfunction overloads the lungs during breathing and results in progressive hypoxemia and respiratory acidosis in preterm infants [7].

Most premature infants born before 30 weeks of gestation possess underdeveloped lungs, and almost half of these infants continue to require surfactant treatment [8]. Improvements in preventing and managing RDS include the use of medications to avert premature births and promote lung development, the replacement of surfactants, and the adoption of innovative mechanical ventilation methods [9]. These advancements are expected to further reduce both death rates and complications linked to this condition [6].

High-flow nasal cannula (HFNC) and nasal continuous positive airway pressure (NCPAP) are the most frequently utilized forms of non-invasive respiratory assistance for premature infants and newborns, for children suffering from bronchiolitis and other underlying causes [10]. Previous research has investigated the effectiveness of HFNC therapy, while other studies have examined the use of continuous positive airway pressure (CPAP), which is noted for its capacity to enhance functional residual capacity and decrease the frequency of apneic episodes [11-13].

HFNC oxygen therapy delivers warm, humidified oxygen at a flow rate exceeding typical inspiratory flow rates. Research indicates that it may be effective in enhancing oxygen levels and reducing the need for mechanical ventilation in pediatric patients experiencing respiratory distress [14-16]. NCPAP represents a treatment option that can be challenging in resource-limited environments, often necessitating technical expertise and proper upkeep [17,18].

Methodology

This systematic review was performed following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. A detailed review protocol was developed before searching and is available upon request. To identify relevant studies, a comprehensive literature search was performed across multiple electronic databases within the last 10 years (2015 to 2025), including PubMed, Web of Science, and Scopus. The search utilized the following keywords: ((“Respiratory Distress Syndrome” OR RDS OR “Hyaline Membrane Disease” OR “neonatal respiratory failure” OR “neonatal respiratory distress”) AND (infant* OR newborn* OR neonat* OR preterm OR prematur*)) AND ((“Continuous Positive Airway Pressure” OR CPAP OR “nasal cpap” OR nCPAP OR “nasal continuous positive airway pressure”) AND (“High-Flow Nasal Cannula” OR HFNC OR “high flow oxygen” OR “high flow therapy” OR “nasal high flow” OR NHF)).

Eligibility criteria

Inclusion criteria

Studies were included if they met the following inclusion criteria:

1. Assessed the use of HFNC and CPAP as a respiratory support in infants diagnosed with RDS.
2. Included the pediatric population, the preterm infants age group.
3. Reported clinical outcomes: safety and efficacy outcomes.
4. Employed RCTs in English-language publications between 2015 and 2025.

Exclusion criteria

Studies were excluded if they:

1. Included infants with other respiratory diseases.
2. Included different age groups (adults or older pediatric populations).
3. Were reviews, meta-analyses, commentaries, letters, or had insufficient reported data.

Selection of articles and data extraction

After the initial database search, two reviewers independently screened the titles and abstracts to identify relevant studies based on predefined inclusion criteria. Full texts of selected articles were assessed for eligibility by the same reviewers, with disagreements resolved through discussion or consultation with a third reviewer. Data were extracted using a standardized form, including study characteristics (author, year, design, country), patient demographics (total sample size, mean age and range, gender distribution, gestational age, birthweight,

apgar score, and antenatal steroids), intervention details (NCPAP vs. HFNC and their adjustments), safety, and efficacy outcomes.

Quality assessment

The Cochrane risk-of-bias tool for randomized trials (RoB2) [19] was used to assess the risk of bias (RoB) in the studies. It evaluates the potential for bias in randomized controlled trials (RCTs) by examining five critical areas: randomization, deviations from planned interventions, handling of missing data, outcome measurement, and the selection of reported outcomes. Each area is classified as having low, some, or high RoB, and the overall bias risk for each study is established based on these evaluations.

Results

PRISMA diagram

The literature search identified a total of 565 records across the selected databases. After removal of 229 duplicate records, 336 unique records were screened based on titles and abstracts, resulting in the exclusion of 302 records that did not meet the predefined eligibility criteria. The remaining 34 articles underwent full-text assessment for eligibility. Of these, 22 studies were excluded for the following reasons: inaccessible full text (n = 5), incompatible study design (n = 5), population-related issues (n = 4), irrelevant outcomes (n = 5), and language restrictions (n = 3). Ultimately, 12 studies fulfilled all inclusion criteria and were included in the final qualitative synthesis (Figure 1).

Table 1 describes the included studies on the use of NCPAP versus HFNC in infants with RDS, highlighting several key features. The evidence base primarily consists of RCT studies. This table presents baseline characteristics, including study design, country, sample size, gender distribution, neonatal clinical parameters, and maternal factors. By organizing these details, the table shows both controlled efficacy data and real-world clinical outcomes, allowing comparison across studies and ensuring transparency in study populations and methodologies.

Table 2 summarizes the intervention protocols used in the included studies, including FiO_2 ranges, oxygen saturation targets, flow/pressure settings, and interface types for both CPAP and HFNC.

Table 3 compiles the primary and secondary outcomes reported in the studies, covering treatment success/failure, mortality, comorbidities, adverse events, and the need for escalation of care.

We considered the RoB when interpreting findings, as shown in Table 4.

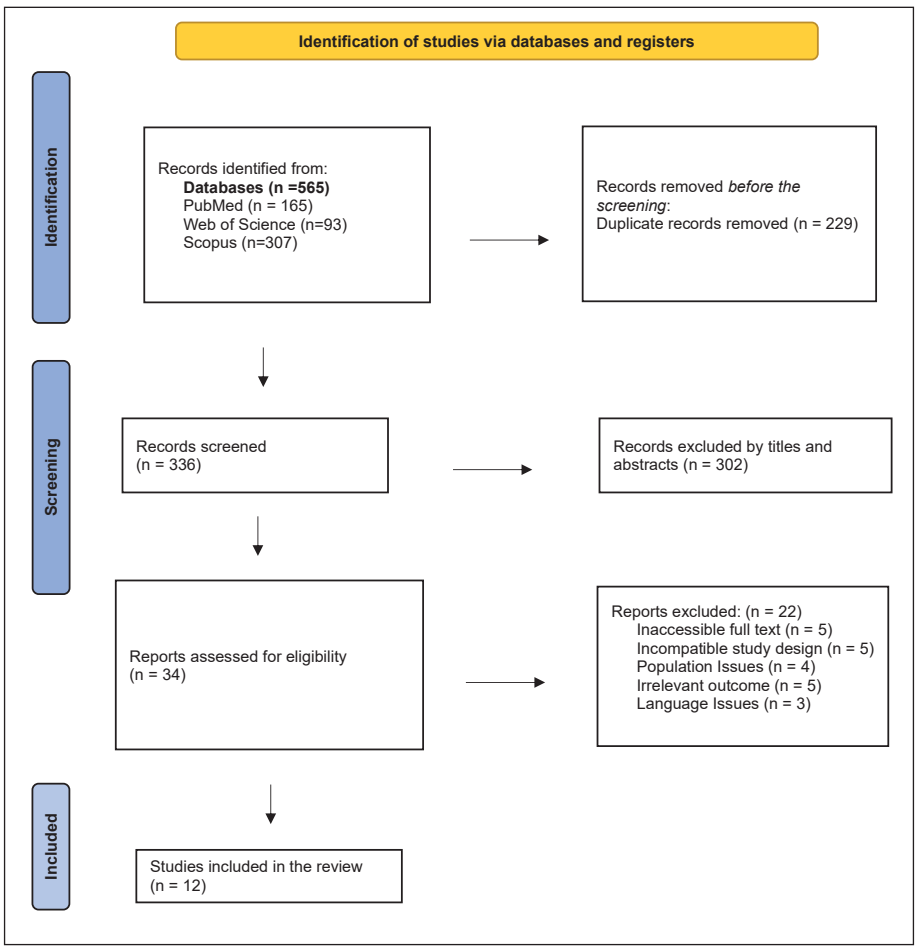

Figure 1. *Schematic representation of the criteria for choosing included studies.*

