Devices and pressure sources for administration of nasal continuous positive airway pressure (NCPAP) in preterm neonates (Review)

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[Intervention Review]

Devices and pressure sources for administration of nasal continuous positive airway pressure (NCPAP) in preterm neonates

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ABSTRACT

Background

Nasal continuous positive airway pressure (NCPAP) is used to support preterm infants recently extubated, those experiencing significant apnoea of prematurity and those with respiratory distress soon after birth as an alternative to intubation and ventilation. This review focuses exclusively on identifying the most effective pressure source and interface for NCPAP delivery in preterm infants.

Objectives

To determine which technique of pressure generation and which type of nasal interface for NCPAP delivery most effectively reduces the need for additional respiratory support in preterm infants extubated to NCPAP following intermittent positive pressure ventilation (IPPV) for respiratory distress syndrome (RDS) or in those treated with NCPAP soon after birth.

Search strategy

The strategy included searches of MEDLINE (1966 - 2006), the Cochrane Central Register of Controlled Trials (CENTRAL, The Cochrane Library, Issue 4, 2006) CINAHL, abstracts from conference proceedings, cross-referencing of previous reviews and the use of expert informants.

Selection criteria

Randomised or quasi-randomised trials comparing different techniques of NCPAP pressure generation and/or nasal interfaces in preterm infants extubated to NCPAP following IPPV for RDS or treated with NCPAP soon after birth.

Data collection and analysis

Data was extracted and analysed by the first three authors. Dichotomous results were analysed using the relative risk (RR), risk difference (RD) and number needed to treat (NNT).

Main results

1. Preterm infants being extubated to NCPAP following a period of IPPV for RDS:

Meta-analysis of the results from Davis 2001 and Roukema 1999a demonstrated that short binasal prongs are more effective at preventing re-intubation than single nasal or nasopharyngeal prongs [typical RR 0.59 (CI: 0.41, 0.85), typical RD -0.21 (CI: -0.35, -0.07), NNT 5 (CI: 3, 14)]. In one study comparing short binasal prong devices (Sun 1999), the re-intubation rate was significantly lower with the Infant Flow Driver than with the Medicorp prong [RR 0.33 (CI: 0.17, 0.67), RD -0.32 (CI: -0.49, -0.15), NNT 3 (CI: 2, 7)]. The other study comparing short binasal prong devices (Infant Flow Driver versus INCA prongs, Stefanescu 2003) demonstrated no significant difference in the re-intubation rate but did show a significant reduction in the total days in hospital in the Infant Flow Driver group [MD -12.60 (95% CI: -22.81, -2.39) days].

2. Preterm infants primarily treated with NCPAP soon after birth:

In the one trial identified, Mazzella 2001 found a significantly lower oxygen requirement and respiratory rate in those randomised to short binasal prongs when compared with CPAP delivered via nasopharyngeal prong. The requirement for intubation beyond 48 hours from randomisation was not assessed.

3. Studies randomising preterm infants to different NCPAP systems using broad inclusion criteria

The studies of Rego 2002 and Buettiker 2004 did not examine the primary outcomes of this review. Of the secondary outcomes, Rego 2002 demonstrated a significantly higher incidence of nasal hyperaemia with the use of the Argyle prong compared with Hudson prongs [RR 2.39 (95% CI: 1.27, 4.50), RD 0.28 (95% CI: 0.10, 0.46)].

One study comparing different techniques of pressure generation is awaiting further assessment as it is currently available in abstract form only.

Authors' conclusions

Short binasal prong devices are more effective than single prongs in reducing the rate of re-intubation. Although the Infant Flow Driver appears more effective than Medicorp prongs the most effective short binasal prong device remains to be determined. The improvement in respiratory parameters with short binasal prongs suggests they are more effective than nasopharyngeal CPAP in the treatment of early RDS. Further studies incorporating longer-term outcomes are required. Studies are also needed to determine the optimal pressure source for the delivery of NCPAP.

PLAIN LANGUAGE SUMMARY

Devices and pressure sources for administration of nasal continuous positive airway pressure (NCPAP) in preterm neonates

After weaning preterm babies from a ventilator, short binasal prong devices for NCPAP (nasal continuous positive airways pressure) are more effective than single prong devices. Nasal continuous positive airway pressure (NCPAP) is a form of breathing support that is less invasive than mechanical ventilation (where a tube goes down into a baby's lungs). NCPAP usually delivers oxygen to a baby through tubes into the nose, or less commonly, through face masks. It can be used after weaning a baby from ventilation (extubation), or to help babies who need help for lung problems, but do not need ventilation. The review of trials found that short binasal prongs (entering both nostrils) are better than single prong NCPAP for preterm babies. More research is needed on the best pressure delivery system and the best pressure levels to use.

BACKGROUND

Nasal continuous positive airway pressure (NCPAP) is used widely to provide respiratory support for preterm neonates. In physiological terms NCPAP has been shown to:

1. increase functional residual capacity (Richardson 1978) and improve oxygenation (Krouskop 1975; Harris 1976; Yu 1977),

2. dilate the larynx (Gaon 1999), reduce supraglottic airway resistance (Miller 1990) and lessen the incidence of obstructive apnoea (Miller 1985),

3. improve the synchrony of respiratory thoracoabdominal movements (Locke 1991) and

4. enhance the Hering-Breuer inflation reflex following airway occlusion (Martin 1977).

NCPAP is clinically effective in the post-extubation period; however, the optimal method of administration is an area requiring further research (Davis 2000). NCPAP is also an alternative to intubation and mechanical ventilation for the support of preterm neonates with respiratory distress soon after birth. However, a systematic review found insufficient evidence to provide recommendations for its application in this clinical setting (Subramaniam 2000).

CPAP has been applied to preterm infants using an array of devices. Its first application to the preterm neonate with respiratory distress was via an endotracheal tube or by enclosure of the head in a plastic pressure chamber (Gregory 1971). Subsequent CPAP devices included a pressurised plastic bag fitted over the infant's head (Barrie 1972), face chambers (Ahlstrom 1973) and face masks (Harris 1972; Rhodes 1973; Ackerman 1974). The use of tight-fitting facial masks and devices requiring a neck seal declined as a consequence of serious complications associated with their application, including an increased incidence of cerebellar haemorrhage (Pape 1976) and post-haemorrhagic hydrocephalus (Vert 1973). Nasal devices remained popular, as they facilitated better access to the infants (Chernick 1973). Given the infrequent use of other methods of CPAP in current clinical practice, this review will focus exclusively on nasal interfaces and modes of pressure generation used in NCPAP delivery.

NASAL INTERFACES

Nasal masks, nasal cannulae, and single and binasal tubes/prongs of varying lengths, ending at either the nasal or nasopharyngeal level, have been developed.

- Nasal masks

An early means of applying CPAP to neonates (Chernick 1973; Cox 1974), nasal masks lost popularity because of the difficulty in maintaining an adequate seal and a tendency to cause nasal airway obstruction (Kattwinkel 1973). Although new masks have been developed and are in clinical use, they have not been subjected to comparison with other devices.

- Single prong

Single prong CPAP, either nasopharyngeal or short nasal, is a relatively simple technique (Ahluwalia 1998). Single prong CPAP continues to be widely used despite a criticism of inefficiency (Field 1985). The comparison of single with binasal prong interfaces comprises part of this review.

- Binasal prongs

Binasal prongs, when introduced to deliver CPAP, proved simple, effective and safe to use, but had the potential to cause nasal trauma (Kattwinkel 1973; Agostino 1973). A number of binasal devices are now in use including Argyle prongs (Kamper 1990), Hudson prongs (Wung 1975; So 1992) and INCA prongs (Courtney 2001). With the realisation that binasal prongs might result in a significant increase in work of breathing (Goldman 1979), efforts were directed at designing a nasal interface that would minimise this by reducing airway resistance and fluctuations in airway pressure (Moa 1988). The resultant short-pronged binasal devices, currently known as Infant Flow or Aladdin Generators (EME, UK), are engineered to allow sufficient flow to the infant on inspiration while minimising expiratory resistance. Work with lung models (Moa 1988; Klausner 1996) and a small study on preterm neonates with minimal lung disease (Pandit 2001) demonstrated a reduced work of breathing when compared with conventional devices. However, limited randomised cross-over (Ahluwalia 1998) and non-randomised (Kavvadia 2000) clinical studies found no significant difference in short-term physiological parameters when comparing the Infant Flow system with single prong NCPAP.

- Nasopharyngeal prongs

Prongs inserted to the nasopharyngeal level have been used to deliver CPAP since the 1970's (Novogroder 1973; Boros 1976). Nasopharyngeal prongs received early criticism because they were perceived to be poorly tolerated and difficult to insert when compared with short nasal tube insertion (Caliumi-Pell. 1974). However, the use of nasopharyngeal tubes became established in clinical practice and featured in trials which examined both binasal (Higgins 1991) and single (Annibale 1994) forms.

- Nasal cannulae

Nasal cannulae are most often used in neonates to deliver supplemental oxygen at low flows (<0.5 L/min) with no intention of generating significant airway pressure. Despite their relatively small

calibre, nasal cannulae with an outer diameter of 3 mm and flows up to 2 L/min were reported to increase intra-oesophageal pressure and reduce thoracoabdominal motion asynchrony (Locke 1993). CPAP via nasal cannulae (flow up to 2.5 L/min) has been reported to be comparable with conventional NCPAP via nasal prongs in the management of apnoea of prematurity (Sreenan 2000). Optimal flow settings, appropriate cannula size, the delivery of adequate humidification and the effect on important outcomes with this nasal interface require further research.

In common with naso-endotracheal tubes, NCPAP interfaces have the potential to cause nasal excoriation and scarring if inappropriately applied or infrequently monitored (Loftus 1994; Robertson 1996). It is not clear which NCPAP device is least likely to cause nasal trauma.

TECHNIQUES FOR PRESSURE GENERATION

Techniques for CPAP generation include:

- Expiratory flow valve (e.g. ventilator)

The use of variable resistance valves on the expiratory limb of NCPAP circuits is a common method of generating pressure. This is usually achieved through the use of a ventilator.

- Underwater tube 'bubble' CPAP (underwater expiratory resistance)

Underwater bubble CPAP remains in use since first devised in the early 1970's (Gregory 1971). It is a simple and effective technique for generating pressure. A comparison of underwater bubble endotracheal (ET) CPAP with ventilator derived ETCPAP in preterm neonates suggested that the bubbling contributed to gas exchange (Lee 1998); however, this effect not been studied when applied via the nasal route.

- Benveniste device (pressure generation at nasal level: gas jet device connected to nasal prong/s)

The Benveniste paediatric gas jet device first delivered CPAP to the neonate via a face mask or by endotracheal tube (Benveniste 1976). Subsequent study of this device for NCPAP demonstrated that a high gas flow of 14 L/minute was required to create a pressure of between 3 and 10.5 cm H_2O in the oropharynx. No significant difference in oropharyngeal pressure was noted whether the flow was delivered by single or binasal tube (Pedersen 1994). The Benveniste jet device, in conjunction with a binasal tube (Argyle prong), has been described as a simple and effective NCPAP system for preterm infants (Kamper 1990).

- Infant Flow Driver (IFD) system (pressure generation in Infant Flow 'Generator' at nasal level: adapted directly to Infant Flow short binasal prongs)

The IFD system (EME, UK) has a conventional flow source with a manometer. Pressure in the system is created at the level of the nasal device ('Generator') to which short binasal prongs, specifically made by EME for this device, are attached. The pressure generated in this device is controlled directly by adjusting the flow. Owing to their design the IFD prongs cannot be connected to other CPAP pressure systems.

OBJECTIVES

The two primary objectives for each group were to determine:

a) Which technique of pressure generation for the delivery of NCPAP most effectively reduces the need for additional respiratory support and,

b) Which type of NCPAP interface most effectively reduces the need for additional respiratory support?

The two groups to be investigated were:

1. Preterm infants extubated to NCPAP following a period of intermittent positive pressure ventilation (IPPV) for respiratory distress syndrome (RDS) and,

2. Preterm infants initially treated with NCPAP soon after birth, either prophylactically or as treatment for RDS.

METHODS

Criteria for considering studies for this review

Types of studies

Only randomised and quasi-randomised studies were included.

Types of participants

1. Preterm infants (<37 weeks gestation) extubated to NCPAP following a period of intermittent positive pressure ventilation (IPPV) for respiratory distress syndrome. Infants were intubated and ventilated at the time of study entry.
2. Preterm infants (<37 weeks gestation) initially treated with NCPAP soon after birth, either prophylactically or as treatment for respiratory distress syndrome. NCPAP treatment was begun within 24 hours of birth.

