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## High-flow nasal cannula therapy for respiratory support in children (Review)

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[Intervention Review]

# High-flow nasal cannula therapy for respiratory support in children

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## ABSTRACT

### Background

Respiratory support is a central component of the management of critically ill children. It can be delivered invasively via an endotracheal tube or non-invasively via face mask, nasal mask, nasal cannula or oxygen hood/tent. Invasive ventilation can be damaging to the lungs, and the tendency to use non-invasive forms is growing. However, non-invasive delivery is often poorly tolerated by children. High-flow nasal cannula (HFNC) oxygen delivery is a relatively new therapy that shows the potential to reduce the need for intubation and be better tolerated by children than other non-invasive forms of support. HFNC therapy differs from other non-invasive forms of treatment in that it delivers heated, humidified and blended air/oxygen via nasal cannula at rates  $\geq 2$  L/kg/min. This allows the user to deliver high concentrations of oxygen and to potentially deliver continuous distending pressure; this treatment often is better tolerated by the child.

### Objectives

To determine whether HFNC therapy is more effective than other forms of non-invasive therapy in paediatric patients who require respiratory support.

### Search methods

We searched the Cochrane Central Register of Controlled Trials (CENTRAL) (2013, Issue 4); MEDLINE via PubMed (January 1966 to April 2013); EMBASE (January 1980 to April 2013); CINAHL (1982 to April 2013); and LILACS (1982 to April 2013). Abstracts from conference proceedings, theses and dissertations and bibliographical references to relevant studies were also searched. We applied no restriction on language.

### Selection criteria

We planned to include randomized controlled trials (RCTs) and quas-randomized trials comparing HFNC therapy with other forms of non-invasive respiratory support for children. Non-invasive support encompassed cot, hood or tent oxygen; low-flow nasal cannulae (flow rates  $\leq 2$  L/min); and continuous positive airway pressure (CPAP) or bilevel positive airway pressure (BiPAP) delivered via facial or nasal mask/cannula. Treatment failure was defined by the need for additional respiratory support. We excluded children with a diagnosis of bronchiolitis.

## Data collection and analysis

Two review authors independently assessed all studies for selection and data extraction. We used standard methodological procedures expected by The Cochrane Collaboration.

## Main results

Our search yielded 922 records. A total of 109 relevant records were retrieved with reference to our search criteria. After duplicates and irrelevant studies were removed, 69 studies were further scrutinized. Of these, 11 studies involved children. No study matched our inclusion criteria.

## Authors' conclusions

Based on the results of this review, no evidence is available to allow determination of the safety or effectiveness of HFNC as a form of respiratory support in children.

## PLAIN LANGUAGE SUMMARY

### High-flow nasal cannula therapy for support of breathing in children

We reviewed evidence on the effectiveness of high-flow nasal cannula (HFNC) therapy in supporting children's breathing. We found 11 studies in children.

### Background

HFNC therapy delivers a mixture of air and oxygen via tubing that sits just inside the nostrils. For children hospitalized with breathing difficulties caused by conditions such as pneumonia or trauma or after surgery, HFNC therapy may help to support their breathing. This may reduce the need for other forms of breathing support such as life support. HFNC therapy can be used within the hospital ward setting, the emergency department or the intensive care unit. This Cochrane review is important because it assesses available evidence on the safety and effectiveness of HFNC compared with other forms of respiratory support, to help inform clinicians caring for children with breathing difficulties.

### Search date

We searched medical databases from the 1950s until April 2013.

### Study characteristics

We included studies on children from four weeks to 16 years of age. We searched for randomized controlled trials; however we excluded studies involving infants with bronchiolitis (a respiratory illness affecting infants that typically mimics a common cold) because children with this condition are included in another Cochrane review.

### Results

We found 11 studies involving children; however none matched our criteria.

### Conclusion

It is important that good-quality studies are completed to identify indications as to the use and effectiveness of HFNC therapy in supporting the breathing of ill children.

## BACKGROUND

### Description of the condition

Respiratory support is central to the care of critically ill children. Support may be needed because of underlying disease processes such as respiratory infection or pneumonia, neuromuscular disorders, cardiac conditions or cardiac failure, and as the result of other mechanisms such as upper airway obstruction, trauma and injury or postsurgical interventions. Respiratory support can be delivered non-invasively in the form of oxygen therapy, continuous positive airway pressure (CPAP) or bilevel positive airway pressure (BiPAP), or invasively via mechanical ventilation. Children with significant respiratory distress and hypoxaemia often require the latter. This may result in various forms of trauma to the lungs and airways, collectively known as ventilator-induced lung injury (VILI) (Dahlem 2003; The ARDS Network 2000).

Although VILI is the major concern with intubation and mechanical ventilation, other effects on the body need to be considered. Increased use of sedative drugs may lead to neuropathy or myopathy, which can increase recovery time. In turn, cardiovascular support in the form of drug infusions may be needed to maintain blood pressure. These requirements increase the costs of care provided to the child. Non-invasive methods of ventilation are an ideal method of providing respiratory support without the need for intubation and may avoid some of the additional harms associated with positive-pressure ventilation, such as ventilator-associated pneumonia (VAP) (Glossop 2012).

Non-invasive ventilation can be as simple as oxygen therapy delivered via face mask, nasal cannula or head box or devices delivering CPAP/BiPAP via face mask or nasopharyngeal tubes, with pressure generated by a dedicated driver or water column (i.e. bubble CPAP) (Frey 2001; Frey 2003; Klein 1986). Devices delivering CPAP/BiPAP can reduce the work of breathing and improve functional residual capacity, potentially avoiding intubation, reducing VILI and VAP and preventing other possible causes of harm (Reid 1984; Thorsteinsson 2002).