Table 1. *Characteristics of studies included in the review (NCPAP vs. HFNC in infants with RDS).*

Author, Year	Study Design, Country	Total Sample Size	Gender Distribution (M/F)	Gestational Age (mean ± SD)	SGA (mean ± SD)	LGA (mean ± SD)	Birthweight (mean ± SD)	Apgar score, median (IQR)	Antenatal Steroid Use (mean ± SD)
Grover et al., 2022 [20]	Non-inferiority RCT in India	124 63 in NCPAP 61 in HFNC	NCPAP: 27 (42.9) F HFNC: 32 (52.5) F	NCPAP: 33.0 (2.27) HFNC: 33.3 (2.13)	NCPAP: 22 (34.9) HFNC: 23 (37.7)	NCPAP: 3 (4.8) HFNC:1 (1.6)	NCPAP: 1778 (575) HFNC: 1844 (539)	At 1 min.: NCPAP: 7 (6-8) HFNC: 8 (7-8) At 5 min.: NCPAP: 9 (8-9) HFNC: 9 (8-9)	NCPAP (n/%): 32 (96.9) (N=33) HFNC (n/%): 30 (100) (N=30)
Singh et al., 2022 [21]	Non-inferiority RCT in India	30 15 in NCPAP 15 in HFNC	NCPAP: 6 M HFNC: 9 M	NCPAP: 30 weeks (1.8) HFNC: 31 weeks (2.1)	NR	NR	NCPAP: 1440.7 (293.8) HFNC: 1478.4 (289.6)	NR	NCPAP: 13 HFNC: 12
Demirel et al., 2021 [22]	Prospective randomized study in Turkey	107 54 in CPAP 53 in HFNC	CPAP: 25 (46.2) F HFNC: 23 (43.3) F	Median (IQR): CPAP: 31.0 (1.8) HFNC: 31.2 (2.3)	NR	NR	Median (IQR): CPAP: 1505 (580) HFNC: 1570 (455)	NR	CPAP: 40 (74) HFNC: 38 (71.6)
Chen et al., 2020 [23]	RCT in China	94 46 in the CPAP group 48 in HFNC group	CPAP: 29/17 HFNC group: 30/18	CPAP: 27.5 ± 3.2 HFNC group: 27.2 ± 2.8	CPAP: 8 (17.39) HFNC group: 9 (18.75)	NR	CPAP: 794 ± 31.0 HFNC group: 827 ± 23.0	At 1 min: CPAP: 5.4 ± 0.4 HFNC group: 5.2 ± 0.6	CPAP: 36 (78.26) HFNC group: 38 (79.17)
Charki et al., 2020 [24]	A Noninferiority trial in India	106 52 in NCPAP 54 in HFNC	NCPAP: 36/16 HFNC: 39/15	28-34WKS: NCPAP: 30 HFNC: 20 34-37WKS: NCPAP: 18 HFNC: 30 NVD: NCPAP: 33 HFNC: 31	NR	NR	1-1.5: NCPAP: 10 HFNC: 9 1.5-2.5: NCPAP: 34 HFNC: 40 >2.5: NCPAP: 5 HFNC: 3	NR	NCPAP: 3 HFNC: 4
Akbarian-rad et al., 2020 [25]	RCT in Iran	64 32 in NCPAP 32 in HFNC	NCPAP: 15/19 HFNC: 13/17	NCPAP: 1.83 ± 30.98 HFNC: 2.00 ± 30.45	NR	NR	NCPAP: 334.71 ± 1348.97 HFNC: 493.26 ± 1416.00	NR	NCPAP:19 (55.9) HFNC:23 (76.7)
Armanian et al., 2019 [26]	RCT in Iran	72 37 in NCPAP 35 in HFNC	NR	NR	NR	NR	NR	NR	NR
Skariah et al., 2019 [27]	A prospective study in India	84 Two groups: 27-32 weeks: 22 in NCPAP, 15 in HFNC 33-36 weeks: 21 in NCPAP, 26 in HFNC	27-32 weeks: NCPAP: 9/13 HFNC: 9/6 33-36 weeks: NCPAP: 12/9 HFNC: 17/9	27-32 weeks: NCPAP: 30.7±1.31 HFNC: 30.8±1.45 33-36 weeks: NCPAP: 33.72±1.7 HFNC: 34.7±1.00	NR	NR	27-32 weeks: NCPAP: 1342±318.14 HFNC: 1413±311.41 33-36 weeks: NCPAP: 1898±463.37 HFNC: 2396±512.08	NR	27-32 weeks: NCPAP: 21/22(30.2) HFNC: 9/15 (45.5) 33-36 weeks: NCPAP: 6/11 (54.5) HFNC: 11/26 (63.6)
Murki et al., 2018 [28]	RCT in India	272 139 in NCPAP 133 in HFNC	NCPAP: 77 (55) M HFNC group: 73 (55) M	NCPAP: 31.6±2.2 HFNC: 31.8±1.9	NR	NR	NCPAP: 1,642±437 HFNC: 1,632±431	At 1 min.: NCPAP: 7 (6-7) HFNC:7 (6-7) At 5 min.: NCPAP: 8 (7-8) HFNC: 8 (7-8)	Complete: NCPAP: 78 (56) HFNC: 83 (62) Partial: NCPAP: 40 (29) HFNC: 34 (26)

Continued

Author, Year	Study Design, Country	Total Sample Size	Gender Distribution (M/F)	Gestational Age (mean ± SD)	SGA (mean ± SD)	LGA (mean ± SD)	Birthweight (mean ± SD)	Apgar score, median (IQR)	Antenatal Steroid Use (mean ± SD)
Farhat et al., 2018 [29]	RCT in Iran	160 53 in NCPAP 53 in NIPPV 54 in HFNC	NCPAP: 64.2% M HFNC: 61.1% M	NCPAP: 31.1 (2) HFNC: 31.3 (1.9)	NR	NR	NCPAP: 1650 (486) HFNC: 1624 (425)	At 1 min.: NCPAP: 6.4 HFNC: 6.9 At 5 min.: NCPAP: 7.7 HFNC: 8	NCPAP: 83% HFNC: 88.9%
Shin et al., 2017 [30]	RCT non-inferiority study in Korea	85 43 in NCPAP 42 in HFNC	NCPAP: 24 (55.8) males HFNC: 23 (54.8) M	NCPAP: 33.0 ± 1.2 HFNC: 32.5 ± 1.5	NR	NR	NCPAP: 1,996 ± 374 HFNC: 2,058 ± 371	At 1 min.: NCPAP: 7 (5-8) HFNC:7 (6-8) At 5 min.: NCPAP: 9 (8-9) HFNC: 9 (8-9)	NCPAP: 23 (53.5) HFNC: 27 (64.3)
Glackin et al., 2017 [31]	Single-center RCT in Ireland	44 22 in CPAP 22 in HFNC	NR	NCPAP: 27.3±1.5 HFNC: 26.9±1.5	NR	NR	NCPAP: 891±202 HFNC: 868±160	At 1 min.: NCPAP: 5 (4-6) HFNC: 6 (5-7) At 5 min.: NCPAP: 8 (6-8) HFNC: 8 (7-8)	NCPAP: 86 HFNC: 77

CPAP, Continuous Positive Airway Pressure; F, Female; GA, Gestational Age; HFNC, High-Flow Nasal Cannula; IQR, Interquartile Range; LGA, Large for Gestational Age; M, Male; NCPAP, Nasal Continuous Positive Airway Pressure; NIPPV, Nasal Intermittent Positive Pressure Ventilation; NR, Not Reported; RCT, Randomized Controlled Trial; SD, Standard Deviation; SGA, Small for Gestational Age; WKS, Weeks.