Types of interventions

Interventions in each group of participants were to comprise:
a) A comparison of the following techniques of pressure generation for the delivery of NCPAP:

i) Underwater bubble NCPAP vs. NCPAP delivered by ventilator
ii) Underwater bubble NCPAP vs. NCPAP delivered by Benveniste device
iii) NCPAP delivered by ventilator vs. NCPAP delivered by Benveniste device
b) A comparison of NCPAP interfaces categorised as:
i) Short single vs. short binasal (double) prongs (nasal cannulae, Hudson prongs, Argyle prongs, IFD devices, INCA prongs or other double nasal prong interfaces) ii) Any short binasal prong vs. any other short binasal prong
iii) Single nasal (short) vs. long (nasopharyngeal) prongs
iv) Short binasal vs. long prongs
v) Single nasal or long prong vs. short binasal prongs*
Comparisons conducted after review of available data, i.e. not included in the published protocol, are asterixed (*).

Types of outcome measures

Primary outcome for both groups of participants:
The proportion requiring additional respiratory support either by endotracheal intubation and IPPV or nasal intermittent positive pressure ventilation (NIPPV) within a period of 7 days* following randomisation.
Secondary outcomes for both groups of participants:
a) Symptoms of respiratory failure*
b) 'Rescue' by alternate NCPAP device or mode of pressure generation*
c) Chronic lung disease incidence by comparison of:

- supplemental oxygen requirement at 28 days of life
- supplemental oxygen requirement at 36 weeks postmenstrual age
- requirement for home oxygen therapy

d) Incidence of air leak following randomisation: pneumothorax, pulmonary interstitial emphysema, pneumomediastinum
e) Incidence of apnoea and bradycardia expressed as events per hour
f) Effectiveness of gas exchange by comparison of mean:

- arterial or capillary pH
- arterial, capillary or transcutaneous oxygen and carbon dioxide partial pressures
- oxygen saturation and fraction of inspired oxygen
- respiratory rate*

g) Total duration of NCPAP or endotracheal intubation in days
h) Rates of gastrointestinal complications:

- necrotising enterocolitis (NEC)
- gastrointestinal perforation
- feeding intolerance as determined by days to establish enteral feeds of 150 mls/kg/day
- feeding intolerance as defined by large or bilious gastric aspirates*
- abdominal distension resulting in cessation of enteral feeding

i) Weight gain:

- time to regain birth weight
- weight at 28 days of life
- weight gain from extubation to discharge*
- weight gain in the week post-extubation*

j) Rate of sepsis: culture positive and suspected
k) Incidence of intraventricular haemorrhage (IVH) and periventricular leukomalacia (PVL) identified post-randomisation
l) Incidence of retinopathy of prematurity (ROP)
m) Long-term neurosensory outcomes at 2 years corrected age or older as defined by the incidence of:

- cerebral palsy
- moderate to severe developmental delay
- blindness
- deafness

n) Mortality
o) Utilisation of resources as defined by days in hospital and total days in oxygen (see (g) above for days of ventilation and NCPAP)
Subgroup analysis was planned according to trials using, or not using, methylxanthines to determine the impact of methylxanthine use on these outcomes. Additional subgroup analysis based on participant characteristics (e.g. stratification on birth weight or gestational age at intervention) was planned if appropriate. The subgroup of trials randomising to different NCPAP interfaces was also planned, to determine the incidence of nasal scarring.
A sensitivity analysis including only true randomised trials was planned if quasi-randomised trials were identified.
Outcome measures not specified a priori (included or modified after review of the available trials) are asterixed (*).

Search methods for identification of studies

The standard search strategy of the Neonatal Review Group of the Cochrane Collaboration was used. MEDLINE (1966 - December 2006) was searched using the MeSH terms: infant, newborn (exp) and positive-pressure respiration (exp) with keywords/phrases: continuous positive airway pressure or continuous distending pressure. The Cochrane Central Register of Controlled Trials (CENTRAL, The Cochrane Library, Issue 4, 2006) and CINAHL were also searched. Language restrictions were not applied. Abstracts published by the Society for Pediatric Research and the European Society for Pediatric Research were searched for

the period 1996 to 2006. Cross referencing of previous reviews and expert informants were also used.

Data collection and analysis

The standard method of the Cochrane Collaboration and its Neonatal Review Group was used. Trial searching, methodologic assessment and data extraction were performed independently by the first three authors before comparison and resolution of differences at each stage. Methodology was assessed by adequacy of blinding of randomisation, blinding of intervention, completeness of follow-up and blinding of outcome measurement. The authors were contacted for further information for completeness of data or study methodology. Additional unpublished data were supplied by Drs Sun (results for the outcomes: 'Death', 'Chronic lung disease', 'Air leak', 'Sepsis', 'NEC' and 'Days of respiratory support') and Davis (results for the outcome: 'NEC', and means and standard deviations for the outcomes: 'Days of respiratory support' and 'Days in level III hospital').
Categorical data (e.g. number requiring additional respiratory support) were analysed using relative risk (RR), risk difference (RD) and number needed to treat (NNT). Meta-analysis of continuous data (e.g. number of days of CPAP) was to be performed with the weighted mean difference (WMD) using the fixed effect model. Confidence intervals of 95% were adopted.

RESULTS

Description of studies

See: Characteristics of included studies; Characteristics of excluded studies.

1. Preterm infants extubated to NCPAP following a period of IPPV for RDS

Four studies (Stefanescu 2003; Davis 2001; Roukema 1999a and Sun 1999) that compared different NCPAP devices in the period following endotracheal intubation and ventilation for RDS were identified for inclusion. The studies of Stefanescu 2003 (162 infants) and Davis 2001 (87 infants) were available as a full journal publications, whereas the studies of Roukema 1999a (93 infants) and Sun 1999 (100 infants) remain available in abstract form only. The study by Stefanescu 2003 could also be considered in the category of studies comparing different methods of NCPAP pressure generation. It is included in the comparison of different nasal interfaces ('Any short binasal prong vs. any other short binasal prong') as the different nasal interfaces used were considered the main point of difference between the two systems compared in this trial. Details of these studies are included in the table 'Characteristics of Included Studies'.

All four studies randomised intubated, very low birth weight, preterm infants at the time of extubation. Detailed extubation criteria are available only for Davis 2001; Stefanescu 2003 and Sun 1999 (low ventilatory requirements). Details of methylxanthine usage are only available for Davis 2001, where all infants were loaded with theophylline at the time of extubation, and Stefanescu 2003, where the study protocol mandated universal methylxanthine treatment prior to extubation.

The NCPAP interventions in each study were:

- Stefanescu 2003 randomised infants to either Infant Flow Driver (short binasal prongs) or INCA prongs (short binasal prongs)
- Davis 2001 randomised infants to either single prong or to binasal (Hudson) prong NCPAP
- Sun 1999 randomised infants to NCPAP via Medicorp prongs (short binasal prongs) or Infant Flow Driver (short binasal prongs)
- Roukema 1999a randomised infants to NCPAP via nasopharyngeal prong or Infant Flow Driver

The initial NCPAP pressure settings are known for the studies of Stefanescu 2003 (4-6 cmH_2O), Davis 2001 (7 cmH_2O) and Sun 1999 (5 cmH_2O). The initial set NCPAP flow is known only for the study of Davis 2001 (6 L/min). The starting pressure and flow settings were the same for both treatment arms in these studies.
Davis 2001 and Sun 1999 defined their primary outcome as meeting respiratory failure criteria within the seven days following extubation. The decision to re-intubate in Davis 2001 was at the discretion of the attending physician, whereas re-intubation was performed in Sun 1999 if the pre-determined failure criteria were met. For Stefanescu 2003 and Roukema 1999a the primary outcome was defined as remaining extubated in the seven days post-extubation. Crossover to, or 'rescue' by the alternative mode of NCPAP was not permitted by any study.

2. Preterm infants initially treated with NCPAP soon after birth, either prophylactically or as treatment for RDS

Mazzella 2001 was the only study published in full that randomised only preterm neonates with early RDS to different NCPAP devices. Infants of less than 36 weeks' gestation with RDS at less than 12 hours of age were randomly allocated to receive NCPAP either via single nasopharyngeal tube or via the Infant Flow system (short binasal prongs). These infants were on average more mature (32 - 33 weeks' gestation) than those enrolled in the studies comparing NCPAP devices in the post-extubation period (26 weeks' gestation). Those infants who had received antenatal corticosteroids or were intubated at delivery were excluded. The initial NCPAP pressure setting for both groups was 4 cmH_2O, with the study protocol limiting the maximum pressure to 6 cmH_2O. The set flow rates for nasopharyngeal CPAP, usually 4 to 7 L/min, were reported as being sufficient to meet an infant's inspiratory flow

demand. For the Infant Flow system flows of 6 to 8 L/min were required to generate a pressure of 4 to 5 cmH_2O at the device. Caffeine citrate was begun in each infant from the time of enrolment.

The primary outcome was change in the oxygen requirement and/or respiratory rate within 48 hours. Secondary outcomes included the success rate of weaning and complications including death, intraventricular haemorrhage, air leak and chronic lung disease.

Cross-over to the alternative mode of NCPAP or intubation for surfactant treatment could be considered if an infant met respiratory failure criteria.

3. Studies randomising preterm infants to different NCPAP systems using broad inclusion criteria

Two studies, Rego 2002 and Buettiker 2004, randomised preterm infants to different NCPAP systems using inclusion criteria that resulted in significant heterogeneity in the clinical conditions of those randomised. Consequently, infants with early respiratory distress, infants requiring post-extubation support and infants with other indications for respiratory support were potentially eligible and were randomised. The infants in these studies were comparatively more mature than those included in the trials randomising infants only in the post-extubation setting.

Rego 2002 randomised a total of 71 neonates ≤ 2500 g with RDS, transient tachypnoea of the newborn, apnoea of prematurity, pneumonia and those requiring post-extubation support. Infants were randomised to NCPAP delivered either by Argyle prongs or via Hudson prongs, with pressure in both groups generated by conventional ventilator. Analysis was by mode of NCPAP treatment, stratified by weight category (≤ 1000 g, 1000 to 1500 g, 1500 to 2500 g) but not by clinical inclusion criteria, thus rendering the study difficult to assess according to the *a priori* criteria of this review. The primary outcome was CPAP 'success' defined as avoiding intubation and weaning off CPAP without requiring recommencement of respiratory support in the 72 hours following cessation. This primary outcome does not meet the *a priori* requirements of this review however some of the secondary outcomes, including the incidence of air leak and nasal trauma, are applicable.

Buettiker 2004 randomised a total of 40 newborn infants with respiratory distress to three different NCPAP systems: Infant Flow NCPAP system, single prong nasopharyngeal CPAP and Hudson prong NCPAP. Only six out of a total of 20 patients in the strata with weight > 2500 g were preterm infants and therefore this subgroup was not considered for analysis as the subjects did not meet the *a priori* inclusion criteria for this review. The strata of infants of weight 1250 to 2500 g (median 1790 g) were all preterm (<37 weeks gestation) and hence could be considered for analysis. Inclusion criteria were heterogeneous with randomised infants in the 1250 to 2500 g (median 1790 g) strata requiring support for respiratory distress syndrome, post-extubation support (randomisation pre-extubation not specified), meconium aspiration syndrome, respiratory syncytial virus infection, neuromuscular disorders and necrotising enterocolitis. The primary outcomes of this study included the length of NCPAP treatment and the incidence of nasal trauma but did not encompass the *a priori* primary outcome of this review.

4. Studies awaiting further assessment

Colaizy 2004: This study is currently published in abstract form only. Very low birth weight and preterm infants (< 1500 g; 24 to 32 weeks gestation) with early RDS were randomised to NCPAP generated either via an underwater bubble system or via a conventional ventilator. Hudson prongs were used as the nasal interface in each arm of the trial. Each group was treated with a NCPAP pressure of 5 cmH_2O. Outcomes included 'CPAP failures', 'CPAP complications', days of supplemental oxygen, days of mechanical ventilation, length of hospital stay, incidence of chronic lung disease and surfactant use. Further information on this study is required to allow further assessment and inclusion in this review.

None of the included studies examined long-term neurodevelopment as an outcome.

Risk of bias in included studies

The criteria of the Neonatal Cochrane Review Group was used to assess methodological quality.

Allocation concealment

Allocation concealment was adequate for Stefanescu 2003; Davis 2001; Sun 1999 and Mazzella 2001. Rego 2002 randomised infants by drawing lots. Further information on allocation concealment is required on the studies of Roukema 1999a and Buettiker 2004.

Blinding of intervention

No study attempted to blind the intervention.