Disadvantages of this method of delivery are that it is cumbersome, and the masks and tubes are poorly tolerated by young children and infants (McGinley 2009; Spentzas 2009; Yong 2005). Obtaining an adequate seal around the face of small children can be difficult, thereby making delivery of CPAP/BiPAP variable and resulting in ineffective ventilation. This is often due to the limited choice of face masks developed for children with a wide range of ages and stages of facial development. The need for a system that can deliver CPAP while being comfortable and well tolerated by children is an important consideration in providing non-invasive respiratory support.

### Description of the intervention

High-flow nasal cannula (HFNC) therapy has recently been introduced for a range of patients from preterm infants to adults, addressing the need for a simple, effective method of providing respiratory support (Campbell 2006; McGinley 2009; McKiernan 2010; Shoemaker 2007). It offers an advantage over simple oxygen therapy in that the gas mixture can be heated and humidified, thereby reducing damage to upper airway mucosa, and the concentration of inspired oxygen can be titrated as required. This can prevent inflammatory reactions and the naso-pulmonary

bronchoconstrictor reflex triggered by cold, dry air (Spentzas 2009). The mixed gas is delivered via a nasal cannula that sits just inside the nares. The flow rate delivered varies depending on the type of cannula used but can range from 4 to 70 L/min.

### How the intervention might work

It has been shown that delivery of nasal air at high flow rates may cause incidental delivery of CPAP (Dysart 2009; Spence 2007; Wilkinson 2008). The effects of this are yet to be fully understood. It may be that the high flow flushes the dead space of the nasopharyngeal cavity, resulting in alveolar ventilation as a greater fraction of minute ventilation. It may also assist in the washout of carbon dioxide, which may then reduce apnoea secondary to hypercapnia and improve ventilation (Dysart 2009). High flow rates may also provide some amount of positive pressure and thereby overcome upper airway obstruction, again improving ventilation (McGinley 2009).

The amount of CPAP generated depends on the flow delivered relative to the size of the patient, the size of the nasal cannula used and the potential for leak around the nasal cannula (Kubicka 2008; Lampland 2009; Sreenan 2001). Three retrospective studies in paediatric populations assessing HFNC therapy have demonstrated that overall, ventilator days were significantly decreased after introduction of this therapy when compared with retrospective historical control groups (McKiernan 2010; Schibler 2011; Shoemaker 2007).

HFNC therapy has also been reported to be better tolerated by the patient than other forms of non-invasive ventilation (Roca 2010). This can reduce the need for the sedation required to help patients tolerate more invasive or uncomfortable forms of respiratory support.

### Why it is important to do this review

HFNC therapy is an emerging treatment option for the respiratory support of children, especially in the intensive care unit. To date, most findings have been derived from neonatal and adult studies, with little clinical experience reported in the paediatric population (McKiernan 2010). Clinical experience in the paediatric population is reported in case reports and observational studies; few randomized controlled trials are reported (Mayfield 2013; McGinley 2009; Spentzas 2009). The Cochrane review of HFNC therapy from the Cochrane Neonatal Group found only four eligible, randomized controlled trials and concluded that evidence was insufficient to determine effectiveness, and more research was needed (Wilkinson 2011). Two further reviews of HFNC therapy are under way: in the adult population (Corley 2012) and in infants with bronchiolitis (Beggs 2012). This review differs in that it includes studies of children with a broader age range and more diverse pathophysiologies such as type 1 and 2 respiratory failure, parenchymal lung disease, neuromuscular disorders, respiratory drive disorders and airway obstruction.

HFNC therapy has the potential to improve outcomes such as reduced intubation and invasive ventilation (McKiernan 2010; Schibler 2011; Wing 2012) in critically ill children. It is readily applied and is not resource or cost intensive. Staff can easily be trained in the application of HFNC therapy and in the care of children using this therapy. It may also reduce the length of intubation, as HFNC holds potential to transition between

extubation and low-flow nasal cannula oxygen delivery. An additional advantage is that children requiring this therapy may be cared for outside of the paediatric intensive care unit (PICU). However potential risks are associated with its use, such as air leak syndrome, which has been described in a case report (Hedge 2013), and other risks extrapolated from the neonatal population, such as nasal trauma and abdominal overdistention (Kopelman 2003). These potential risks and benefits need to be assessed in the paediatric population.

## OBJECTIVES

To determine whether HFNC therapy is more effective than other forms of non-invasive therapy in paediatric patients who require respiratory support.

## METHODS

### Criteria for considering studies for this review

#### Types of studies

We included prospective randomized controlled trials (RCTs) and quasi-randomized studies.

#### Types of participants

We included paediatric participants from four weeks corrected age to 16 years of age requiring respiratory support for type 1 and 2 respiratory failure, parenchymal lung disease, neuromuscular disorders, respiratory drive and airway obstruction. We excluded a study in children with bronchiolitis.

#### Types of interventions

What constitutes 'high flow' has not been well described in the literature, nor has it been universally determined. Most paediatric studies have been limited to using devices that deliver flow rates in infants from 4 to 8 L/min (Arora 2012; Schibler 2011). Older children may have up to 30 L/min delivered (McGinley 2009). For the purposes of this review, high-flow nasal oxygen was defined as the delivery of heated, humidified oxygen or blended oxygen with air via nasal cannula at flow rates greater than 2 L/min. HFNC therapy was compared with other means of non-invasive respiratory support, such as cot, hood or tent oxygen; low-flow nasal cannula (flow rates  $\leq$  2 L/min); and continuous positive airway pressure (CPAP) or bilevel positive airway pressure (BiPAP).