The RoB across the 12 included studies was generally "low" to "some concerns" (Figure 2). Singh et al. [21] display low RoB across all key domains, indicating a rigorous design and conduct with proper randomization, adherence to interventions, complete outcome data, reliable measurements, and transparent reporting. Most studies demonstrated a low RoB in outcome measurement and reporting (Domains 4 and 5). However, concerns were noted in randomization procedures and deviations from intended interventions (Domains 1 and 2) in several studies. In particular, three studies [22, 28] were judged to have a high overall RoB, mainly due to issues with randomization or missing outcome data. These limitations should be considered when interpreting the pooled evidence.

Discussion

This systematic review of 12 studies involving preterm infants with respiratory distress indicates that HFNC is a safe and effective alternative to NCPAP. In infants over 28 weeks' gestation, HFNC demonstrated comparable efficacy to NCPAP regarding key respiratory outcomes, including RDS, BPD, duration of non-invasive ventilation, and need for invasive mechanical ventilation. Additional advantages, such as ease of use, patient comfort, and suitability for the delivery room, make HFNC a viable first-line or alternative non-invasive ventilation strategy when NCPAP is unavailable. Some studies further suggested potential benefits in shorter hospital stays and reduced non-invasive ventilation duration, though these results were not always statistically significant.

Consistent with our review, the included study observed no statistically significant differences between HFNC and NCPAP in demographic characteristics, respiratory outcomes, or complications such as NEC, BPD, pneumothorax, and mortality. Although the HFNC group showed trends toward shorter hospitalization, reduced intubation, and decreased need for full nutritional and oxygen support, these differences were not statistically significant, supporting the general conclusion that HFNC is a safe and effective alternative to NCPAP [19].

Similar to the studies included in this review, a trial involving 120 preterm neonates (51 males, 69 females) found no statistically significant differences between HFNC and NCPAP in major clinical outcomes, including NEC, IVH, pneumothorax, chronic lung disease, treatment failure, and mortality. Additionally, GA, birth weight, Apgar scores, RDS severity, and duration of oxygen therapy and hospitalization were comparable between groups. Notably, the HFNC group experienced a lower incidence of nasal trauma, although they required more surfactant therapy and had a longer duration of intervention. These findings are consistent with the overall evidence that HFNC is a safe and generally effective alternative to NCPAP, with some advantages in patient comfort and airway safety [20].

In line with several studies reviewed, a comparison of nCPAP and HFNC demonstrated no significant differences in major neonatal outcomes, including mortality, intubation rates, or discharge without ventilation. Interestingly, the HFNC group had shorter

Table 2. *Intervention parameters: nasal CPAP and HFNC.*

Author, Year	HFNC FiO_2	HFNC SpO_2	HFNC Pressure and/or Flow	CPAP interface	CPAP Pressure and/ or Flow	CPAP FiO_2	CPAP SpO_2	CPAP Interface
Grover et al., 2022 [18]	21 (21-25)	90%-94%	4 L/min up to 8 L/ min	NR	5 cm of water up to 8 cm	21 (21-25)	90%-94%	Binasal prongs
Singh et al., 2022 [19]	60%	91%-95%	2 L/min up to 8 L/ min	NR	5 cm of water up to 7 cm	60%	91%-95%	Nasal prongs
Demirel et al., 2021 [20]	Respiratory outcome of neonates ≤28 gestational weeks: 40 (45) Neonates >28 gestational weeks: 30 [20]	90%-95%	6 L/min up to 8 L/ min	NR	6 cm of H2O	Respiratory outcome of neonates ≤28 gestational weeks: 40 (7.5) Neonates >28 gestational weeks: 40 (12.5)	90%-95%	Binasal prongs
Chen et al., 2020 [23]	30-40%	NR	4-6 L/min	NR	Flow 6-8 L/min	40%	NR	NR
Charki et al., 2020 [24]	21-40%	NR	Weight-based (2 L/kg)	Nasal prongs	Flow 5-8 L/min	21-40%	NR	Binasal midline prongs
Akbarian-rad et al., 2020 [25]	Up to 40%	NR	3-5 l/min	Short binasal prongs	5 cm of H_2O	30%	NR	Face mask
Armanian et al., 2019 [26]	>30%	<91%	Flow: <1000 g → 2.5 L/min; 1000-1500 g → 3 L/min; Temp: 37°C	Nasal cannula, 2 mm external diameter + oxygen interface tubes, joints, warm humidifier	5-6 cm of H_2O; Flow 8-10 L/min	>30%	<91%	Nasal prongs + joints
Skariah et al., 2019 [27]	Adjusted as needed (no fixed value), titrated according to center protocol	Target range not specified; adjusted per center protocol	Flow 8 L/min (initial)	Nasal cannula	5 cm of H_2O	Adjusted as needed (no fixed value), titrated according to center protocol	Target range not specified; adjusted per center protocol	Nasal mask
Murki et al., 2018 [28]	50 (30-50)	Target 90-95%	Flow 5 L/min	Nasal prongs	5 cm of H_2O	40 (30-50)	Target 90-95%	Short binasal prongs
Farhat et al., 2018 [29]	Not specified, likely adjusted per oxygen need	Not specified	≥2 L/min (weight-based); increased as needed up to 5 L/min	Humidified high-flow nasal cannula	Initial 6 cm H_2O; could be increased up to 8 cm H_2O	Not specified, likely adjusted per oxygen need	Not specified	Nasal prongs/mask with CPAP system
Shin et al., 2017 [30]	Started at 0.40; adjusted; weaning to 0.25 then 0.21.	Target 88-94%	Initial 5 L/min; adjusted 3-7 L/min; weaning at 3 L/min.	Short binasal prongs	4-7 cm of H_2O based on respiratory condition (guided by blood gas results)	Started at 0.40; adjusted; weaning to 0.25 then 0.21	Target 88-94%	Short binasal prongs

Cm H_2O, Centimeters of Water (unit of pressure); CPAP, Continuous Positive Airway Pressure; FiO_2, Fraction of Inspired Oxygen; g, Gram; HFNC, High-Flow Nasal Cannula; H_2O, Water (used in pressure measurement; cm H_2O); L/min, Liters per Minute (flow rate); NR, Not Reported; SpO_2, Peripheral Oxygen Saturation; Temp, Temperature.

durations of non-invasive ventilator support and hospital stay, suggesting potential efficiency benefits. However, HFNC was associated with more nasal mucosal injury, whereas sepsis was more common in the nCPAP group. Treatment failure was also slightly higher in the HFNC group, indicating that while HFNC is generally safe and effective, clinicians should monitor for specific adverse effects and individualize respiratory support strategies [21,22].