Completeness of follow-up

Adequate follow-up was accomplished in all trials except Rego 2002 where three infants were excluded from analysis for complications as their time on NCPAP was less than two hours.

Blinding of outcome assessment

In the study by Stefanescu 2003, the radiologists assessing cranial ultrasounds were blinded to the treatment allocation. Blinding of outcome assessment was not attempted in any of the other trials.

Effects of interventions

A total of seven studies met inclusion criteria for the review. Four studies (Stefanescu 2003; Davis 2001; Roukema 1999a and Sun 1999) compared NCPAP interfaces in the prevention of extubation failure. One study (Mazzella 2001) compared NCPAP interfaces in the treatment of early respiratory distress. Two studies (Buettiker 2004 and Rego 2002) compared different NCPAP devices for a mixed group of neonatal respiratory conditions. While the primary outcomes of Buettiker 2004 and Rego 2002 did not

satisfy the a priori criteria of this review some of the secondary outcomes were relevant.

PRETERM INFANTS EXTUBATED TO NCPAP FOLLOWING A PERIOD OF IPPV

INFANT FLOW DRIVER (SHORT BINASAL) VS. INCA PRONG (SHORT BINASAL) NCPAP TO PREVENT EXTUBATION FAILURE (COMPARISON 05): Stefanescu 2003

- ***Endotracheal intubation within 7 days post-extubation (Outcome 05.01):***

There was no significant difference in the rate of re-intubation between those randomised to Infant Flow Driver versus INCA prong NCPAP [RR 1.01 (95% CI: 0.68, 1.49), RD 0.00 (95% CI: -0.15, 0.15)].

- ***Other outcomes (Outcomes 05.02 - 05.06):***

Comparing infants randomised to the Infant Flow Driver versus the INCA prong there were no statistically significant differences in the outcomes of death [RR 2.87 (95% CI: 0.79, 10.44), RD 0.07 (95% CI: -0.01, 0.15) trend favouring INCA prong], chronic lung disease [at 36 weeks postmenstrual age, RR 0.86 (95% CI: 0.65, 1.14), RD -0.08 (95% CI: -0.24, 0.07)], grade 3 and 4 intraventricular haemorrhage [RR 0.85 (95% CI: 0.41, 1.75), RD -0.03 (95% CI: -0.14, 0.09)], periventricular leukomalacia, retinopathy of prematurity, air leak, sepsis and necrotising enterocolitis. However, in the Infant Flow Driver group there was a significantly lower duration of hospital stay [MD -12.60 (95% CI: -22.81, -2.39) days] and lower total days of supplemental oxygen [MD -11.50 (95% CI: -21.74, -1.26) days] when compared to the INCA prong group.

SHORT BINASAL PRONG VS. SINGLE NASAL PRONG CPAP TO PREVENT EXTUBATION FAILURE (Comparison 01): Davis 2001

- ***Endotracheal intubation within 7 days post-extubation (Outcome 01.01.01):***

A trend, not reaching statistical significance, favoured the use of short binasal prongs in preventing re-intubation [RR 0.53 (CI: 0.27, 1.04), RD -0.19 (CI: -0.38, 0.00)].

- ***Respiratory failure within 7 days post-extubation (Outcome 01.01.02):***

Infants extubated to NCPAP using short binasal prongs had a statistically and clinically significantly lower incidence of respiratory failure [RR 0.43 (CI: 0.24, 0.78), RD -0.32 (CI: -0.52, -0.13)]. Three (CI: 2, 8) infants would need to be treated with short binasal rather than single nasal prongs to avoid respiratory failure in one infant.

- ***Other outcomes (Outcomes 01.02 - 01.07):***

No statistically significant differences were found for rates of complications including death [RR 1.68 (CI: 0.30, 9.58), RD 0.03 (CI: -0.07, 0.13)], chronic lung disease [at 36 weeks postmenstrual age: RR 0.80 (CI: 0.54, 1.18), RD -0.12 (CI: -0.33, 0.09)], intraventricular haemorrhage [RR 1.68 (CI: 0.30, 9.58), RD 0.03 (CI: -0.07, 0.13)], retinopathy of prematurity, sepsis or feeding intolerance. Weight gain, both in the week post-extubation and to the time of discharge, was not significantly different between the two treatment arms. [See Comparison 01 tables: 'Death', 'Chronic lung disease', 'Non-pulmonary outcomes' (IVH, PVL, ROP, sepsis, feeding intolerance, NEC), 'Weight gain', 'Days of respiratory support' and 'Resource utilisation' (days in level III hospital)].

INFANT FLOW DRIVER (SHORT BINASAL) VS. MEDICORP PRONG (SHORT BINASAL) NCPAP TO PREVENT EXTUBATION FAILURE (Comparison 02): Sun 1999

- ***Endotracheal intubation within 7 days following extubation (Outcome 02.01):***

Infants in both arms of this study were extubated to short binasal prongs. However, the likelihood of re-intubation in the week following extubation in those randomised to the Infant Flow Driver was lower at a statistically and clinically significant level [RR 0.33 (CI: 0.17, 0.67), RD -0.32 (CI: -0.49, -0.15), NNT 3 (CI: 2, 7)]. All those infants that met respiratory failure criteria were re-intubated.

- ***Other outcomes (Outcomes 02.02 - 02.05):***

No statistically significant differences were present for the outcomes of death (no deaths in either group), chronic lung disease [at 36 weeks postmenstrual age: RR 0.86 (CI: 0.31, 2.37), RD -0.02 (CI: -0.15, 0.11)], air leak, sepsis or necrotising enterocolitis. [See Comparison 02 tables: 'Death', 'Pulmonary outcomes' (chronic lung disease and air leak), 'Non-pulmonary outcomes' (sepsis and NEC), and 'Days of respiratory support'].

SHORT BINASAL PRONG (INFANT FLOW DRIVER) VS. NASOPHARYNGEAL PRONG CPAP TO PREVENT EXTUBATION FAILURE (COMPARISON 03): Roukema 1999a

- ***Endotracheal intubation within 7 days following extubation (Outcome 03.01):***

Those extubated to the short binasal prong (Infant Flow Driver) had a lower rate of re-intubation [RR 0.63 (CI: 0.40, 0.97), RD -0.23 (CI: -0.42, -0.03), NNT 4 (CI: 2, 33)] when compared with the nasopharyngeal prong group. This result is statistically and clinically significant.

- ***Other outcomes***

Results for other outcomes are not yet available.

SHORT BINASAL PRONG VS. SINGLE PRONG (NASAL OR NASOPHARYNGEAL) NCPAP TO PREVENT EXTUBATION FAILURE (COMPARISON 04): Davis 2001 and Roukema 1999a

- ***Endotracheal intubation within 7 days following extubation (Outcome 04.01):***

Meta-analysis of this outcome in the studies by Davis 2001 and Roukema 1999a showed a statistically significant and clinically important benefit for those extubated to short binasal prongs [typical RR 0.59 (CI: 0.41, 0.85), typical RD -0.21 (CI: -0.35, -0.07), NNT 5 (CI: 3, 14)].

- ***Other outcomes (Outcomes 04.02 - 04.07):***

Meta-analysis of other outcomes will not be possible until results from the full publication of the study by Roukema 1999a are available. The available results in the remaining tables for Comparison 04 are as per Comparison 01 (Davis 2001).
Subgroup analysis in these studies according to methylxanthine use is not possible. Methylxanthine use was universal in Davis 2001 and almost universal in Stefanescu 2003 (3 in the Infant Flow Driver group and 7 in the INCA prong group did not receive methylxanthine therapy pre-extubation) but is not yet known for Roukema 1999a or Sun 1999. No information on rates of nasal trauma is available for these trials.

PRETERM INFANTS INITIALLY TREATED WITH NCPAP SOON AFTER BIRTH, EITHER PROPHYLACTICALLY OR AS A TREATMENT FOR RDS

SHORT BINASAL PRONG VS. NASOPHARYNGEAL (SINGLE TUBE) CPAP FOR EARLY RESPIRATORY DISTRESS (COMPARISON 06): Mazzella 2001

- ***Endotracheal intubation and respiratory failure within 7 days post-randomisation (Outcome 06.01):***

These outcomes were not assessed beyond 48 hours from randomisation. There was no significant difference in these outcomes for this limited period.

- ***Oxygen requirement and respiratory rate***

The oxygen requirement and respiratory rate were significantly lower ($p < 0.0001$, as calculated by Mazzella 2001) in the short binasal prong group over the 48 hours following randomisation. This outcome is not able to be represented as a mean difference as the study used univariate repeated measures analysis.

- ***Other outcomes (Outcomes 06.02 - 06.05):***

There were no cases of death, chronic lung disease or IVH in either group. No significant differences were found for the rates of pneumothorax or nasal trauma. [See Comparison 06 tables: 'Death', 'Pulmonary outcomes' (chronic lung disease and pneumothorax), 'Non-pulmonary outcomes' (IVH and nasal trauma), 'Total days of respiratory support'].
Subgroup analysis according to methylxanthine use was not possible as all infants in Mazzella 2001 received caffeine citrate.

STUDIES RANDOMISING PRETERM INFANTS TO DIFFERENT NCPAP SYSTEMS USING BROAD INCLUSION CRITERIA

ARGYLE PRONG (SHORT BINASAL) VS. HUDSON PRONG (SHORT BINASAL) CPAP FOR PRETERM INFANTS REQUIRING RESPIRATORY SUPPORT (COMPARISON 07): Rego 2002

- ***Respiratory failure and endotracheal intubation within 7 days post-randomization for respiratory distress syndrome or post-extubation support***

This outcome was not assessed in this study. The primary outcome assessed in this trial of successful weaning from NCPAP was not an *a priori* outcome of this review. NCPAP was considered to have failed in those patients who required intubation to receive surfactant at the attending clinician's discretion. It is not possible from the published results to determine the number of infants that were intubated in each clinical category (apnoea, respiratory distress syndrome, pneumonia, transient tachypnoea of the newborn and post-extubation support) or in each treatment arm (Argyle prong versus Hudson prong). It is also important to note that no respiratory failure or intubation criteria were specified. The absence of such criteria may lead to intervention bias as the clinicians are not blinded to the mode of NCPAP.

- ***Other outcomes (Outcomes 07.01 - 07.02):***

Infants randomised to Argyle prong NCPAP had a significantly higher incidence of nasal hyperaemia compared to those treated with Hudson prong NCPAP when the results of all weight categories are combined [RR 2.39 (95% CI: 1.27, 4.50), RD 0.28 (95% CI: 0.10, 0.46)]. When the authors analysed the incidence of nasal hyperaemia in each of the three weight strata ($\leq$ 1000 g, 1000-1500 g, 1500-2500 g) the increase in nasal hyperaemia in the Argyle prong group only reached statistical significance for those infants in the $\leq$ 1000 g subgroup. There was no significant difference in the incidence of nasal bleeding and there were no cases of nasal septum necrosis. The published results do not permit sub-analysis of the nasal trauma incidence according to the clinical category of the infants at the time of randomisation. There were no cases of pneumothorax in either arm of the study.

INFANT FLOW DRIVER (SHORT BINASAL) VS. HUDSON PRONG (SHORT BINASAL) VS. NASOPHARYNGEAL (SINGLE PRONG) CPAP FOR NEWBORN INFANTS REQUIRING RESPIRATORY SUPPORT - Buettiker 2004
The results for infants in the > 2500 g weight strata were excluded as these infants were predominantly term.

- ***Respiratory failure and endotracheal intubation within 7 days post-randomization for respiratory distress syndrome or post-extubation support***

This was not the primary outcome for this trial. In the 1250 to 2500 g weight strata four infants required intubation (two for respiratory distress syndrome and two for neuromuscular disease). The results do not specify the NCPAP devices to which these four infants were randomised.

- ***Other outcomes***

The primary outcomes in this trial included the duration of nasal CPAP treatment and the frequency of nasal trauma. In the 1250 to 2500 g weight strata the overall median duration of CPAP was 1.1 (range 0.1 - 7) days with no significant difference between the three groups. Of the 20 infants in this stratum, 3 infants of 6 on Infant Flow Driver, 2 infants of 6 on Hudson prong and 2 infants of 8 on nasopharyngeal CPAP developed a nasal injury with no statistically significant difference between these groups.

DISCUSSION

1. Preterm infants being extubated to NCPAP following a period of IPPV for RDS

The four included studies are methodologically sound, although further information is awaited on the study of Roukema 1999a on allocation concealment. As it is impractical to blind caregivers to the NCPAP intervention it is possible that bias in the use of co-interventions may have occurred. Only Stefanescu 2003 and Davis 2001 at present account for the use of methylxanthines. Criteria for respiratory failure and/or indications for intubation are clearly described in Stefanescu 2003; Davis 2001 and Sun 1999 reducing the potential for bias, however this information is not available for the study of Roukema 1999a.