#### Types of outcome measures

##### Primary outcomes

1. Hospital mortality.
2. Intubation rate.
3. Treatment failure (defined as the need for additional respiratory support).

##### Secondary outcomes

1. Duration of any form of respiratory support in hours (mechanical ventilation, non-invasive ventilation, high-flow nasal cannula).
2. Length of stay in hospital in days.
3. Clinical severity score.
4. Length of paediatric intensive care unit (PICU) stay in days.
5. Complications.

- Air leaks (pneumothorax, pneumomediastinum, pneumopericardium or pulmonary interstitial emphysema (PIE)) reported individually or as a composite outcome.
- Nasal trauma (defined as erythema or erosion of the nasal mucosa, nares or septum as assessed by a blinded observer).
- Barotrauma.
- Gastrointestinal distention.

## Search methods for identification of studies

### Electronic searches

We obtained all relevant studies irrespective of language or publication status (published, unpublished, in press and in progress) using the following methods. We applied no limits in terms of language or year of publication.

We searched Issue 4, 2013 of the Cochrane Central Register of Controlled Trials (CENTRAL, see Appendix 1); MEDLINE via Ovid SP (January 1966 to April 2013, see Appendix 2); EMBASE via Ovid SP (January 1980 to April 2013, see Appendix 3); CINAHL via EBSCO Host (1982 to April 2013, see Appendix 4); and LILACS via the BIREME interface (1982 to April 2013, see Appendix 5).

We also searched the electronic databases of higher-degree theses for relevant unpublished trials: Index to Theses (1950 to date), Australian Digital Theses Program (1997 to April 2013) and Proquest Digital Dissertations (1980 to April 2013).

We then combined our MEDLINE search strategy with the Cochrane highly sensitive search strategy for identifying RCTs, as suggested in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We adopted the MEDLINE search strategy for searching in all other databases.

For ongoing trials, we searched the MetaRegister of Controlled Trials (<http://www.controlledtrials.com/>) and the National Research Register (<http://clinicaltrials.gov/>).

### Searching other resources

We handsearched citations from included studies.

### Data collection and analysis

We used standard methodological procedures expected by The Cochrane Collaboration.

### Selection of studies

We used the search strategy described to obtain titles and abstracts of studies that may be relevant to the review. Two review authors (SM and JJ-C) independently performed this screening. Studies that were not applicable were discarded. We found no ongoing studies that matched our search criteria.

### Data extraction and management

We adapted the standardized Cochrane Anesthesia Review Group (CARG) data extraction form (Appendix 6) to capture relevant data specific to this review. We (SM and JJ-C) used this form independently to extract and collect data from the relevant study. No disagreements arose.

### Assessment of risk of bias in included studies

No studies were eligible for assessment of risk of bias. However, we planned to assess risk of bias using the following domains with judgements of high, low or uncertain.

1. Selection bias: incorporating random sequence generation and allocation concealment.
2. Performance bias: blinding of participants and personnel.
3. Detection bias: blinding of outcome assessment.
4. Attrition bias: incomplete outcome data.
5. Reporting bias: selective reporting.
6. Other bias: other sources of bias.

### Measures of treatment effect

No studies were found that could be included in this review. Excluded studies were tabulated with the reasons for exclusion documented in the [Characteristics of excluded studies](#).

We planned to manage dichotomous outcome data, such as mortality, by using risk ratios (RRs) to determine effect and by displaying them in a table. For continuous data, we planned to collect means and standard deviations and to display them in a table. If different scales were used to measure continuous data, we would have calculated the standardized mean difference. Outcomes from comparable trials would have used 95% confidence intervals to estimate treatment effect. We would use forest plots to graphically compare treatment effect with risk ratio for dichotomous data and with mean difference for continuous outcomes.

### Unit of analysis issues

The unit of analysis was the individual child. We expected to find parallel-group study designs and no cross-over studies. As none of the studies included in this review were randomized at cluster level, unit of analysis was not an issue.

### Dealing with missing data

If eligible studies with missing data were found, we planned to contact the corresponding author.

### Assessment of heterogeneity

We planned to analyse heterogeneity using the Chi<sup>2</sup> test on N-1 degrees of freedom, with an alpha of 0.1 used for statistical significance, along with the I<sup>2</sup> statistic ([Higgins 2011](#)).

### Assessment of reporting biases

We planned to assess publication bias or small-study effects by preparing a funnel plot. We planned to test for funnel plot asymmetry if more than 10 studies were included in the meta-analysis. We planned to obtain published and unpublished studies as a way of addressing reporting bias.

### Data synthesis

We planned to review the summary tables of included trials to identify clinical heterogeneity amongst trials. If two or more randomized trials had been found with comparable populations undergoing similar interventions, we would have conducted a meta-analysis with a random-effects model using [RevMan 5.2](#).

### Subgroup analysis and investigation of heterogeneity

No studies were found to permit subgroup analyses or exploration of heterogeneity ([Sutton 2008](#)).

### Sensitivity analysis

No studies were found to allow sensitivity analysis.

### Summary of findings

We planned to use the principles of the GRADE system ([Guyatt 2008](#)) to assess the quality of the body of evidence associated with the following specific outcomes in our review.

1. Mortality.
2. Intubation.
3. Failure of treatment or escalation to non-invasive ventilation.
4. Length of PICU stay.
5. Length of time on any form of respiratory support.
6. Oxygenation and respiratory assessment tools.