Several of the included studies specifically evaluated the comparative effectiveness of HFNC and NCPAP in preterm infants with respiratory distress, including high-risk neonates and those in the delivery room. A study assessing preterm neonates with gestational ages of 28–36 weeks demonstrated that HFNC provided comparable efficacy and safety to NCPAP for delivery room respiratory support, although the authors noted that noninferiority could not be conclusively established [23]. Similarly, a study focusing on neonates of 32 weeks' gestation reported no significant differences between HFNC and NCPAP in terms of primary respiratory support, time to weaning from the devices, or oxygen requirements during the first hour of life [24,25]. Collectively, these findings reinforce the broader evidence from this review, suggesting that HFNC is generally as safe and effective as NCPAP for moderately preterm infants, while also offering practical advantages such as ease of use and patient comfort.

One trial in infants >28 weeks and >1 kg with RDS found no difference in treatment failure within 7 days post-INSURE, but reported a lower incidence of nasal injury with HFNC, suggesting non-inferiority to NCPAP [26]. Another study in extremely low-birth-weight infants (ELBWI) demonstrated that HFNC was effective in preventing extubation failure, while also reducing oxygen use, nasal trauma, necrotizing enterocolitis, hospital stay, and associated costs [27]. Similarly, a trial evaluating postextubation respiratory support showed comparable primary and secondary outcomes between HFNC and NCPAP, with HFNC again deemed a safe and acceptable alternative. Collectively, these findings support the potential role of HFNC as a non-inferior and better-tolerated modality compared to NCPAP in preterm neonates requiring non-invasive respiratory support [28,29].

One study reported that HFNC was as effective as NCPAP in managing neonates with RDS following surfactant administration, indicating its potential as an alternative support modality [30]. In contrast, another investigation found higher treatment failure rates with HFNC compared to NCPAP and nasal intermittent mandatory ventilation (NIMV), cautioning against its use as first-line therapy [31]. A further study demonstrated that early application of HFNC yielded comparable outcomes to NCPAP as a primary non-invasive respiratory support, although it did not prove superior. Collectively, these findings suggest that while HFNC may be a feasible alternative in selected contexts, its effectiveness relative to established modalities such as NCPAP and NIMV remains inconclusive [32].

Table 3. *Reported Efficacy and Safety Outcomes.*

Author, Year	Treatment failure within 24 h of randomization, n (%)	Failure of assigned means of respiratory support (N)	Causes of treatment failure at 24 h, number (%)	Treatment failure at 72 h, n (%)	Comorbidities Outcomes	Need for mechanical ventilation within 72 h, n (%)	Surfactant Administration (n/%)	Caffeine Therapy (n/%)	Conclusion
Grover et al., 2022 [18]	NCPAP: 7 (11.1) HFNC: 8 (13.1)	NR	Apnea: NCPAP: 2 (28.6) HFNC: 1 (12.5) FiO2 requirement ≥0.4: NCPAP: 3 (42.9) HFNC: 6 (75) ABG criteria: NCPAP: 1 (14.3) HFNC: 1 (12.5)	NCPAP: 11 (17.5) HFNC: 10 (16.4)	NR	NCPAP: 11 (17.5) HFNC: 7 (11.5)	HFNC: 71 (56.8)	NCPAP: 25 (39.7)	The High-Flow Humidified Nasal Cannula (HFNC) is an effective and safe option for respiratory stabilization in preterm infants over 28 weeks' gestation, although its non-inferiority to NCPAP remains unclear. It offers ease of use and comfort, making it suitable for use in the delivery room. Larger multicentric studies involving extremely preterm neonates are needed to confirm these findings.

Continued

Author, Year	Treatment failure within 24 h of randomization, n (%)	Failure of assigned means of respiratory support (N)	Causes of treatment failure at 24 h, number (%)	Treatment failure at 72 h, n (%)	Comorbidities Outcomes	Need for mechanical ventilation within 72 h, n (%)	Surfactant Administration (n/%)	Caffeine Therapy (n/%)	Conclusion
Singh et al., 2022 [19]	NR	NR	NR	NR	IVH NCPAP: 4 HFNC: 3 BPD: NCPAP: 4 ROP: NCPAP: 3 HFNC: 1 Sepsis: NCPAP: 6 HFNC: 5 Hs-PDA: NCPAP: 12 HFNC: 12	NR	NCPAP: 5 (7.9)	HFNC: 18 (29.5)	In summary, HFNC seems to be at least as effective as NCPAP for preterm infants over 28 weeks of gestation with RDS when used as a ventilatory option following INSURE.
Demirel et al., 2021 [20]	NR	NR	NR	NR	Non-respiratory outcomes: Patent ductus Arteriosus: NCPAP: 6 (11.1%) HFNC: 5 (9.4%) Sepsis: NCPAP: 7 (12.9%) HFNC: 6 (11.3%) Intraventricular Hemorrhage: NCPAP: 1 (1.8%) HFNC: 2 (3.7%) Necrotizing Enterocolitis: NCPAP: 1 (1.8%) HFNC: 1 (1.8%) Retinopathy of Prematurity: NCPAP: 1 (1.8%) HFNC group: 2 (3.7%) Respiratory Outcomes: Respiratory outcome of neonates ≤28 gestational weeks: Bronchopulmonary Dysplasia: NCPAP: 6 (75%) HFNC: 2 (28.5%) Respiratory outcome of neonates >28 gestational weeks: Pneumothorax: NCPAP: 1 (2.1%) HFNC: 2 (4.3%) Bronchopulmonary Dysplasia: HFNC: 2 (4.3%)	NR	HFNC: 4 (6.6)	NCPAP: 15	HFNC and nCPAP show no significant differences as primary respiratory support for preterm infants regarding weaning time, incidence of respiratory distress syndrome and bronchopulmonary dysplasia, hospital stay duration, and complications from prematurity.