Short binasal prong devices appear to be more effective than single prong devices in reducing both the symptoms of respiratory failure and the rate of re-intubation. It is likely that short binasal prongs are more effective at transmitting the prescribed pressure to the airway than single prong devices and as a result reduce the chances of respiratory failure. While the infant's own nasal airway has resistance to air flow, the passage of a nasopharyngeal prong through the nasal passage reduces the diameter of the airway and increases this resistance. Air-leak out through the contralateral nostril (which has no prong *in situ*) is likely to significantly diminish the applied pressure. Other outcomes such as chronic lung disease and gastrointestinal complications appear not to be influenced by device type. However, the numbers randomised to date are small and further data from completed trials is awaited.

In the direct comparisons of short binasal prong devices the Infant Flow Driver was shown to be more effective than Medicorp prongs (Sun 1999) at preventing re-intubation in the week post-extubation. This should not be extrapolated to the type of pressure generation (i.e. that the Infant Flow system is more effective than a ventilator at generating CPAP) as the result may be attributable to a higher resistance to flow in the Medicorp prong. The appearance of the Medicorp prong (personal communication with Dr Shyan Sun) closely resembles that of the Argyle prong which has a relatively higher resistance to flow compared to other types of double prong (De Paoli 2002).

The trial of Stefanescu 2003 comparing the Infant Flow Driver with the INCA prong demonstrated that there was a significantly lower duration of hospital stay in the Infant Flow Driver group. However, there were no significant differences in other clinically important outcomes.

The design of the included studies did not permit a direct comparison of techniques of pressure generation. Although the structure of the Infant Flow binasal prong is such that it cannot be connected to other systems, a comparison of the Infant Flow system of pressure generation with another (e.g. ventilator or underwater bubbler) remains feasible. This can be achieved if the resistance of the binasal prongs to flow in each arm of the study (Infant Flow prongs have a low resistance) is comparable to allow equivalent transmission of pressure to the airway. The most effective and least traumatic short binasal device remains to be determined.

2. Preterm infants initially treated with NCPAP soon after birth, either prophylactically or as treatment for RDS

The single study comparing a nasopharyngeal with a short binasal prong in this population of infants (Mazzella 2001) was powered to detect significant changes in oxygen requirement. Although oxygen requirements and respiratory rates were lower in the short binasal prong group any important differences in other outcomes, such as requirement for endotracheal intubation, would be difficult to detect because of the small number of infants randomised. The greater relative maturity of these infants and the exclusion of any who had received antenatal steroids reduces the generalizability of these results.

3. Studies randomising preterm infants to different NCPAP systems using broad inclusion criteria

Any conclusions that may be drawn from the studies of Rego 2002 and Buettiker 2004 are limited by their broad inclusion of more mature preterm infants requiring respiratory support for many different clinical indications, although many of those included required treatment for respiratory distress syndrome or post-extubation support. The primary outcomes as specified in this review were not examined. In both studies, there was no significant difference between the NCPAP devices used for the outcome of air leak. Rego 2002 showed that Argyle prongs were more likely to cause nasal hyperaemia when compared with Hudson prongs. Buettiker 2004 showed no significant difference in the rates of nasal trauma between the NCPAP devices investigated. Both of these trials were limited in their capacity to show significant differences in the rates of nasal trauma because the more mature preterm infants enrolled in these studies required relatively short times on NCPAP.

AUTHORS' CONCLUSIONS

Implications for practice

1. Preterm infants being extubated to NCPAP following a period of IPPV for RDS

Short binasal prong devices are more effective than single prongs in reducing the likelihood of the short-term adverse outcomes of re-intubation and respiratory failure. In a single study (available in abstract form only) the Infant Flow system appears more effective than Medicorp prongs. Although the comparison of the Infant Flow Driver with INCA prong NCPAP demonstrated a shorter hospital stay for the Infant Flow Driver treated group, there were no significant differences in the primary outcome or in other more important secondary outcomes. Consequently, the most effective short binasal prong device remains to be determined. It is unclear whether the superiority of the Infant Flow system demonstrated in these studies is attributable to its prongs or to its method of generating pressure.

2. Preterm infants initially treated with NCPAP soon after birth, either prophylactically or as treatment for RDS

The reduction in oxygen requirements and respiratory rate with short binasal prongs suggests they are more effective than single prong nasopharyngeal CPAP in the treatment of RDS. The short-term primary outcomes of this trial do not allow conclusions to be made on some medium-term (e.g. chronic lung disease at 36 weeks postmenstrual age) and long-term outcomes.

At present the only randomised trial directly comparing different pressure sources for NCPAP delivery (Colaizy 2004) is only available in abstract form and further data is required before its inclusion in this review. The choice of pressure source may then be based on cost-effectiveness and ease of use.

Implications for research

Further research in preterm infants requiring NCPAP for respiratory support is required to focus on defining the optimal short binasal prong devices. In addition to assessing important longer-term outcomes such as mortality, chronic lung disease, time on respiratory support, length of hospital stay, gastrointestinal complications and neurodevelopment, attention should also be directed at determining which device is least traumatic to the infant nose, particularly in very low birth weight infants. Studies comparing nasal devices should ensure that the prescribed starting pressure at the nasal level is the same and that sufficient flow to meet inspiratory demands is applied in each treatment arm. Randomised studies comparing different techniques of pressure generation need to control for the resistance of the nasal prong in each group. Comparisons of pressure generation via the Infant Flow system, underwater bubble system and via ventilator would be of most interest.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Buettiker 2004

Methods	Method of randomisation: not specified. Intervention blinded: no Follow-up complete. Blinding of outcome assessment not specified.
Participants	Neonates with respiratory distress of birthweight 1250g or greater and less than or equal to 28 days of life. Total number randomised: 40 (1250-2500g: 20, >2500g: 20) Inclusion criteria for both non-intubated infants and those after extubation: 1. Clinical signs of respiratory distress and, 2. FiO2 >0.4 and PaCO2 >52mmHg (or capillary PCO2> 56mmHg) Exclusions: 1. Congenital heart disease 2. Necrotising enterocolitis 3. Upper airway anomalies One infant with neuromuscular disease and one with Jeune syndrome included.
Interventions	1. Naso- pharyngeal CPAP via a single tube attached to a conventional ventilator (n = 16) 2. NCPAP via Hudson prongs attached to a conventional ventilator (n = 12) 3. NCPAP via IFD CPAP pressure routinely used: 3-5 cmH2O. Flow not specified.
Outcomes	1. Nasal trauma 2. Air leak syndromes 3. CPAP tube blockage
Notes	

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Davis 2001

Methods	Blinding of randomisation: yes; sealed, opaque, sequentially numbered envelopes Intervention blinded: no Complete follow-up: yes Outcome assessment blinded: no
Participants	Ventilated preterm infants prior to extubation Total randomised: 87 1. BW <1000g 2. Intubated 3. Ventilator rate <= 20/min 4. FiO2 <= 0.5 5. Clinician agrees to extubation 6. Loaded with aminophylline
Interventions	Experimental: NCPAP via Hudson prongs attached to conventional ventilator (n = 41) Control: NCPAP via single prong (Portex tube size 2.5 or 3.0) inserted to 2.5 cm, attached to conventional ventilator (n = 46) Both groups had set flows of 6 L/min and initial pressures of 7 cmH2O
Outcomes	Respiratory failure defined as 1. frequent apnoea requiring stimulation or episode requiring bag and mask ventilation, 2. FiO2 15% above extubation level, 3. pH< 7.25 with PCO2 > 50 mmHg Other outcomes included: Need for additional respiratory support within the 7 days following removal of the endotracheal tube death, BPD, IVH, PVL, ROP sepsis, feeding intolerance, weight gain, days of respiratory support, days in level III hospital
Notes	Planned sample size of 130 however trial was stopped after 87 on the advice of an external monitoring committee, based on a prespecified stopping rule.

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	A - Adequate

Mazzella 2001

Methods	Blinding of randomisation: yes; sealed, numbered envelopes Intervention blinded: no Complete follow-up: yes Outcome assessment blinded: no
Participants	Non-intubated preterm infants with early respiratory distress Total randomised: 36 1. GA < 36 weeks 2. age < 12 hours 3. PCO2 < 65 mmHg 4. FiO2 > 30% 5. CXR showing poor lung expansion

Mazzella 2001 (*Continued*)

	Exclusion: 1. Major congenital malformation 2. Neuromuscular diseases 3. Severe birth asphyxia 4. Overwhelming infection 5. Severe apnoea 6. PDA 7. Intubation at delivery 8. Antenatal steroids
Interventions	Experimental: NCPAP via IFD (n = 18) Control: Single nasopharyngeal tube, pressure generated by underwater seal (n = 18) Both groups' starting pressure: 4 cmH2O (could be increased to a maximum of 6 cmH2O) Flow in IFD group 6-8L/min Flow in nasopharyngeal group 4-7 L/min
Outcomes	Primary: change in O2 requirement and / or respiratory rate Secondary: included success rate of weaning from NCPAP, death, IVH, oxygen dependency at day 28, pneumothorax, nasal trauma
Notes	

Risk of bias

Item	**Authors' judgement**	**Description**
Allocation concealment?	Yes	A - Adequate

Rego 2002

Methods	Randomisation by drawing lots. Intervention blinded: no Follow-up: incomplete as 3 infants were excluded from analysis for complications as their time on NCPAP was less than 2 hours. Blinding of outcome assessment not specified.
Participants	Neonates (total randomised = 99) requiring NCPAP for primary respiratory support (n=71) or for post-extubation support (n=28) of weight <= 2500g. Primary respiratory support inclusion criteria: 1. Silverman-Anderson retraction score of >3 or, 2. Increasing FiO2 to maintain PaO2>50mmHg or, 3. PaCO2 >60mmHg and pH<7.20 or, 4. Three or more apnoeic episodes during a 4 hour period or apnoeic episodes requiring vigorous stimulation, increased FiO2 or mask ventilation. Primary respiratory support diagnoses: 1. Respiratory distress syndrome [n=34] 2. Transient tachypnoea of the newborn [n=21], 3. Apnoea of prematurity (n=12)

Rego 2002 (*Continued*)

	4. Pneumonia (n=4) Post-extubation: Ventilated infants placed on NCPAP when peak inspiratory pressure <16cmH2O and respiratory rate <20/minute Exclusions: major cardiac disease or facial malformations.
Interventions	1. Hudson prong NCPAP delivered by conventional ventilator with pressure fixed at 5cmH2O and flow from 5 to 10 L/minute. 2. Argyle prong CPAP delivered by conventional ventilator with pressure fixed at 5cmH2O and flow from 5 to 10 L/minute.
Outcomes	1. CPAP 'success' defined as avoiding intubation and weaning off CPAP without requiring recommencement of CPAP in the 72 hours following cessation. Discontinuation of CPAP was at the discretion of attending staff. 2. Respiratory rate 3. Heart rate 3. Silverman-Anderson retraction score 4. pH and pCO2 before, and 2, 24, and 48 hours after commencement of NCPAP (arterial and capillary specimens). 5. Hours on NCPAP. 6. Frequency of abdominal distension. 7. Frequency per 24 hours of requirement for device removal from the nostrils 8. Nasal trauma (hyperaemia, bleeding, septum necrosis)
Notes	Heterogeneous diagnoses in primary respiratory support group (including respiratory distress and apnoea of prematurity).

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	A - Adequate

Roukema 1999a

Methods	Blinding of randomisation: unclear Intervention blinded: no Complete follow-up: yes Outcome assessment blinded: no
Participants	Ventilated preterm infants prior to extubation Total randomised: 93 1. BW < 1251g 2. Intubated 3. Decision made to extubate Exclusion: 1. Signs of upper airway obstruction 2. Airway anomalies

Roukema 1999a (*Continued*)

Interventions	Experimental: NCPAP via IFD (n = 48) Control: 'Conventional' nasopharyngeal CPAP. Pressure and flow not stated (n = 45)
Outcomes	Primary outcome: remaining extubated for 7 days Indications for intubation or respiratory failure criteria not stated
Notes	Randomisation was blocked into three weight groups (250g increments).