However, no studies were identified for inclusion.

## RESULTS

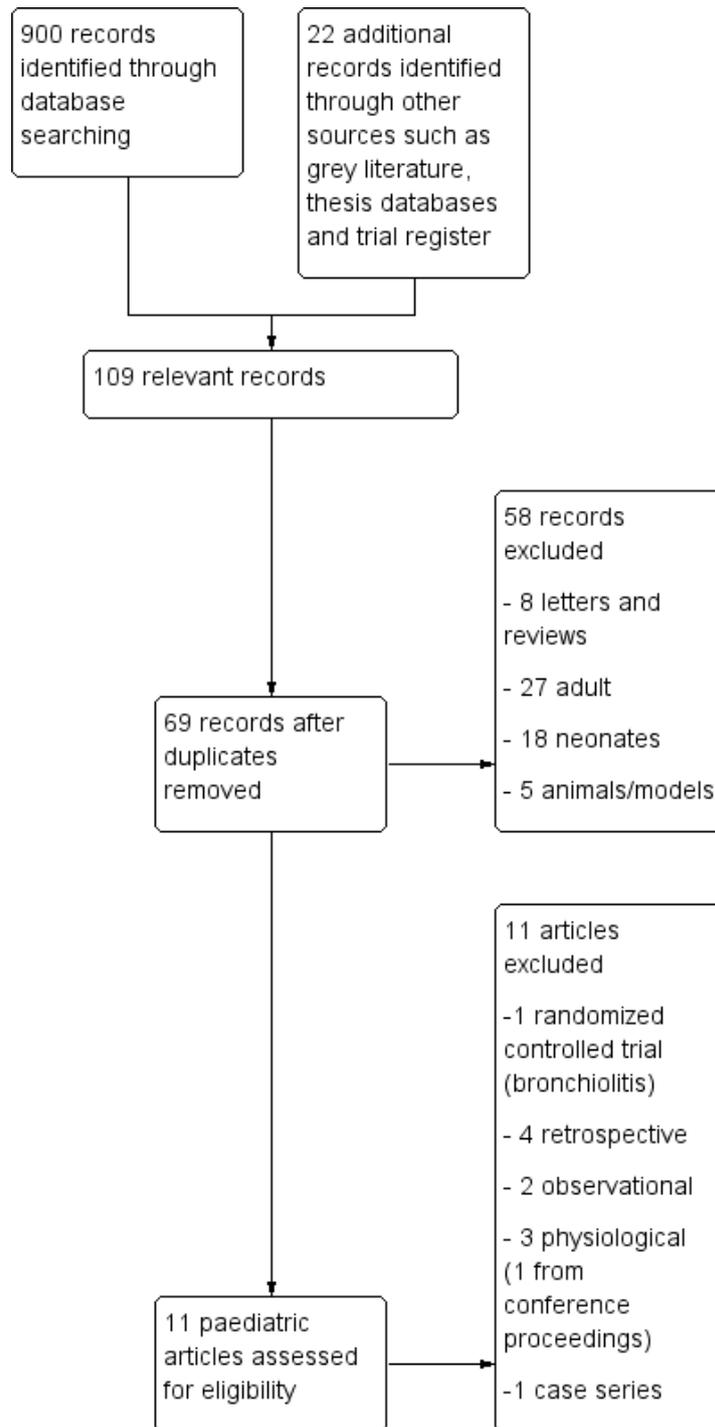
### Description of studies

See [Characteristics of excluded studies](#).

### Results of the search

Our search yielded 922 records. After duplicates and irrelevant references were removed, 69 were further scrutinized. Eleven studies involved children. No study met our criteria ([Figure 1](#)).

**Figure 1. Study flow diagram.**



**Included studies**

No studies met our inclusion criteria.

**Excluded studies**

Ten studies did not meet the criteria of being randomized or quasi-randomized (Abboud 2012; Arora 2012; Hedge 2013; Hough 2011; McGinley 2009; McKiernan 2010; Milesi 2013; Schibler 2011; Spentzas 2009; Wing 2012). One randomized controlled trial was

excluded because it included infants with bronchiolitis (Hilliard 2012). Details are listed in the [Characteristics of excluded studies](#).

**Risk of bias in included studies**

N/A.

**Allocation**

N/A.

**Blinding**

N/A.

**Incomplete outcome data**

N/A.

**Selective reporting**

N/A.

**Other potential sources of bias**

N/A.

**Effects of interventions**

N/A.

**DISCUSSION****Summary of main results**

We found no randomized controlled trials of HFNC therapy in children older than four weeks of age requiring respiratory support for type 1 or 2 respiratory failure, parenchymal lung disease, neuromuscular disorders, respiratory drive or airway obstruction.

**Overall completeness and applicability of evidence**

N/A.

**Quality of the evidence**

N/A.

**Potential biases in the review process**

We believe that any bias in this review is of low probability. We ensured that language would not be a bias by imposing no restrictions on such. We used a well-constructed search strategy to minimize the chance of missing randomized controlled trials that fulfilled our inclusion criteria.

**Agreements and disagreements with other studies or reviews**

This review supports the conclusion of other studies and reviews conducted to evaluate HFNC therapy (Lee 2013; Wilkinson 2011) in that evidence of robust quality is insufficient to permit determination of the superiority of HFNC therapy over other established forms of non-invasive ventilation for children with moderate to severe respiratory compromise. Further studies are needed to quantify this and to identify clinical indicators regarding its use.

**AUTHORS' CONCLUSIONS****Implications for practice**

Based on the results of this review, no evidence can be found to allow determination of the safety or effectiveness of HFNC therapy as a form of respiratory support in children.