Continued

Author, Year	Treatment failure within 24 h of randomization, n (%)	Failure of assigned means of respiratory support (N)	Causes of treatment failure at 24 h, number (%)	Treatment failure at 72 h, n (%)	Comorbidities Outcomes	Need for mechanical ventilation within 72 h, n (%)	Surfactant Administration (n/%)	Caffeine Therapy (n/%)	Conclusion
Chen et al., 2020 [23]	NR	NR	NR	NR	Intracerebral hemorrhage: NCPAP: 7 (15.21) HFNC: 7 (14.58) Retinopathy of prematurity: NCPAP: 18 (39.13) HFNC: 17 (35.42) Patent ductus arteriosus: NCPAP: 16 (34.78) HFNC: 16 (33.33) Bronchopulmonary dysplasia: NCPAP: 15 (32.61) HFNC: 16 (33.33) Necrotizing enterocolitis: NCPAP: 13 (28.26) HFNC: 5 (10.42) Nasal injury: NCPAP: 17 (36.96) HFNC: 3 (6.25)	NR	NR	HFNC: 14	HFNC is more effective than NCPAP in preventing extubation failure in preterm ELBWI. It reduces oxygen use time, lowers the risk of nasal injury and necrotizing enterocolitis, and decreases both length of stay and hospitalization costs.
Charki et al., 2020 [24]	NR	NCPAP: 3 HFNC: 5	NR	NR	Retinopathy of Prematurity: NCPAP: 2 (3.8%) HFNC: 2 (3.7%) Intraventricular Hemorrhage: NCPAP: 2(3.8%) HFNC: 2 (3.7%) Nosocomial Infection: NCPAP group: 8 (15.4%) HFNC: 8 (14.8%) Necrotizing Enterocolitis: NCPAP: 13 (25%) HFNC: 1 (1.9%) Nasal Trauma: NCPAP: 30 (57.7%) HFNC: 1 (1.9%)	NR	NCPAP: 2 HFNC: 1	NR	Infants on High-Flow Humidified Nasal Cannula (HFNC) had fewer nasal injuries and necrotizing enterocolitis (NEC) and reached full feeding faster than those on NCPAP. HFNC was found to be noninferior to NCPAP, making it a safe and effective choice for respiratory support in preterm infants.
Akbarian-rad et al., 2020 [25]	NR	NCPAP: 4 (11.8%) HFNC: 5 (16.7%)	NR	NR	Pneumothorax: NCPAP: 2 HFNC: 2 IVH: NCPAP: 2 HFNC: 3	NR	NR	NR	The use of HFNC in preterm infants experiencing respiratory distress might be comparably effective to NCPAP for treating neonates with respiratory distress syndrome (RDS) following surfactant treatment. If NCPAP is unavailable, HFNC presents a suitable alternative with a similar failure rate and effective respiratory care.

Continued

Author, Year	Treatment failure within 24 h of randomization, n (%)	Failure of assigned means of respiratory support (N)	Causes of treatment failure at 24 h, number (%)	Treatment failure at 72 h, n (%)	Comorbidities Outcomes	Need for mechanical ventilation within 72 h, n (%)	Surfactant Administration (n/%)	Caffeine Therapy (n/%)	Conclusion
Armanian et al., 2019 [26]	NR	NCPAP: 13 (35.1) HFNC: 19 (54.3)	Hypoxia (need to FiO2 ≥40%): NCPAP: 5 (38.4) HFNC: 14 (73.6) Respiratory acidosis: NCPAP: 2 (15.4) HFNC: 1 (5.3) Urgent need for intubation : HFNC: 1 (5.3) Severe apnea: NCPAP: 3 (23.1) Frequent apnea: NCPAP: 3 (23.1) HFNC: 3 (15.8)	NR	IVH: NCPAP: 5 (13.5) HFNC: 1 (2.9) PDA: NCPAP: 8 (21.6) HFNC: 10 (28.6) Pneumothorax: NCPAP: 5 (13.5) HFNC: 2 (5.7)	NR	NCPAP: 26 (70.3) HFNC: 22 (62.9)	NR	Using High-High-Flow Nasal Cannula (HFNC) as the initial treatment for very low birth weight (VLBW) preterm infants with respiratory distress syndrome (RDS) is associated with higher failure rates than Nasal Continuous Positive Airway Pressure (NCPAP). While some secondary outcomes may improve with HFNC, it should not be considered the primary treatment.
Skariah et al., 2019 [27]	NR	27-32 weeks: NCPAP: 5/22(22.7) HFNC: 4/15 (26.7) 33-36 weeks: NCPAP: 2/21(9.5) HFNC: 2/26(7.7)	NR	Necrotizing enterocolitis: 27-32 weeks: NCPAP: Nil HFNC: 1/15(2.7) 33-36 weeks: HFNC: 1/26(2.7) Intraventricular hemorrhage: 27-32 weeks: NCPAP: 1/22 (2.8) HFNC: 3/15 (8.3) 33-36 weeks: NCPAP group: 0 HFNC group: 1/26(2.1) Retinopathy of prematurity: 27-32 weeks: NCPAP group: 3/22 (8.3) HFNC group: 2/15 (5.4) 33-36 weeks: NCPAP group: 0 HFNC group: 1/26 (2.1)	NR	NR	INSURE techniques: 27-32 weeks: NCPAP: 9/22 (24.3) HFNC: 4/15 (10.8) 33-36 weeks: HFNC: 1/25 (2.1)	NR	HFNC does not lower the need for invasive mechanical ventilation compared to NCPAP in the first 72 hours. However, it shows similar clinical efficacy and safety as a primary non-invasive ventilation method, with a shorter overall duration of NIV support in the HFNC group. More large randomized trials are needed to confirm its use and establish a protocol for all gestational ages.

Continued

Author, Year	Treatment failure within 24 h of randomization, n (%)	Failure of assigned means of respiratory support (N)	Causes of treatment failure at 24 h, number (%)	Treatment failure at 72 h, n (%)	Comorbidities Outcomes	Need for mechanical ventilation within 72 h, n (%)	Surfactant Administration (n/%)	Caffeine Therapy (n/%)	Conclusion
Murki et al., 2018 [28]	NR	NR	Increased oxygen need: NCPAP: 3/11 [27] HFNC: 16/35 (46) Increased respiratory distress: NCPAP: 4/11 (36) HFNC: 14/35 (40) Apnea: NCPAP: 3/11 (27.3) HFNC: 3/35 (8.6) Shock or other reasons: NCPAP: 1/11 (9.1) HFNC: 2/35 (5.6)	NCPAP: 11 (7.9) HFNC: 35 (26.3) Subgroup with SAS >5: NCPAP: 6/64 (9.4) HFNC: 21/54 (38.9) Subgroup with SAS ≤5: NCPAP: 5/75 (6.7) HFNC: 14/79 (17.7) Subgroup of infants with gestation <32 weeks: NCPAP: 7/68 (10.3) HFNC: 22/58 (37.9) Subgroup of infants with gestation ≥32 weeks NCPAP: 6/71 (8.5) HFNC: 15/75 (20.0)	Pneumothorax: NCPAP: 1 (0.7) HS-PDA: NCPAP: 13 (9.4) HFNC: 8 (6.0) Culture-positive sepsis: NCPAP: 13 (9.4) HFNC: 13 (9.8) NEC Bell's stage II or more: HFNC: 2 (1.5) Nasal injury: NCPAP: 13 (9.4) HFNC: 7 (5.3) Oxygen supplementation at 36 weeks: HFNC: 1 (0.7) IVH grade III or IV: NCPAP: 1 (0.7) Cystic periventricular leukomalacia: NCPAP: 1 (0.7) Retinopathy of Prematurity: NCPAP: 7 (5.0) HFNC: 6 (4.5)	Ventilation within 3 days: NCPAP: 11 (7.9) HFNC: 8 (6.0) Ventilation within 7 days: NCPAP: 13 (9.4) HFNC: 9 (6.8) Subgroup with SAS >5: Ventilation within 3 days: NCPAP: 6/64 (9.4) HFNC: 4/54 (7.4) Ventilation within 7 days: NCPAP: 7/64 (10.9) HFNC: 4/54 (7.4) Subgroup with SAS ≤5: Ventilation within 3 days: NCPAP group: 5/75 (6.7) HFNC: 4/79 (5.1) Ventilation within 7 days: NCPAP: 6/75 (8.0) HFNC: 5/79 (6.3)	Dose 1: NCPAP: 68 (48.9) HFNC: 58 (43.6) Dose 2: NCPAP: 24 (17.3) HFNC: 18 (13.5)	NR	In preterm infants with respiratory distress, high-flow nasal cannula (HFNC) is less effective than nasal continuous positive airway pressure (nCPAP) at preventing the need for higher respiratory support within the first 72 hours of life.
Farhat et al., 2018 [29]	NR	NR	NR	NR	Comorbidities during nasal ventilation: IVH: NCPAP: 17% HFNC: 16.7% Apnea: NCPAP: 17% HFNC: 18.5% Hypercapnia: NCPAP: 11.3% HFNC: 13% Sepsis: NCPAP: 11.3% HFNC: 5.6% Air leak: NCPAP: 9.4% HFNC: 13% Pneumonia: NCPAP: 5.7% HFNC: 5.6% Collapse: NCPAP: 6.7% HFNC: 7.4% GI complications: NCPAP: 7.5% HFNC: 5.6%	NR	NCPAP: 49.1% HFNC: 48.1%	NR	The study indicates that HFNC is a safe method for preterm infants with respiratory distress at birth, despite differing research methods from previous studies.