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Stefanescu 2003

Methods	Blinding of randomisation: yes; table of random numbers and sealed opaque envelopes. Randomisation stratified into three birth weight blocks: <= 600g, 601 to 800g, and 801 to 1000g. Intervention blinded: no Complete follow-up: yes. Outcome assessment blinding: limited to blinding of radiologists (assessing cranial ultrasounds)to treatment allocation.
Participants	Ventilated preterm infants of birth weight <= 1000g prior to first extubation attempt. Suggested extubation criteria: 1. Mean airway pressure <= 5 cmH2O on conventional ventilation or <= 7cmH2O on high frequency ventilation 2. FiO2 <= 0.3 3. pH >= 7.25 4. pCO2 <= 65 mmHg Total randomised: 162 Exclusions: 1. Major chromosomal anomalies. 2. Known airway anomalies. 3. Neuromuscular disorders 4. Other major congenital malformations 5. Participation in a concurrent randomised controlled trial.
Interventions	Experimental: Infant Flow NCPAP system. Control: INCA binasal prongs with pressure generation via conventional ventilator. Commencing NCPAP pressure for both treatment arms: 4-6 cmH2O. Flow not specified for either treatment arm. Minimum of 24 hours of NCPAP treatment for both arms. Protocol specified administration of methylxanthine therapy to all infants prior to extubation.

Stefanescu 2003 (*Continued*)

Outcomes	Primary outcome: reduction in the percentage of infants failing extubation defined as the requirement for re-intubation within 168 hours (7 days) of extubation. Criteria for re-intubation: 1. SaO2 < 88% in FiO2 >= 0.5. 2. PaCO2 >= 65 mmHg with arterial pH < 7.25 3. CPAP requirement > 8 cmH2O. 4. Recurrent significant apnoea or bradycardia. Secondary outcomes: 1. Death 2. Survival without BPD 3. Number of days on CPAP 4. Days on supplemental oxygen 5. Length of hospitalisation 6. Necrotising enterocolitis 7. Patent ductus arteriosus 8. Sepsis 9. Intraventricular haemorrhage
Notes	

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	A - Adequate

Sun 1999

Methods	Blinding of randomisation: yes, sealed envelopes, mixed and picked at random Intervention blinded: no Complete follow-up: yes Outcome assessment blinded: no
Participants	Ventilated preterm infants prior to extubation Total randomised: 100 1. GA < 31 weeks 2. BW < 1251g 3. Respiratory distress syndrome 4. Intubated 5. MAP < 7 cmH2O 6. FiO2 <= 0.30 7. Daily caloric intake: >= 50 kcal/kg/day for >=12 hours
Interventions	Experimental: NCPAP via IFD Control: 'Conventional' NCPAP system (Medicorp nasal prongs: short binasal) Commencing pressures: IFD: flow adjusted to attain pressure of

Sun 1999 (*Continued*)

	5 cmH2O (n = 50) Conventional: expiratory valve adjusted to attain pressure of 5 cmH2O (n = 50)
Outcomes	Failure of extubation defined as: 1. NCPAP required > 8 cmH2O, 2. FiO2 > 0.60 to maintain SaO2 at 88-95%, 3. PCO2 > 65 mmHg with pH < 7.25, 4. recurrent apnoeas / bradycardias
Notes	

Risk of bias

Item	**Authors' judgement**	**Description**
Allocation concealment?	Yes	A - Adequate

BPD: bronchopulmonary dysplasia
PVL: periventricular leucomalacia
ROP: retinopathy of prematurity
IVH: intraventricular haemorrhage
GA: gestational age
PDA: patent ductus arteriosus
IFD: Infant flow driver
MAP: mean airway pressure

Characteristics of excluded studies *[ordered by study ID]*

Ahluwalia 1998	This randomised study did not examine the target preterm population for this review (ie immediately post-extubation or needing primary treatment for respiratory distress syndrome). Any infant treated with NCPAP and supplemental oxygen was eligible.
Bhandari 1996	This comparison of nasal versus naso-pharyngeal CPAP was non randomized and retrospective.
Campbell 2004	This study compared Infant Flow CPAP with high-flow nasal cannulae. High-flow nasal cannulae is not a CPAP system that has an intrinsic pressure monitoring or pressure relief/blow-off system and does not meet the inclusion criteria for this review.
Courtney 2001	Although randomising infants to different NCPAP devices this study did not examine the target population for the review. They examined preterm infants treated with NCPAP for apnoea or mild respiratory distress.
Jonsson 1998	Although randomised this study did not examine the target population for this review. Infants were randomised on day 3 of life after prior NCPAP treatment.

(*Continued*)

Kavvadia 2000	This study was non-randomised. Single prong and Infant Flow NCPAP were compared in the post-extubation period.
Liptsen 2005	This study compared bubble NCPAP with variable-flow NCPAP in preterm infants, however the outcome measures of work of breathing and breathing asynchrony did not meet the inclusion criteria for this review.
Massaro 2005	This study was a non-randomized and retrospective comparison of bubble (underwater seal) CPAP and ventilator-derived CPAP and hence did not meet the inclusion criteria for this review.
Nair 2005	This study compared the Vapotherm system (high flow nasal cannula system) with bubble nasal CPAP (prong type not specified)in preterm infants. Vapotherm (high-flow nasal cannula system) is not a NCPAP system that monitors pressure or has a pressure relief/blow-off system and hence was not included in this review.
Narendran 2002	This study in extremely low birth weight infants used historical controls to compare bubble nasal CPAP with conventional CPAP (specific CPAP type not specified)and hence did not meet the inclusion criteria.
Pandit 2001	This study did not examine the target population for this review (infants with minimal lung disease were studied) or a priori outcomes applicable to the review.
Pelligra 2006	This study of CPAP in preterm infants used historical controls to compare bubble CPAP with conventional, ventilator-derived nasopharyngeal CPAP and hence did not meet inclusion criteria.
Roukema 1999b	Non-randomised evaluation of those 'unsuccessful' infants attempting extubation on second and subsequent attempts, using the alternative CPAP method to that used on the first attempt in the included study: Roukema H, et al, A randomized controlled trial of infant flow continuous positive airway pressure (CPAP) versus nasopharyngeal CPAP in the extubation of babies <=1250g (abstr), Pediatr Res, 1999;45:318A.
Sreenan 2001	This study examined infants with apnoea of prematurity and hence is not the target population for this review.
Telenko 1999	Although randomised did not study the target population for this review. Examined a population of preterm infants with apnoea of prematurity only.
Trevisanuto 2005	This study compared Infant Flow nasal CPAP with CPAP delivered via a polycarbonate helmet. Helmet CPAP does not meet the a priori inclusion criteria of nasal interfaces for CPAP delivery.
Yong 2005	This study randomized very low birth weight infants to either nasal mask or via nasal masks are not currently in our inclusion criteria. to include this trial we would have to include this as a post-hoc comparison of interfaces. No outcomes assessed other than nasal trauma.

DATA AND ANALYSES

Comparison 1. Short binasal prong vs single nasal prong CPAP to prevent extubation failure

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Extubation failure	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 Endotracheal intubation within 7 days post-extubation	1	87	Risk Ratio (M-H, Fixed, 95% CI)	0.53 [0.27, 1.04]
1.2 Respiratory failure within 7 days post-extubation	1	87	Risk Ratio (M-H, Fixed, 95% CI)	0.43 [0.24, 0.78]
2 Death	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
3 Chronic lung disease	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
3.1 Supplemental oxygen at day 28 of life	1	87	Risk Ratio (M-H, Fixed, 95% CI)	0.85 [0.63, 1.15]
3.2 Supplemental oxygen at corrected gestational age of 36 weeks	1	87	Risk Ratio (M-H, Fixed, 95% CI)	0.80 [0.54, 1.18]
4 Non-pulmonary outcomes	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
4.1 Intraventricular haemorrhage	1	87	Risk Ratio (M-H, Fixed, 95% CI)	1.68 [0.30, 9.58]
4.2 Periventricular leukomalacia	1	86	Risk Ratio (M-H, Fixed, 95% CI)	0.16 [0.01, 3.08]
4.3 Retinopathy of prematurity	1	83	Risk Ratio (M-H, Fixed, 95% CI)	1.14 [0.81, 1.60]
4.4 Sepsis: culture positive	1	87	Risk Ratio (M-H, Fixed, 95% CI)	1.02 [0.66, 1.58]
4.5 Sepsis: suspected	1	87	Risk Ratio (M-H, Fixed, 95% CI)	0.93 [0.60, 1.44]
4.6 Feeding intolerance: large or bilious gastric aspirates (in the 7 days after randomisation)	1	87	Risk Ratio (M-H, Fixed, 95% CI)	1.25 [0.76, 2.07]
4.7 Necrotising enterocolitis	1	87	Risk Ratio (M-H, Fixed, 95% CI)	2.24 [0.21, 23.84]
5 Weight gain	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
5.1 Weight gain from extubation to discharge (g/day)	1	87	Mean Difference (IV, Fixed, 95% CI)	1.0 [-1.76, 3.76]
6 Days of respiratory support	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
6.1 Total days on NCPAP	1	87	Mean Difference (IV, Fixed, 95% CI)	-4.19 [-11.74, 3.36]
6.2 Total days intubated	1	87	Mean Difference (IV, Fixed, 95% CI)	-3.39 [-10.22, 3.44]
6.3 Total days of respiratory support (NCPAP and intubation)	1	87	Mean Difference (IV, Fixed, 95% CI)	-6.35 [-16.99, 4.29]
7 Resource utilisation	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
7.1 Total days in level III hospital	1	87	Mean Difference (IV, Fixed, 95% CI)	-4.62 [-23.45, 14.21]

Comparison 2. Infant Flow Driver (short binasal) vs Medicorp prong (short binasal) NCPAP to prevent extubation failure

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Extubation failure	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 Endotracheal intubation within 7 days post-extubation	1	100	Risk Ratio (M-H, Fixed, 95% CI)	0.33 [0.17, 0.67]
2 Death	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
3 Pulmonary outcomes	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
3.1 Chronic lung disease: supplemental oxygen at day 28 of life	1	100	Risk Ratio (M-H, Fixed, 95% CI)	0.6 [0.33, 1.09]
3.2 Chronic lung disease: supplemental oxygen at corrected gestational age of 36 weeks	1	100	Risk Ratio (M-H, Fixed, 95% CI)	0.86 [0.31, 2.37]
3.3 Chronic lung disease: home oxygen therapy	1	100	Risk Ratio (M-H, Fixed, 95% CI)	0.17 [0.02, 1.33]
3.4 Air leak	1	100	Risk Ratio (M-H, Fixed, 95% CI)	1.5 [0.26, 8.60]
4 Non-pulmonary outcomes	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
4.1 Culture positive sepsis	1	100	Risk Ratio (M-H, Fixed, 95% CI)	1.09 [0.53, 2.24]
4.2 Necrotising enterocolitis	1	100	Risk Ratio (M-H, Fixed, 95% CI)	0.8 [0.23, 2.81]
5 Days of respiratory support	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
5.1 Total days of NCPAP	1	100	Mean Difference (IV, Fixed, 95% CI)	1.10 [-3.73, 5.93]

Comparison 3. Short binasal prong (Infant Flow Driver) vs nasopharyngeal prong CPAP to prevent extubation failure

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Extubation failure	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
1.1 Endotracheal intubation within 7 days post-extubation	1		Risk Ratio (M-H, Fixed, 95% CI)	Not estimable

Comparison 4. Short binasal prong vs single prong (nasal or nasopharyngeal) NCPAP to prevent extubation failure

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Extubation failure	2		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 Endotracheal intubation within 7 days post-extubation	2	180	Risk Ratio (M-H, Fixed, 95% CI)	0.59 [0.41, 0.85]
1.2 Respiratory failure within 7 days post-extubation	1	87	Risk Ratio (M-H, Fixed, 95% CI)	0.43 [0.24, 0.78]
2 Death	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
3 Chronic lung disease	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
3.1 Supplemental oxygen at day 28 of life	1	87	Risk Ratio (M-H, Fixed, 95% CI)	0.85 [0.63, 1.15]
3.2 Supplemental oxygen at corrected gestational age of 36 weeks	1	87	Risk Ratio (M-H, Fixed, 95% CI)	0.80 [0.54, 1.18]
4 Non-pulmonary outcomes	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
4.1 Intraventricular haemorrhage	1	87	Risk Ratio (M-H, Fixed, 95% CI)	1.68 [0.30, 9.58]
4.2 Periventricular leukomalacia	1	86	Risk Ratio (M-H, Fixed, 95% CI)	0.16 [0.01, 3.08]
4.3 Retinopathy of prematurity	1	83	Risk Ratio (M-H, Fixed, 95% CI)	1.14 [0.81, 1.60]
4.4 Sepsis: culture positive	1	87	Risk Ratio (M-H, Fixed, 95% CI)	1.02 [0.66, 1.58]
4.5 Sepsis: suspected	1	87	Risk Ratio (M-H, Fixed, 95% CI)	0.93 [0.60, 1.44]
4.6 Feeding intolerance: large or bilious gastric aspirates (in the 7 days following randomisation)	1	87	Risk Ratio (M-H, Fixed, 95% CI)	1.25 [0.76, 2.07]
4.7 Necrotising enterocolitis	1	87	Risk Ratio (M-H, Fixed, 95% CI)	2.24 [0.21, 23.84]
5 Weight gain	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
5.1 Weight gain from extubation to discharge (g/day)	1	87	Mean Difference (IV, Fixed, 95% CI)	1.0 [-1.76, 3.76]
6 Days of respiratory support	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
6.1 Total days on NCPAP	1	87	Mean Difference (IV, Fixed, 95% CI)	-4.19 [-11.74, 3.36]
6.2 Total days intubated	1	87	Mean Difference (IV, Fixed, 95% CI)	-3.39 [-10.22, 3.44]
6.3 Total days of respiratory support (NCPAP and intubation)	1	87	Mean Difference (IV, Fixed, 95% CI)	-6.35 [-16.99, 4.29]
7 Resource utilisation	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
7.1 Total days in level III hospital	1	87	Mean Difference (IV, Fixed, 95% CI)	-4.62 [-23.45, 14.21]