**Implications for research**

It is acknowledged that while the number of retrospective, observational and physiological studies surrounding the support of HFNC therapy for respiratory support in children is increasing, adequately powered randomized controlled trials are needed. HFNC therapy must be compared with CPAP and other forms of non-invasive respiratory support. Clinically important outcomes, such as escalation to CPAP or intubation, length of stay and duration of treatment, need to be assessed. With such a broad range of ages and disease processes in children, an aim of further research should be to establish which subgroups benefit from HFNC therapy.

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Abboud P, Roth P, Skiles C, Stolfi A, Rowin M. Predictors of failure in infants with viral bronchiolitis treated with high-flow, high-humidity nasal cannula therapy. *Pediatric Critical Care* 2012;**13**(6):e343-9. [PUBMED: 22805160]

#### Arora 2012 {published data only}

\* Arora B, Mahajan P, Zidan M, Sethuraman U. Nasopharyngeal airway pressures in bronchiolitis patients treated with high-flow nasal cannula oxygen therapy. *Pediatric Emergency Care* 2012;**28**:1179-84. [PUBMED: 23114244]

#### Hedge 2013 {published data only}

Hedge S, Proadhan P. Serious air leak syndrome complicating high-flow nasal cannula therapy: a report of 3 cases. *Pediatrics* 2013;**131**(3):e1-6. [PUBMED: 23382446]

#### Hilliard 2012 {published data only}

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#### Hough 2011 {published data only}

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**References to other published versions of this review**
**Mayfield 2012**

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support in children. *Cochrane Database of Systematic Reviews* 2012, Issue 5. [DOI: [10.1002/14651858.CD009850](https://doi.org/10.1002/14651858.CD009850)]

\* Indicates the major publication for the study

**CHARACTERISTICS OF STUDIES**
**Characteristics of excluded studies [ordered by study ID]**

Study	Reason for exclusion
<a href="#">Abboud 2012</a>	Retrospective chart review of all patients admitted to intensive care with a diagnosis of viral bronchiolitis from 2006 to 2010. 113 patients met inclusion criteria of < 12 months, initiation of HFNC on admission
<a href="#">Arora 2012</a>	Prospective observational study to measure nasopharyngeal effects of HFNC in infants with bronchiolitis. 25 infants enrolled
<a href="#">Hedge 2013</a>	Case series of three patients with air leak syndrome who were also treated with HFNC
<a href="#">Hilliard 2012</a>	Prospective randomized controlled trial comparing HFNC versus head box oxygen therapy. 19 participants enrolled, all with viral bronchiolitis
<a href="#">Hough 2011</a>	Prospective physiological study comparing HFNC at different flow rates. 13 participants enrolled, all with bronchiolitis
<a href="#">McGinley 2009</a>	Prospective observational study of 12 participants with obstructive apnoea-hypopnoea syndrome treated with nasal insufflation at 20 L/min
<a href="#">McKiernan 2010</a>	Retrospective chart review comparing intubation rates of infants with bronchiolitis admitted before and in the season after HFNC was implemented. 115 participants included in the review
<a href="#">Milesi 2013</a>	Prospective physiological study of 21 infants < six months with viral bronchiolitis and HFNC therapy. Pharyngeal and oesophageal pressures measured at different flow rates
<a href="#">Schibler 2011</a>	Retrospective chart review of infants < 24 months admitted to PICU between January 2005 and December 2009, requiring HFNC therapy. 298 infants included in the review
<a href="#">Spentzas 2009</a>	Observational study of all participants (newborn to 12 years) requiring HFNC, admitted between January 2005 and January 2007 to PICU. 46 participants included in the study
<a href="#">Wing 2012</a>	Retrospective chart review of all patients admitted from ED to PICU with acute respiratory insufficiency from January 2006 to December 2009. Patients admitted before HFNC availability were compared with patients admitted after HFNC became available (two cohorts, before and after implementation of clinical guidelines). 848 participants included in the review

**APPENDICES**
**Appendix 1. CENTRAL search strategy**

#1 MeSH descriptor Oxygen Inhalation Therapy explode all trees

#2 intubation rates\*

#3 (#1 AND #2)

#4 ((high flow (nasal or prong or cannula)) or (nasal near oxygen)):ti,ab

#5 (#3 OR #4)

Search from Issue 4 2013.

### Appendix 2. MEDLINE (Ovid SP) search strategy

1. (exp Oxygen Inhalation Therapy/ and intubation rates\*.af.) or (high flow adj3 (nasal or prong or cannula)).mp. or (nasal adj3 oxygen).mp.
2. ((randomized controlled trial or controlled clinical trial).pt. or randomized.ab. or placebo.ab. or drug therapy.fs. or randomly.ab. or trial.ab. or groups.ab.) not (animals not (humans and animals)).sh.
3. 1 and 2

Search from January 1966- April 2013.

### Appendix 3. EMBASE (Ovid SP) search strategy

1. (exp oxygen therapy/ and intubation rates\*.af.) or (high flow adj3 (nasal or prong or cannula)).mp. or (nasal adj3 oxygen).mp.
2. (randomized-controlled-trial/ or randomization/ or controlled-study/ or multicenter-study/ or phase-3-clinical-trial/ or phase-4-clinical-trial/ or double-blind-procedure/ or single-blind-procedure/ or (random\* or cross?over\* or multicenter\* or factorial\* or placebo\* or volunteer\*).mp. or ((singl\* or doubl\* or trebl\* or tripl\*) adj3 (blind\* or mask\*)).ti,ab. or (latin adj square).mp.) not (animals not (humans and animals)).sh.
3. 1 and 2

Search from January 1980 to April 2013.