Continued

Author, Year	Treatment failure within 24 h of randomization, n (%)	Failure of assigned means of respiratory support (N)	Causes of treatment failure at 24 h, number (%)	Treatment failure at 72 h, n (%)	Comorbidities Outcomes	Need for mechanical ventilation within 72 h, n (%)	Surfactant Administration (n/%)	Caffeine Therapy (n/%)	Conclusion
					Pulmonary hemorrhage: NCPAP: 3.8% HFNC: 7.4% Nasal damage: NCPAP: 24.5% HFNC: 9.2% PDA: NCPAP: 9.4% HFNC: 7.4% Important complications of neonates with very low birth weight: Bronchopulmonary dysplasia: NCPAP: 3.8%				
Shin et al., 2017 [30]	NR	NCPAP: 9 (20.9 HFNC: 16 (38.1)	Hypoxia: NCPAP: 6 (14.0) HFNC: 15 (35.7) Respiratory acidosis: NCPAP: 4 (9.3) HFNC: 2 (4.8)	NR	Bronchopulmonary dysplasia: HFNC: 1 (2.4) Air leak HFNC: 2 (4.8)	NR	RDS treated with surfactant: NCPAP: 7 (16.3) HFNC: 12 (28.6)	Apnea treated with caffeine: NCPAP: 9 (20.9) HFNC: 11 (26.2)	There were no significant differences in respiratory and clinical outcomes or complications between the two groups. While high-flow nasal cannula (HFNC) is safe compared to nasal continuous positive airway pressure (nCPAP), its effectiveness as initial support for preterm infants with respiratory distress remains uncertain.
Glackin et al., 2017 [31]	NR	NR	NR	NR	Chronic lung disease (at 36/40): NCPAP: 68 HFNC: 64 Episodes of apnoea (episodes/day on respiratory support): NCPAP: 0.014 (0-0.151)	NR	NR	NR	Preterm infants receiving HFNC did not reach complete oral feeding at a faster rate than those treated with NCPAP.

ABG, Arterial Blood Gas, BPD, Bronchopulmonary Dysplasia; ELBWI, Extremely Low Birth Weight Infant; FiO_2, Fraction of Inspired Oxygen; GI, Gastrointestinal; HFNC, High-Flow Nasal Cannula; Hs-PDA / HS-PDA, Hemodynamically Significant Patent Ductus Arteriosus; IVH, Intraventricular Hemorrhage; NEC, Necrotizing Enterocolitis; NIV, Non-Invasive Ventilation; NR, Not Reported; NCPAP, Nasal Continuous Positive Airway Pressure; PDA, Patent Ductus Arteriosus; RDS, Respiratory Distress Syndrome; ROP, Retinopathy of Prematurity; SAS, Silverman–Anderson Score; VLBW, Very Low Birth Weight.

Table 4. *RoB: interpretation of the included studies.*

Study	D1	D2	D3	D4	D5	Overall
Grover et al., 2022 [20]	Low	Some concerns	Low	Low	Low	Some concerns
Singh et al., 2022 [21]	Low	Low	Low	Low	Low	Low
Demirel et al., 2021 [22]	Some concerns	High	Low	Some concerns	Low	High
Chen et al., 2020 [23]	Some concerns	Some concerns	Low	Some concerns	Low	Some concerns
Charki et al., 2020 [24]	Some concerns	Some concerns	Low	Some concerns	Low	Some concerns
Akbarian-rad et al., 2020 [25]	Low	Some concerns	Low	Some concerns	Low	Some concerns
Armanian et al., 2019 [26]	Low	Low	Some concerns	Low	Low	Some concerns
Skariah et al., 2019 [27]	High	Some concerns	Low	Low	High	High
Murki et al., 2018 [28]	Some concerns	Some concerns	Low	High	Low	High
Farhat et al., 2018 [29]	Some concerns	Low	Low	Low	Low	Some concerns
Shin et al., 2017 [30]	Low	Low	Some concerns	Some concerns	Low	Some concerns
Glackin et al., 2017 [31]	Low	Low	Low	Some concerns	Low	Some concerns

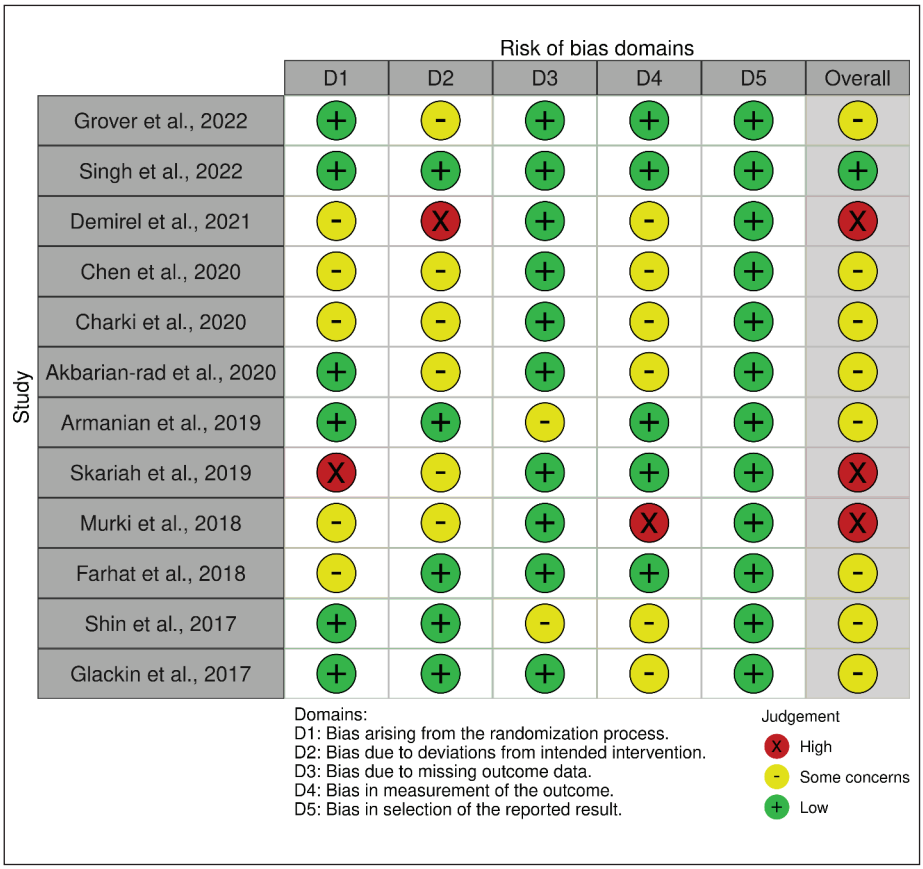

Figure 2*. ROB-2 quality assessment of twelve RCT studies.*

Another investigation, comparing HFNC, nCPAP, and NIMV, reported that while HFNC use at birth appeared safe, it was not more effective than the other two approaches in reducing intubation rates. Comparable findings were noted in another study that observed no significant differences between HFNC and NCPAP in terms of respiratory outcomes, complications, or clinical endpoints, though the non-inferiority of HFNC as an initial treatment could not be firmly established. Beyond respiratory endpoints, one study focused on feeding