Comparison 5. Infant Flow Driver (short binasal) vs INCA prong (short binasal) to prevent extubation failure

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Endotracheal intubation within 7 days post-extubation	1	162	Risk Ratio (M-H, Fixed, 95% CI)	1.01 [0.68, 1.49]
2 Death	1	162	Risk Ratio (M-H, Fixed, 95% CI)	2.87 [0.79, 10.44]
3 Chronic lung disease	1	162	Risk Ratio (M-H, Fixed, 95% CI)	0.86 [0.65, 1.14]
3.1 Supplemental oxygen and CXR changes at corrected gestational age of 36 weeks	1	162	Risk Ratio (M-H, Fixed, 95% CI)	0.86 [0.65, 1.14]
4 PIE and gross air leak	1	162	Risk Ratio (M-H, Fixed, 95% CI)	0.96 [0.61, 1.51]
5 Non-pulmonary outcomes	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
5.1 Necrotising enterocolitis	1		Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
5.2 Sepsis: culture positive and suspected combined	1		Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
5.3 Intraventricular haemorrhage: grade 3 and 4	1		Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
5.4 Periventricular leukomalacia	1		Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
5.5 Retinopathy of prematurity: all grades	1		Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
6 Total days of NCPAP	1	162	Mean Difference (IV, Fixed, 95% CI)	-1.43 [-3.98, 1.12]
7 Days in oxygen	1	162	Mean Difference (IV, Fixed, 95% CI)	-11.5 [-21.74, -1.26]
8 Resource utilisation	1	162	Mean Difference (IV, Fixed, 95% CI)	-12.60 [-22.81, -2.39]
8.1 Total days in hospital	1	162	Mean Difference (IV, Fixed, 95% CI)	-12.60 [-22.81, -2.39]

Comparison 6. Short binasal prong vs nasopharyngeal (single tube) CPAP for early respiratory distress

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Treatment failure	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 Endotracheal intubation within 48 hours of randomisation	1	36	Risk Ratio (M-H, Fixed, 95% CI)	0.33 [0.04, 2.91]
1.2 Respiratory failure within 48 hours of randomisation	1	36	Risk Ratio (M-H, Fixed, 95% CI)	0.2 [0.03, 1.55]
1.3 Rescue by alternate NCPAP device	1	36	Risk Ratio (M-H, Fixed, 95% CI)	0.2 [0.01, 3.89]
2 Death	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
3 Pulmonary outcomes	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
3.1 Chronic lung disease (supplemental oxygen at 28 days)	1	36	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable

3.2 Pneumothorax	1	36	Risk Ratio (M-H, Fixed, 95% CI)	3.0 [0.13, 69.09]
4 Non-pulmonary outcomes	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
4.1 Intraventricular haemorrhage	1	36	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
4.2 Nasal trauma	1	36	Risk Ratio (M-H, Fixed, 95% CI)	9.0 [0.52, 155.86]
5 Total days of respiratory support	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only

Comparison 7. Hudson prong (short binasal) vs Argyle prong (short binasal) CPAP in preterm infants: broad inclusion criteria

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Nasal hyperaemia	1	96	Risk Ratio (M-H, Fixed, 95% CI)	0.42 [0.22, 0.79]
2 Nasal bleeding	1	96	Risk Ratio (M-H, Fixed, 95% CI)	1.34 [0.70, 2.58]

Analysis 1.1. Comparison 1 Short binasal prong vs single nasal prong CPAP to prevent extubation failure, Outcome 1 Extubation failure.

Review: Devices and pressure sources for administration of nasal continuous positive airway pressure (NCPAP) in preterm neonates

Comparison: 1 Short binasal prong vs single nasal prong CPAP to prevent extubation failure

Outcome: 1 Extubation failure

Study or subgroup	Short binasal n/N	Single nasal prong n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 Endotracheal intubation within 7 days post-extubation					
Davis 2001	9/41	19/46		100.0 %	0.53 [0.27, 1.04]
Subtotal (95% CI)	**41**	**46**		**100.0 %**	**0.53 [0.27, 1.04]**
Total events: 9 (Short binasal), 19 (Single nasal prong)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.84 (P = 0.065)					
2 Respiratory failure within 7 days post-extubation					
Davis 2001	10/41	26/46		100.0 %	0.43 [0.24, 0.78]
Subtotal (95% CI)	**41**	**46**		**100.0 %**	**0.43 [0.24, 0.78]**
Total events: 10 (Short binasal), 26 (Single nasal prong)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.77 (P = 0.0057)					

Analysis 1.2. Comparison 1 Short binasal prong vs single nasal prong CPAP to prevent extubation failure, Outcome 2 Death.

Review: Devices and pressure sources for administration of nasal continuous positive airway pressure (NCPAP) in preterm neonates

Comparison: 1 Short binasal prong vs single nasal prong CPAP to prevent extubation failure

Outcome: 2 Death

Study or subgroup	Short binasal n/N	Single nasal prong n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Davis 2001	3/41	2/46		1.68 [0.30, 9.58]

Analysis 1.3. Comparison 1 Short binasal prong vs single nasal prong CPAP to prevent extubation failure, Outcome 3 Chronic lung disease.

Review: Devices and pressure sources for administration of nasal continuous positive airway pressure (NCPAP) in preterm neonates

Comparison: 1 Short binasal prong vs single nasal prong CPAP to prevent extubation failure

Outcome: 3 Chronic lung disease

Study or subgroup	Short binasal n/N	Single nasal prong n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 Supplemental oxygen at day 28 of life					
Davis 2001	25/41	33/46		100.0 %	0.85 [0.63, 1.15]
Subtotal (95% CI)	**41**	**46**		**100.0 %**	**0.85 [0.63, 1.15]**
Total events: 25 (Short binasal), 33 (Single nasal prong)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.05 (P = 0.30)					
2 Supplemental oxygen at corrected gestational age of 36 weeks					
Davis 2001	20/41	28/46		100.0 %	0.80 [0.54, 1.18]
Subtotal (95% CI)	**41**	**46**		**100.0 %**	**0.80 [0.54, 1.18]**
Total events: 20 (Short binasal), 28 (Single nasal prong)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.11 (P = 0.27)					

Analysis 1.4. Comparison 1 Short binasal prong vs single nasal prong CPAP to prevent extubation failure, Outcome 4 Non-pulmonary outcomes.

Review: Devices and pressure sources for administration of nasal continuous positive airway pressure (NCPAP) in preterm neonates

Comparison: 1 Short binasal prong vs single nasal prong CPAP to prevent extubation failure

Outcome: 4 Non-pulmonary outcomes

Study or subgroup	Short binasal n/N	Single nasal prong n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 Intraventricular haemorrhage					
Davis 2001	3/41	2/46		100.0 %	1.68 [0.30, 9.58]
Subtotal (95% CI)	**41**	**46**		**100.0 %**	**1.68 [0.30, 9.58]**
Total events: 3 (Short binasal), 2 (Single nasal prong)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.59 (P = 0.56)					
2 Periventricular leukomalacia					
Davis 2001	0/40	3/46		100.0 %	0.16 [0.01, 3.08]
Subtotal (95% CI)	**40**	**46**		**100.0 %**	**0.16 [0.01, 3.08]**
Total events: 0 (Short binasal), 3 (Single nasal prong)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.21 (P = 0.23)					
3 Retinopathy of prematurity					
Davis 2001	25/38	26/45		100.0 %	1.14 [0.81, 1.60]
Subtotal (95% CI)	**38**	**45**		**100.0 %**	**1.14 [0.81, 1.60]**
Total events: 25 (Short binasal), 26 (Single nasal prong)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.75 (P = 0.45)					
4 Sepsis: culture positive					
Davis 2001	20/41	22/46		100.0 %	1.02 [0.66, 1.58]
Subtotal (95% CI)	**41**	**46**		**100.0 %**	**1.02 [0.66, 1.58]**
Total events: 20 (Short binasal), 22 (Single nasal prong)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.09 (P = 0.93)					
5 Sepsis: suspected					
Davis 2001	19/41	23/46		100.0 %	0.93 [0.60, 1.44]
Subtotal (95% CI)	**41**	**46**		**100.0 %**	**0.93 [0.60, 1.44]**
Total events: 19 (Short binasal), 23 (Single nasal prong)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.34 (P = 0.73)					
6 Feeding intolerance: large or bilious gastric aspirates (in the 7 days after randomisation)					
Davis 2001	19/41	17/46		100.0 %	1.25 [0.76, 2.07]
Subtotal (95% CI)	**41**	**46**		**100.0 %**	**1.25 [0.76, 2.07]**

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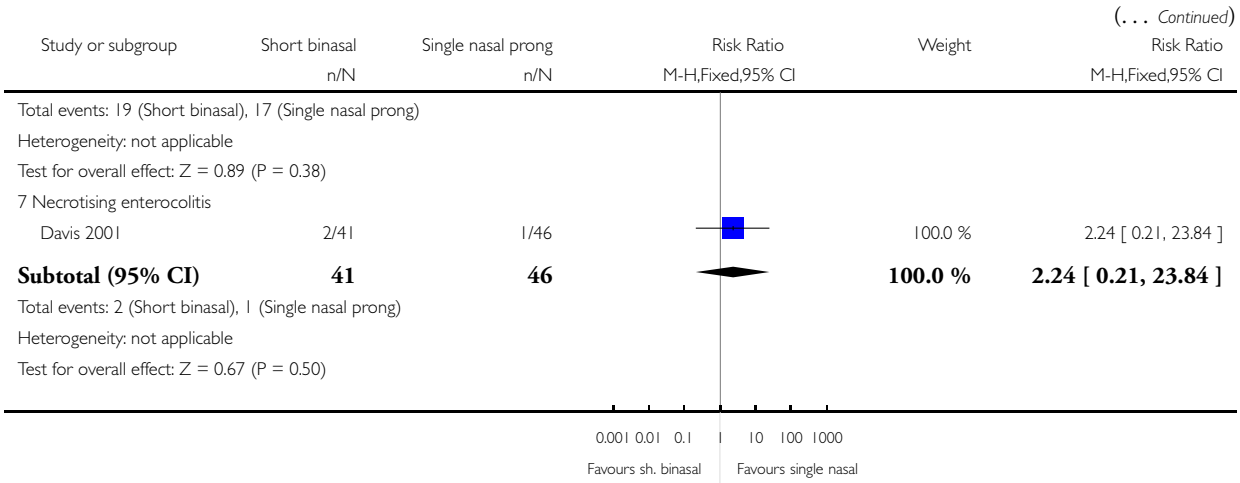
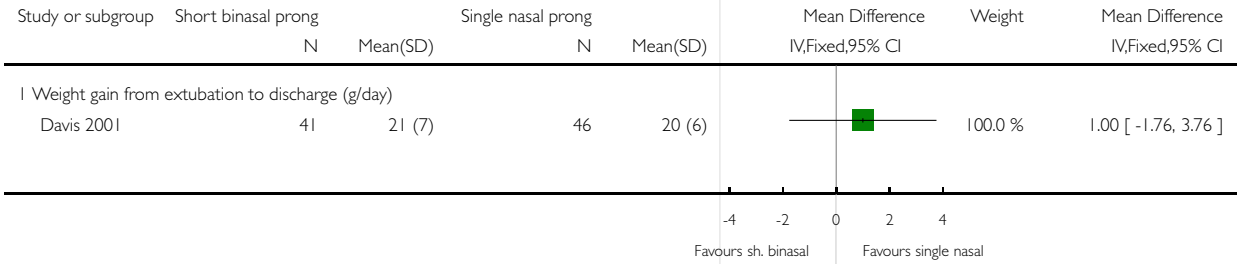


Analysis 1.5. Comparison 1 Short binasal prong vs single nasal prong CPAP to prevent extubation failure, Outcome 5 Weight gain.