### Appendix 4. CINAHL (EBSCO host) search strategy

- S1 (((MH "Oxygen Therapy") and intubation rates\*)) OR ((high flow and (nasal or prong or cannula))) OR (nasal and oxygen)  
S2 (MM "Randomized Controlled Trials") OR (MM "Random Assignment") OR (MH "Clinical Trials+") OR (MM "Multicenter Studies") OR (MM "Prospective Studies") OR (MM "Placebos") OR (MM "Double-Blind Studies") OR (MM "Triple-Blind Studies") OR (MM "Single-Blind Studies")  
S3 S1 and S2

Search from 1982-April 2013.

### Appendix 5. LILACS search strategy

(oxygen therapy and intubation rates\$) or (high flow and (nasal or prong or cannula)) or (nasal and oxygen) [Palabras]

Search from 1982 to April 2013.

### Appendix 6. Data extraction form

---

**Review title or ID**

---

---

---

**Study ID** (*surname of first author and year first full report of study was published e.g. Smith 2001*)

---

---

---

**Report IDs of other reports of this study** (*e.g. duplicate publications, follow-up studies*)

---

---

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**Notes:**

---

## 1. General information

---

**Date form completed** *(dd/mm/yyyy)*

---

**Name/ID of person extracting data**

---

**Report title**

*(title of paper/abstract/report from which data are extracted)*

---

**Report ID**

*(ID for this paper/abstract/report)*

---

**Reference details**

---

**Report author contact details**

---

**Publication type**

*(e.g. full report, abstract, letter)*

---

**Study funding sources**

*(including role of funders)*

---

**Possible conflicts of interest**

*(for study authors)*

---

**Notes:**

---

## 2. Study eligibility

Study characteristics	Eligibility criteria <i>(insert eligibility criteria for each characteristic as defined in the protocol)</i>	Yes	No	Unclear	Location in text <i>(pg &amp; ¶/fig/table)</i>
<b>Type of study</b>	Randomized controlled trial  Controlled clinical trial  <i>(quasi-randomized trial)</i>				
<b>Participants</b>	Paediatric patients from four weeks corrected to 16 years of age				
<b>Types of interventions</b>	High-flow nasal oxygen (heated/humidified, flow > 2 L/kg/min)  Comparator: non-invasive respiratory support such as cot/tent/hood, low-flow oxygen or CPAP				
<b>Types of outcome measures</b>	Hospital mortality; intubation rate; treatment failure  Secondary: duration of any form of respiratory support; length of hospital stay; clinical severity score; length of PICU stay; complications—air leak, nasal trauma, nosocomial sepsis, barotrauma, gastrointestinal distention				
<b>INCLUDE</b>	<b>EXCLUDE</b>				
<b>Reason for exclusion</b>					
<b>Notes:</b>					

DO NOT PROCEED IF STUDY EXCLUDED FROM REVIEW.

### 3. Methods

Aim of study	Descriptions as stated in report/paper	Location in text <i>(pg &amp; ¶/fig/table)</i>

(Continued)

**Design** (e.g. parallel, cross-over, cluster)

**Unit of allocation**

(by individuals, cluster/groups or body parts)

**Start date**

**End date**

**Total study duration**

**Ethical approval needed/obtained for study**

Yes No Unclear

**Notes:**

#### 4. Risk of bias assessment

See Chapter 8 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

Domain	Risk of bias			Support for judgement	Location in text <i>(pg &amp; ¶/fig/table)</i>
	Low risk	High risk	Unclear		
<b>Random sequence generation</b> <i>(selection bias)</i>					
<b>Allocation concealment</b> <i>(selection bias)</i>					
<b>Blinding of participants and personnel</b> <i>(performance bias)</i>				<b>Outcome group: all/</b>	
<i>(if required)</i>				<b>Outcome group:</b>	
<b>Blinding of outcome assessment</b> <i>(detection bias)</i>				<b>Outcome group: all/</b>	
<i>(if required)</i>				<b>Outcome group:</b>	

*(Continued)*

**Incomplete outcome data**

*(attrition bias)*

**Selective outcome reporting?**

*(reporting bias)*

**Other bias**

**Notes:**

**5. Participants**

*Provide overall data and, if available, comparative data for each intervention or comparison group.*

**Description as  
stated in re-  
port/paper**

**Location in text**  
*(pg & ¶/fig/table)*

**Total no. randomly assigned**

*(or total population at start of study for NRCTs)*

**Clusters**

*(if applicable, no., type, no. people per cluster)*

**Withdrawals and exclusions**

*(if not provided below by outcome)*

**Age**

**Sex**

**Severity of illness**

**Co-morbidities**

**Other treatment received** *(additional to study intervention)*

**Subgroups measured**

**Subgroups reported**

**Notes:**

## 6. Intervention groups

Copy and paste table for each intervention and comparison group.