outcomes in preterm infants with evolving chronic lung disease, noting that both HFNC and nCPAP offered comparable support in achieving full oral feeding [33].

However, the evidence for ELBW infants (<1,000 g) and very early preterm neonates is less consistent. Some studies reported higher failure rates, increased need for escalation to invasive support, or slightly better outcomes with NCPAP in this population [34]. These results align with prior research indicating that very fragile neonates may require more aggressive or closely monitored respiratory support. Clinicians should consider gestational age, respiratory effectiveness, and patient tolerance when choosing between HFNC and NCPAP. HFNC may be particularly useful for improving comfort, reducing nasal injury, and facilitating early feeding in preterm infants over 28 weeks' gestation. However, for ELBW infants or those at the highest risk of respiratory failure, NCPAP may still be preferred as the initial respiratory support.

Limitations

This systematic review has several limitations that should be acknowledged. Because the included studies varied widely in design, outcome definitions, and patient populations, meta-analysis was not feasible. We therefore conducted a structured narrative synthesis following PRISMA guidelines. The overall certainty of evidence across the included studies was low to moderate, primarily due to small sample sizes, methodological heterogeneity, and the absence of a formal GRADE assessment. Follow-up in most studies was brief, with long-term outcomes, such as neurodevelopmental status or chronic lung disease, rarely reported. Finally, the generalizability of the findings is limited. Most of the included studies were conducted in high-resource neonatal intensive care units using specific devices, which may not reflect outcomes in lower resource settings or with different equipment. These factors should be considered when interpreting the results of this review.

Conclusion

HFNC is a safe and effective alternative to NCPAP for preterm infants over 28 weeks' gestation, with similar respiratory outcomes and benefits like reduced nasal trauma and lower rates of NEC. HFNC offers ease of use and comfort, particularly in delivery rooms. However, results for ELBW infants and very early preterm neonates have been inconsistent, with some studies showing higher failure rates and increased need for invasive support. While most studies found no significant differences in major outcomes, careful patient selection and monitoring are essential. HFNC can be considered a viable first-line or alternative non-invasive ventilation option, but further multicenter randomized trials are needed to validate its effectiveness across all gestational ages and improve protocols for ELBW infants.

Conflict of Interest
The authors declare that there is no conflict of interest regarding the publication of this article.

Acknowledgment
Nil.

Funding
None

Ethical Approval
Not applicable.

Author details
Yara Hamed Abo Sabaah[1,2,3], Rasha Ahmed Almumlah[2], Mohammed Hamed Abosabaah[1,2,3], Abdulrahman Sultan Al Qattoumah[4], Ali Ibrahim Almoghassl[5], Hussain Abdullah Alqahtani[5], Hams Oudah Aljadani[2], Amal Saleh Alzahrani[2], Sulaiman Al Queflie[6]

1. College of Medicine, King Saud bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia
2. College of Medicine, University of Jeddah, Jeddah, Saudi Arabia
3. King Abdullah International Medical Research Center (KAIMRC), Riyadh, Saudi Arabia
4. Faculty of Medicine, Alexandria University, Alexandria, Egypt
5. College of Medicine, Dar Al Uloom University, Riyadh, Saudi Arabia
6. King Abdullah Specialized Children's Hospital & King Saud bin Abdulaziz University for Health Sciences (KSAU-HS), Ministry of National Guard Health Affairs, Riyadh, Saudi Arabia

Supplementary content (If any) is available online.

Reference

1. Franklin D, Dalziel S, Schlapbach LJ, Babl FE, Oakley E, Craig SS, et al. Early high flow nasal cannula therapy in bronchiolitis, a prospective randomised control trial (protocol): a paediatric acute respiratory intervention study (PARIS). BMC Pediatrics. 2015;15(1):183. https://doi.org/10.1186/s12887-015-0501-x
2. Verder H, Heiring C, Clark H, Sweet D, Jessen TE, Ebbesen F, et al. Rapid test for lung maturity, based on spectroscopy of gastric aspirate, predicted respiratory distress syndrome with high sensitivity. Acta Paediatrica. 2017;106(3):430–7. https://doi.org/10.1111/apa.13683
3. Teague WG. Noninvasive ventilation in the pediatric intensive care unit for children with acute respiratory failure. Pediatric Pulmonol. 2003;35(6):418–26. https://doi.org/10.1002/ppul.10281
4. Oakley E, Borland M, Neutze J, Acworth J, Krieser D, Dalziel S, et al. Nasogastric hydration versus intravenous hydration for infants with bronchiolitis: a randomised trial. Lancet Respir Med. 2013;1(2):113–20. https://doi.org/10.1016/S2213-2600(12)70053-X
5. Steinhorn DM, Green TP. The treatment of acute respiratory failure in children: a historical examination of landmark advances. J Pediatrics. 2001;139(4):604–8. https://doi.org/10.1067/mpd.2001.118196
6. Holme N, Chetcuti P. The pathophysiology of respiratory distress syndrome in neonates. Paediatrics Child Health. 2012;22(12):507–12. https://doi.org/10.1016/j.paed.2012.09.001
7. Greenough A, Murthy V. Respiratory distress syndrome. Fetal Maternal Med Rev. 2008;19(3):203–5. https://doi.org/10.1017/S0965539508002222
8. Zhu XW, Shi Y, Shi LP, Liu L, Xue J, Ramanathan R. Non-invasive high-frequency oscillatory ventilation versus nasal continuous positive airway pressure in preterm

infants with respiratory distress syndrome: study protocol for a multi-center prospective randomized controlled trial. Trials. 2018;19(1):319. https://doi.org/10.1186/s13063-018-2673-9