Review: Devices and pressure sources for administration of nasal continuous positive airway pressure (NCPAP) in preterm neonates

Comparison: 1 Short binasal prong vs single nasal prong CPAP to prevent extubation failure

Outcome: 5 Weight gain



Analysis 1.6. Comparison 1 Short binasal prong vs single nasal prong CPAP to prevent extubation failure, Outcome 6 Days of respiratory support.

Review: Devices and pressure sources for administration of nasal continuous positive airway pressure (NCPAP) in preterm neonates

Comparison: 1 Short binasal prong vs single nasal prong CPAP to prevent extubation failure

Outcome: 6 Days of respiratory support

Study or subgroup	Short binasal prong N	Mean(SD)	Single nasal prong N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Total days on NCPAP							
Davis 2001	41	26.7 (16.59)	46	30.89 (19.34)		100.0 %	-4.19 [-11.74, 3.36]
Subtotal (95% CI)	**41**		**46**			**100.0 %**	**-4.19 [-11.74, 3.36]**
Heterogeneity: not applicable							
Test for overall effect: Z = 1.09 (P = 0.28)							
2 Total days intubated							
Davis 2001	41	13.85 (14.82)	46	17.24 (17.69)		100.0 %	-3.39 [-10.22, 3.44]
Subtotal (95% CI)	**41**		**46**			**100.0 %**	**-3.39 [-10.22, 3.44]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.97 (P = 0.33)							
3 Total days of respiratory support (NCPAP and intubation)							
Davis 2001	41	39.93 (24.68)	46	46.28 (25.91)		100.0 %	-6.35 [-16.99, 4.29]
Subtotal (95% CI)	**41**		**46**			**100.0 %**	**-6.35 [-16.99, 4.29]**
Heterogeneity: not applicable							
Test for overall effect: Z = 1.17 (P = 0.24)							
Test for subgroup differences: Chi^2 = 0.21, df = 2 (P = 0.90), I^2 =0.0%							

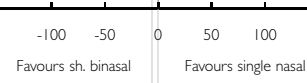
Analysis 1.7. Comparison 1 Short binasal prong vs single nasal prong CPAP to prevent extubation failure, Outcome 7 Resource utilisation.

Review: Devices and pressure sources for administration of nasal continuous positive airway pressure (NCPAP) in preterm neonates

Comparison: 1 Short binasal prong vs single nasal prong CPAP to prevent extubation failure

Outcome: 7 Resource utilisation

Study or subgroup	Short binasal prong N	Mean(SD)	Single nasal prong N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Total days in level III hospital							
Davis 2001	41	77.1 (35.5)	46	81.72 (53.2)		100.0 %	-4.62 [-23.45, 14.21]

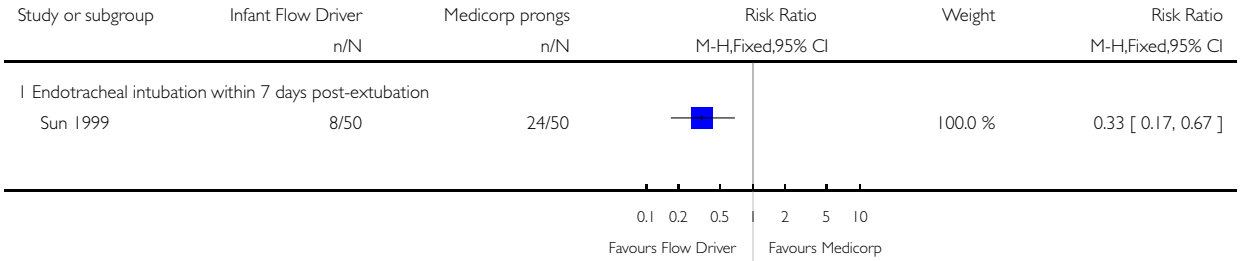


Analysis 2.1. Comparison 2 Infant Flow Driver (short binasal) vs Medicorp prong (short binasal) NCPAP to prevent extubation failure, Outcome 1 Extubation failure.

Review: Devices and pressure sources for administration of nasal continuous positive airway pressure (NCPAP) in preterm neonates

Comparison: 2 Infant Flow Driver (short binasal) vs Medicorp prong (short binasal) NCPAP to prevent extubation failure

Outcome: 1 Extubation failure

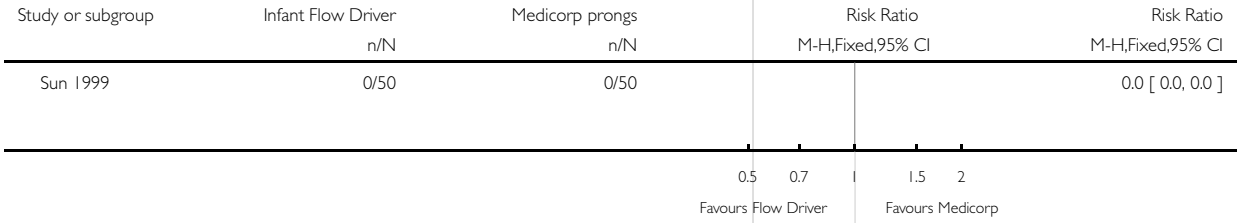


Analysis 2.2. Comparison 2 Infant Flow Driver (short binasal) vs Medicorp prong (short binasal) NCPAP to prevent extubation failure, Outcome 2 Death.

Review: Devices and pressure sources for administration of nasal continuous positive airway pressure (NCPAP) in preterm neonates

Comparison: 2 Infant Flow Driver (short binasal) vs Medicorp prong (short binasal) NCPAP to prevent extubation failure

Outcome: 2 Death

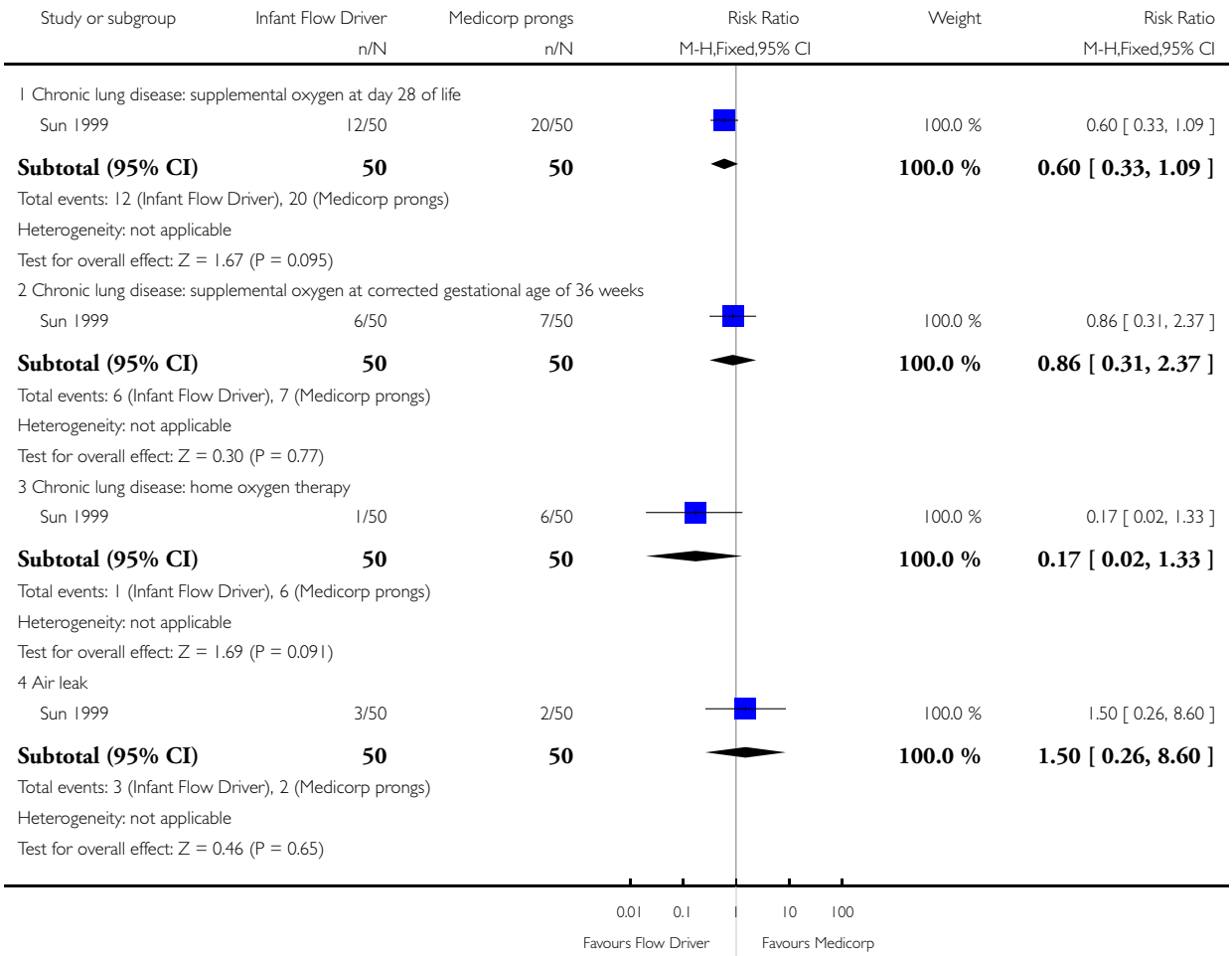


Analysis 2.3. Comparison 2 Infant Flow Driver (short binasal) vs Medicorp prong (short binasal) NCPAP to prevent extubation failure, Outcome 3 Pulmonary outcomes.

Review: Devices and pressure sources for administration of nasal continuous positive airway pressure (NCPAP) in preterm neonates

Comparison: 2 Infant Flow Driver (short binasal) vs Medicorp prong (short binasal) NCPAP to prevent extubation failure

Outcome: 3 Pulmonary outcomes

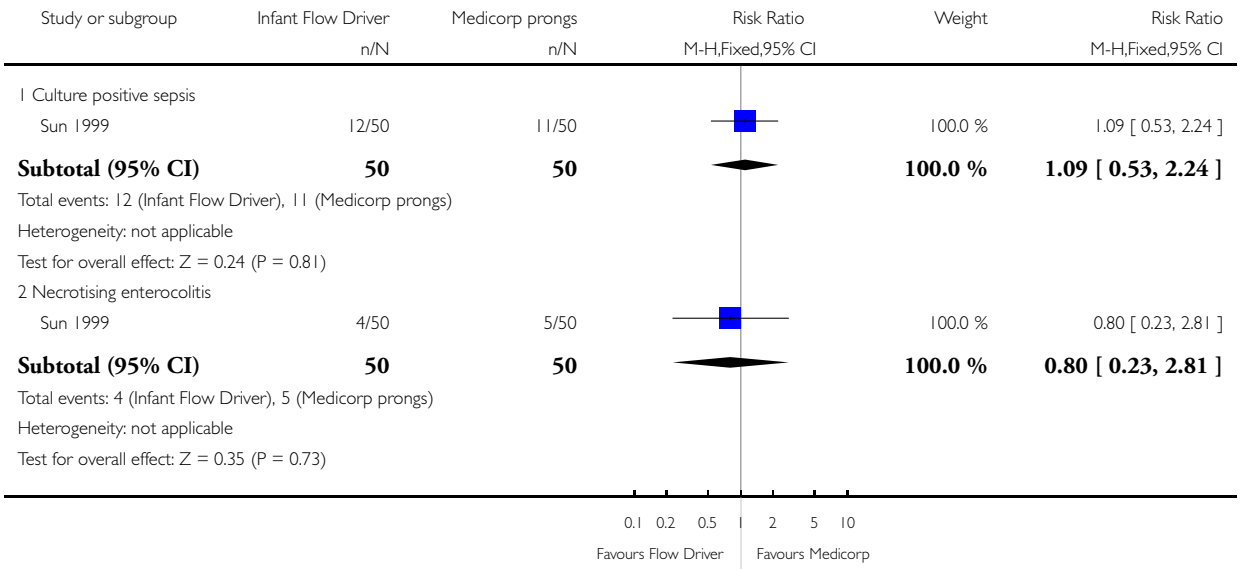


Analysis 2.4. Comparison 2 Infant Flow Driver (short binasal) vs Medicorp prong (short binasal) NCPAP to prevent extubation failure, Outcome 4 Non-pulmonary outcomes.