### Intervention group 1

	Description as stated in report/paper	Location in text (pg & ¶/fig/table)
<b>Group name</b>	HFNC	
<b>No. randomly assigned to group</b> <i>(specify whether no. people or clusters)</i>		
<b>Description</b> <i>(include sufficient detail for replication, e.g. content, dose, components)</i>		
<b>Duration of treatment period</b>		
<b>Timing</b> <i>(e.g. frequency, duration of each episode)</i>		
<b>Delivery</b> <i>(e.g. mechanism, medium, intensity, fidelity)</i>		
<b>Co-interventions</b>		
<b>Notes:</b>		

### Comparison group 1

	Description as stated in report/paper	Location in text (pg & ¶/fig/table)
<b>Group name</b>	Invasive ventilation	
<b>No. randomly assigned to group</b> <i>(specify whether no. people or clusters)</i>		

(Continued)

**Description** (include sufficient detail for replication, e.g. content, dose, components)

**Duration of treatment period**

**Timing** (e.g. frequency, duration of each episode)

**Delivery** (e.g. mechanism, medium, intensity, fidelity)

**Co-interventions**

**Notes:**

## Comparison group 2

	Description as stated in report/paper	Location in text (pg & ¶/fig/table)
<b>Group name</b>	<b>Noninvasive ventilation</b>	
<b>No. randomly assigned to group</b> (specify whether no. people or clusters)		
<b>Description</b> (include sufficient detail for replication, e.g. content, dose, components)		
<b>Duration of treatment period</b>		
<b>Timing</b> (e.g. frequency, duration of each episode)		
<b>Delivery</b> (e.g. mechanism, medium, intensity, fidelity)		
<b>Co-interventions</b>		
<b>Notes:</b>		

## 7. Outcomes

Copy and paste table for each outcome.

### Outcome 1

	Description as stated in re- port/paper	Location in text  (pg & ¶/fig/ta- ble)
<b>Outcome name</b>	<b>Hospital mortality</b>	
<b>Time points measured</b>		
<b>Time points reported</b>		
<b>Outcome definition</b> <i>(with diagnostic criteria if relevant)</i>		
<b>Person measuring/reporting</b>		
<b>Unit of measurement</b>  <i>(if relevant)</i>		
<b>Scales: upper and lower limits</b> <i>(indicate whether high or low score is good)</i>		
<b>Is outcome/tool validated?</b>	Yes No Un- clear	
<b>Imputation of missing data</b> <i>(e.g. assumptions made for ITT analysis)</i>		
<b>Assumed risk estimate</b>  <i>(e.g. baseline or population risk noted in Background)</i>		
<b>Power</b>		
<b>Notes:</b>		

**Outcome 2**

	Description as stated in re- port/paper	Location in text  (pg & ¶/fig/ta- ble)
<b>Outcome name</b>	<b>Intubation rate</b>	

(Continued)

**Time points measured**

**Time points reported**

**Outcome definition** (with diagnostic criteria if relevant)

**Person measuring/reporting**

**Unit of measurement**

(if relevant)

**Scales: upper and lower limits** (indicate whether high or low score is good)

**Is outcome/tool validated?**

Yes No Un-  
clear

**Imputation of missing data**

(e.g. assumptions made for ITT analysis)

**Assumed risk estimate**

(e.g. baseline or population risk noted in Background)

**Power**

**Notes:**

**Outcome 3**

	Description as stated in report/paper	Location in text  (pg & ¶/fig/table)
<b>Outcome name</b>	<b>Treatment failure—escalation to other form of respiratory support</b>	
<b>Time points measured</b>		
<b>Time points reported</b>		
<b>Outcome definition</b> (with diagnostic criteria if relevant)		
<b>Person measuring/reporting</b>		
<b>Unit of measurement</b>		
(if relevant)		

(Continued)

**Scales: upper and lower limits** (indicate whether high or low score is good)

**Is outcome/tool validated?**

Yes No Unclear

**Imputation of missing data**

(e.g. assumptions made for ITT analysis)

**Assumed risk estimate**

(e.g. baseline or population risk noted in Background)

**Power**

**Notes:**

#### Outcome 4

	Description as stated in report/paper	Location in text
		(pg & ¶/fig/table)
<b>Outcome name</b>	<b>Duration of respiratory support</b>	
<b>Time points measured</b>		
<b>Time points reported</b>		
<b>Outcome definition</b> (with diagnostic criteria if relevant)		
<b>Person measuring/reporting</b>		
<b>Unit of measurement</b> (if relevant)		
<b>Scales: upper and lower limits</b> (indicate whether high or low score is good)		
<b>Is outcome/tool validated?</b>	Yes No Unclear	
<b>Imputation of missing data</b> (e.g. assumptions made for ITT analysis)		
<b>Assumed risk estimate</b>		

(Continued)

(e.g. baseline or population risk noted in Background)

**Power**

**Notes:**

**Outcome 5**

Outcome name	Description as stated in report/paper	Location in text <i>(pg &amp; ¶/fig/table)</i>
	Complications—air leak, nasal trauma, nosocomial sepsis, barotrauma, gastrointestinal distention	
<b>Time points measured</b>		
<b>Time points reported</b>		
<b>Outcome definition</b> <i>(with diagnostic criteria if relevant)</i>		
<b>Person measuring/reporting</b>		
<b>Unit of measurement</b> <i>(if relevant)</i>		
<b>Scales: upper and lower limits</b> <i>(indicate whether high or low score is good)</i>		
<b>Is outcome/tool validated?</b>	Yes No Unclear	
<b>Imputation of missing data</b> <i>(e.g. assumptions made for ITT analysis)</i>		
<b>Assumed risk estimate</b> <i>(e.g. baseline or population risk noted in Background)</i>		
<b>Power</b>		
<b>Notes:</b>		