9. Zhao X, Qin Q, Zhang X. Outcomes of high-flow nasal cannula vs. nasal continuous positive airway pressure in young children with respiratory distress: a systematic review and meta-analysis. Front Pediatrics. 2021;9:759297. https://doi.org/10.3389/fped.2021.759297
10. Shokouhi M, Basiri B, Sabzehei MK, Mahdiankhoo M, Pirdehghan A. Efficacy and complications of humidified high-flow nasal cannula versus nasal continuous positive airway pressure in neonates with respiratory distress syndrome after surfactant therapy. Iranian Red Crescent Med J. 2019;21(2): https://doi.org/10.5812/ircmj.83615
11. Esposito S, Leone S. Management of serious bacterial infections: general considerations. Le Infezioni Medicina. 2005; Suppl:3–6.
12. Zimmerman JE, Wagner DP, Knaus WA, Williams JF, Kolakowski D, Draper EA. The use of risk predictions to identify candidates for intermediate care units: implications for intensive care utilization and cost. Chest. 1995;108(2):490–9. https://doi.org/10.1378/chest.108.2.490
13. Chidini G, Piastra M, Marchesi T, De Luca D, Napolitano L, Salvo I, et al. Continuous positive airway pressure with helmet versus mask in infants with bronchiolitis: an RCT. Pediatrics. 2015;135(4):e868–875. https://doi.org/10.1542/peds.2014-1142
14. Lee JH, Rehder KJ, Williford L, Cheifetz IM, Turner DA. Use of high flow nasal cannula in critically ill infants, children, and adults: a critical review of the literature. Intensive Care Med. 2013;39(2):247–57. https://doi.org/10.1007/s00134-012-2743-5
15. Collins CL, Holberton JR, Barfield C, Davis PG. A randomized controlled trial to compare heated humidified high-flow nasal cannulae with nasal continuous positive airway pressure postextubation in premature infants. J Pediatrics. 2013;162(5):949–54. https://doi.org/10.1016/j.jpeds.2012.11.016
16. 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 J Med. 2016;375(12):1142–51. https://doi.org/10.1056/NEJMoa1603694
17. Essouri S, Laurent M, Chevret L, Durand P, Ecochard E, Gajdos V, et al. Improved clinical and economic outcomes in severe bronchiolitis with pre-emptive nCPAP ventilatory strategy. Intensive Care Med. 2014;40(1):84–91. https://doi.org/10.1007/s00134-013-3129-z
18. Pinto VL, Sankari A, Sharma S. Continuous positive airway pressure. Treasure Island, FL:StatPearls Publishing; 2025.
19. Sterne JA, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ. 2019;4898. https://doi.org/10.1136/bmj.l4898
20. Grover R, Singh P, Shubham S, Priyadarshi M, Chaurasia S, Basu S. Delivery room respiratory stabilization of preterm neonates: a randomized, controlled trial. Indian J Pediatrics. 2022;89(8):793–800. https://doi.org/10.1007/s12098-022-04124-0
21. Singh S, Ananthan A, Nanavati R. Post-INSURE administration of heated humidified high-flow therapy versus nasal continuous positive airway pressure in preterm infants more than 28 weeks gestation with respiratory distress syndrome: a randomized non-inferiority trial. J Trop Pediatrics. 2022;68(4):fmac062. https://doi.org/10.1093/tropej/fmac062
22. Demirel G, Vatansever B, Tastekin A. High flow nasal cannula versus nasal continuous positive airway pressure for primary respiratory support in preterm infants: a prospective randomized study. Am J Perinatology. 2021;38(03):237–41. https://doi.org/10.1055/s-0039-1696673
23. Chen J, Lin Y, Du L, Kang M, Chi X, Wang Z, et al. The comparison of HHHFNC and NCPAP in extremely low-birth-weight preterm infants after extubation: a single-center randomized controlled trial. Front Pediatrics. 2020;8:250. https://doi.org/10.3389/fped.2020.00250
24. Charki S, Patil P, Hadalgi L, Kulkarni T, Loni R, Karva M, et al. Heated humidified high-flow nasal cannula versus nasal continuous positive airways pressure for respiratory support in preterm neonates-a noninferiority trial at a tertiary care center. J Clin Neonatology. 2020;1(3):168–74. https://doi.org/10.4103/jcn.JCN_76_19
25. Akbarian-Rad Z, Mohammadi A, Khafri S, Ahmadpour-Kacho M, Zahed-Pasha Y, Haghshenas-Mojaveri M. Comparison of heated humidified high flow nasal cannula and nasal continuous positive airway pressure after surfactant administration in preterm neonates with respiratory distress syndrome. Clin Respiratory J. 2020;14(8):740–7. https://doi.org/10.1111/crj.13191
26. Armanian AM, Iranpour R, Parvaneh M, Salehimehr N, Feizi A, Hajirezaei M. Heated humidified high flow nasal cannula (HHHFNC) is not an effective method for initial treatment of respiratory distress syndrome (RDS) versus nasal intermittent mandatory ventilation (NIMV) and nasal continuous positive airway pressure (NCPAP). J Res Med Sci. 2019;24(1):73. https://doi.org/10.4103/jrms.JRMS_2_19
27. Ann Skariah T, Dias L, Edward Lewis L. Comparison of the Heated Humidified High-flow Nasal Cannula with Nasal Continuous Positive Airway Pressure as Primary Respiratory Support for Preterm Neonates: a Prospective Observational Study. Iranian J Neonatology. 2019;10(3):51–7.
28. Murki S, Singh J, Khant C, Kumar Dash S, Oleti TP, Joy P, et al. High-flow nasal cannula versus nasal continuous positive airway pressure for primary respiratory support in preterm infants with respiratory distress: a randomized controlled trial. Neonatology. 2018;113(3):235–41. https://doi.org/10.1159/000484400
29. Farhat AS, Mohammadzadeh A, Mamuri GA, Saeidi R, Noorizadeh S. Comparison of Nasal Non-invasive Ventilation Methods in Preterm Neonates with Respiratory Distress Syndrome. Iranian J Neonatology. 2018;9(4).
30. Shin J, Park K, Lee EH, Choi BM. Humidified high flow nasal cannula versus nasal continuous positive airway pressure as an initial respiratory support in preterm infants with respiratory distress: a randomized, controlled non-inferiority trial. J Korean Med Sci. 2017;32(4):650. https://doi.org/10.3346/jkms.2017.32.4.650
31. Glackin SJ, O'Sullivan A, George S, Semberova J, Miletin J. High flow nasal cannula versus NCPAP, duration to full oral feeds in preterm infants: a randomised controlled trial. Arch Dis Childhood-Fetal Neonatal Ed. 2017;102(4):F329–32. https://doi.org/10.1136/archdischild-2016-311388

32. Mokhtary-Hassanabad A, Mirjalili SR, Lookzadeh MH, Noorishadkam M. Comparison of treatment outcomes of high-flow nasal cannula and nasal continuous positive airway pressure in preterm neonates with respiratory distress syndrome in the NICU of shahid sadoughi hospital in Yazd. World J Peri Neonatology. 2024;6(2):75–82. https://doi.org/10.18502/wjpn.v6i2.15488

33. Aramesh MR, Majidinezjad S, Dehdashtian M, Malakian A, Mohammadi S. Nasal Continuous Positive Airway Pressure versus High-Flow Nasal Cannula for the Treatment of Respiratory Distress Syndrome in Preterm Neonates: a Randomized Controlled Trial. Curr Respiratory Med Rev. 2025;21(3):296–305. https://doi.org/10.2174/011573398X339994241209170750

34. Yousof Mahboob D, Hassan A, Naheed F, Ali Shah A, Fareed Siddiqui M. Effectiveness of Humidified High Flow Nasal Cannula Versus Continuous Nasal Positive Airway Pressure in Managing Respiratory Failure in Preterm Infants: an Emergency Department Study. Biomedicines. 2025;13(3):602. https://doi.org/10.3390/biomedicines13030602