**Outcome 6**

	Description as stated in report/paper	Location in text <i>(pg &amp; ¶/fig/table)</i>
<b>Outcome name</b>	<b>Length of hospital stay</b>	
<b>Time points measured</b>		
<b>Time points reported</b>		
<b>Outcome definition</b> <i>(with diagnostic criteria if relevant)</i>		
<b>Person measuring/reporting</b>		
<b>Unit of measurement</b> <i>(if relevant)</i>		
<b>Scales: upper and lower limits</b> <i>(indicate whether high or low score is good)</i>		
<b>Is outcome/tool validated?</b>	Yes No Un-clear	
<b>Imputation of missing data</b> <i>(e.g. assumptions made for ITT analysis)</i>		
<b>Assumed risk estimate</b> <i>(e.g. baseline or population risk noted in Background)</i>		
<b>Power</b>		
<b>Notes:</b>		

**Outcome 7**

	Description as stated in report/paper	Location in text <i>(pg &amp; ¶/fig/table)</i>
<b>Outcome name</b>	<b>Clinical severity score</b>	

(Continued)

**Time points measured**

**Time points reported**

**Outcome definition** (with diagnostic criteria if relevant)

**Person measuring/reporting**

**Unit of measurement**

(if relevant)

**Scales: upper and lower limits** (indicate whether high or low score is good)

**Is outcome/tool validated?**

Yes No Un-  
clear

**Imputation of missing data**

(e.g. assumptions made for ITT analysis)

**Assumed risk estimate**

(e.g. baseline or population risk noted in Background)

**Power**

**Notes:**

**Outcome 8: secondary outcome**

	Description as stated in report/paper	Location in text <i>(pg &amp; ¶/fig/table)</i>
<b>Outcome name</b>	<b>Length of PICU stay</b>	
<b>Time points measured</b>		
<b>Time points reported</b>		
<b>Outcome definition</b> (with diagnostic criteria if relevant)		
<b>Person measuring/reporting</b>		

---

(Continued)

**Unit of measurement**

(if relevant)

---

**Scales: upper and lower limits** (indicate whether high or low score is good)

---

**Is outcome/tool validated?**

Yes No Un-  
clear

---

**Imputation of missing data**

(e.g. assumptions made for ITT analysis)

---

**Assumed risk estimate**

(e.g. baseline or population risk noted in Background)

---

**Power**

---

**Notes:**

---

## 8. Results

Copy and paste the appropriate table for each outcome, including additional tables for each time point and subgroup as required.

### Dichotomous outcome

Outcome	HFNC		Invasive ventilation		Non-invasive ventilation		Details
	No. with event	No. without event	No. with event	No. without event	No. with event	No. without event	
Intubation							
Failure of treatment							
Hospital mortality							
Complications							

***Continuous outcome***

Outcome	Unit of measurement	HFNC group			Invasive ventilation group			Non- invasive group			De-tails
		n	M	SD	n	M	SD	n	M	SD	
Length of PICU stay											
Clinical severity score											
Duration of respiratory support											
LOS—hospital											

## 9. Applicability

**Have important populations been excluded from the study?** (*consider disadvantaged populations and possible differences in the intervention effect*)

Yes No Unclear

**Is the intervention likely to be aimed at disadvantaged groups?** (*e.g. lower socioeconomic groups*)

Yes No Unclear

**Does the study directly address the review question?**

(*any issues of partial or indirect applicability*)

Yes No Unclear

**Notes:**

## 10. Other information

**Description as stated in  
report/paper**

**Location in text**  
(*pg & ¶/fig/table*)

**Key conclusions of study authors**

**References to other relevant studies**

**Correspondence required for further study information** (*from whom, what and when*)

**Notes:**

## WHAT'S NEW

Date	Event	Description
20 December 2018	Amended	Editorial team changed to Cochrane Emergency and Critical Care

## CONTRIBUTIONS OF AUTHORS

Conceiving of the review: Sara Mayfield (SM).

Co-ordinating the review: SM.

**High-flow nasal cannula therapy for respiratory support in children (Review)**

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Undertaking manual searches: SM.

Screening search results: SM and Jacqui Jauncey-Cooke (JJ-C).

Organizing retrieval of papers: SM.

Screening retrieved papers against inclusion criteria: SM and JJ-C.

Appraising quality of papers: SM, JJ-C and Judith L Hough (JH).

Abstracting data from papers: SM and JJ-C.

Writing to authors of papers for additional information: SM.

Providing additional data about papers: SM.

Obtaining and screening data on unpublished studies: SM.

Managing data for the review: SM, JJ-C and Fiona Bogossian (FB).

Entering data into Review Manager ([RevMan 5.2](#)): SM.

Interpreting data: SM, JJ-C, FB, JH and Andreas Schibler (AS).

Making statistical inferences: SM, JJ-C, FB and Kristen Gibbons (KG).

Writing the review: SM.

Serving as guarantor for the review (one author): FB.

Taking responsibility for reading and checking the review before submission: JJ-C, FB, AS and JH.

## **DECLARATIONS OF INTEREST**

Sara Mayfield and Andreas Schibler have received financial and equipment support from Fisher Paykel Healthcare to conduct two observational studies involving HFNC therapy. These studies would not be eligible for inclusion in this review.

Jacqueline Jauncey-Cooke: none known.

Judith L Hough: none known:

Kristen Gibbons: none known.

Fiona Bogossian: none known.

## **DIFFERENCES BETWEEN PROTOCOL AND REVIEW**

Initially we planned to include all paediatric patients requiring HFNC therapy; however, because of the overlap with another Cochrane Review of HFNC in infants with bronchiolitis ([Beggs 2012](#)), we excluded children with bronchiolitis from our review.

## **INDEX TERMS**

### **Medical Subject Headings (MeSH)**

Masks; Oxygen Inhalation Therapy [\*methods]; Respiration, Artificial [\*methods]

### **MeSH check words**

Child; Humans