Review: Devices and pressure sources for administration of nasal continuous positive airway pressure (NCPAP) in preterm neonates

Comparison: 2 Infant Flow Driver (short binasal) vs Medicorp prong (short binasal) NCPAP to prevent extubation failure

Outcome: 4 Non-pulmonary outcomes

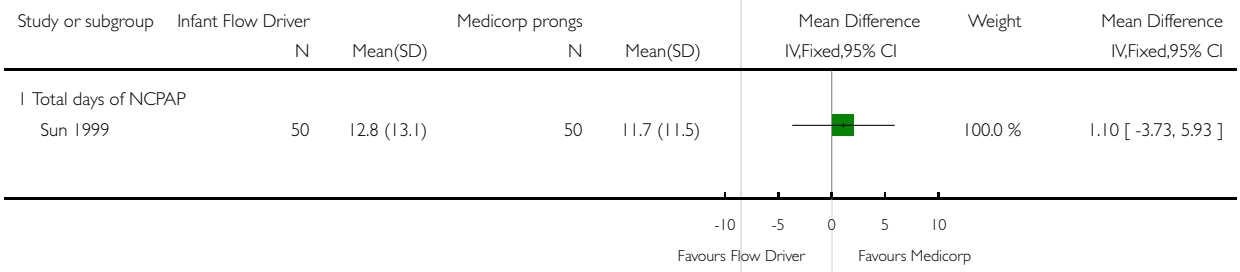


Analysis 2.5. Comparison 2 Infant Flow Driver (short binasal) vs Medicorp prong (short binasal) NCPAP to prevent extubation failure, Outcome 5 Days of respiratory support.

Review: Devices and pressure sources for administration of nasal continuous positive airway pressure (NCPAP) in preterm neonates

Comparison: 2 Infant Flow Driver (short binasal) vs Medicorp prong (short binasal) NCPAP to prevent extubation failure

Outcome: 5 Days of respiratory support



Analysis 3.1. Comparison 3 Short binasal prong (Infant Flow Driver) vs nasopharyngeal prong CPAP to prevent extubation failure, Outcome 1 Extubation failure.

Review: Devices and pressure sources for administration of nasal continuous positive airway pressure (NCPAP) in preterm neonates

Comparison: 3 Short binasal prong (Infant Flow Driver) vs nasopharyngeal prong CPAP to prevent extubation failure

Outcome: 1 Extubation failure

Study or subgroup	Short binasal n/N	Nasopharyngeal n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
1 Endotracheal intubation within 7 days post-extubation				
Roukema 1999a	18/48	27/45		0.63 [0.40, 0.97]

Analysis 4.1. Comparison 4 Short binasal prong vs single prong (nasal or nasopharyngeal) NCPAP to prevent extubation failure, Outcome 1 Extubation failure.

Review: Devices and pressure sources for administration of nasal continuous positive airway pressure (NCPAP) in preterm neonates

Comparison: 4 Short binasal prong vs single prong (nasal or nasopharyngeal) NCPAP to prevent extubation failure

Outcome: 1 Extubation failure

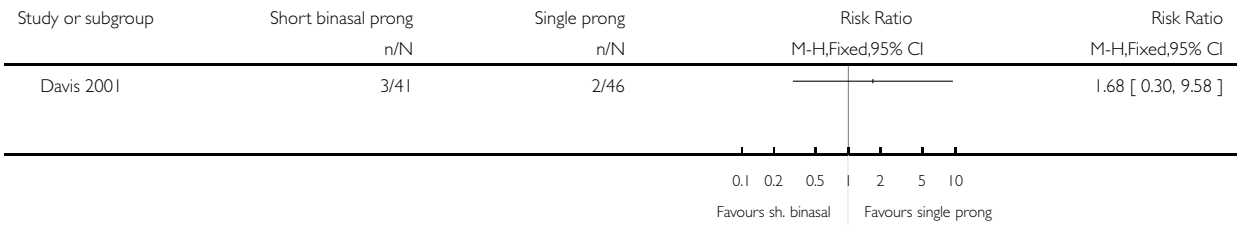
Study or subgroup	Short binasal prong n/N	Single prong n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 Endotracheal intubation within 7 days post-extubation					
Davis 2001	9/41	19/46		39.1 %	0.53 [0.27, 1.04]
Roukema 1999a	18/48	27/45		60.9 %	0.63 [0.40, 0.97]
Subtotal (95% CI)	**89**	**91**		**100.0 %**	**0.59 [0.41, 0.85]**
Total events: 27 (Short binasal prong), 46 (Single prong)					
Heterogeneity: Chi² = 0.16, df = 1 (P = 0.69); I² =0.0%					
Test for overall effect: Z = 2.80 (P = 0.0050)					
2 Respiratory failure within 7 days post-extubation					
Davis 2001	10/41	26/46		100.0 %	0.43 [0.24, 0.78]
Subtotal (95% CI)	**41**	**46**		**100.0 %**	**0.43 [0.24, 0.78]**
Total events: 10 (Short binasal prong), 26 (Single prong)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.77 (P = 0.0057)					

Analysis 4.2. Comparison 4 Short binasal prong vs single prong (nasal or nasopharyngeal) NCPAP to prevent extubation failure, Outcome 2 Death.

Review: Devices and pressure sources for administration of nasal continuous positive airway pressure (NCPAP) in preterm neonates

Comparison: 4 Short binasal prong vs single prong (nasal or nasopharyngeal) NCPAP to prevent extubation failure

Outcome: 2 Death

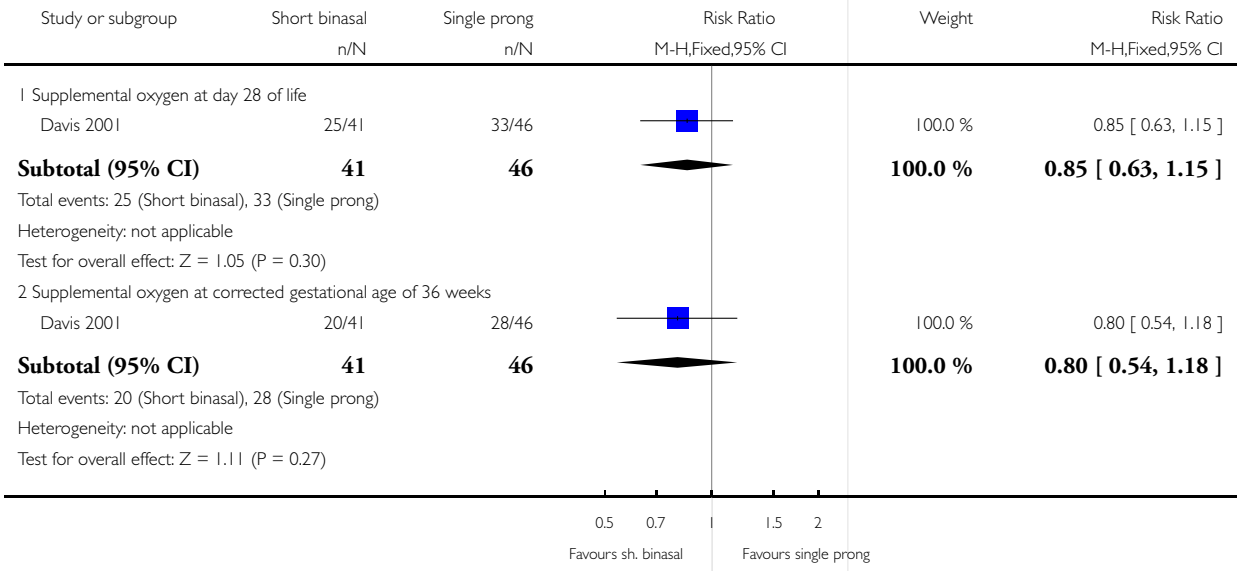


Analysis 4.3. Comparison 4 Short binasal prong vs single prong (nasal or nasopharyngeal) NCPAP to prevent extubation failure, Outcome 3 Chronic lung disease.

Review: Devices and pressure sources for administration of nasal continuous positive airway pressure (NCPAP) in preterm neonates

Comparison: 4 Short binasal prong vs single prong (nasal or nasopharyngeal) NCPAP to prevent extubation failure

Outcome: 3 Chronic lung disease

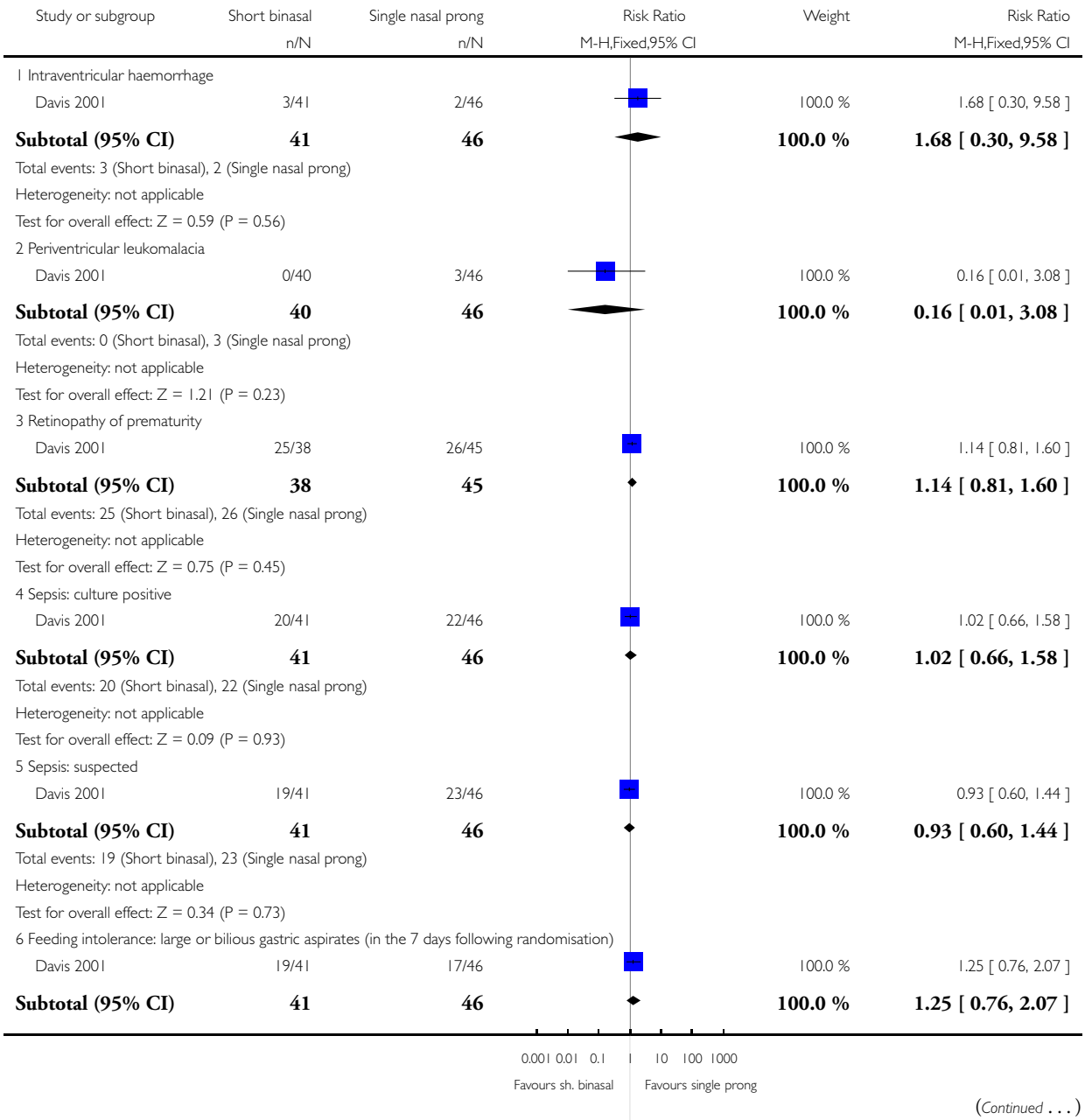


Analysis 4.4. Comparison 4 Short binasal prong vs single prong (nasal or nasopharyngeal) NCPAP to prevent extubation failure, Outcome 4 Non-pulmonary outcomes.

Review: Devices and pressure sources for administration of nasal continuous positive airway pressure (NCPAP) in preterm neonates

Comparison: 4 Short binasal prong vs single prong (nasal or nasopharyngeal) NCPAP to prevent extubation failure

Outcome: 4 Non-pulmonary outcomes



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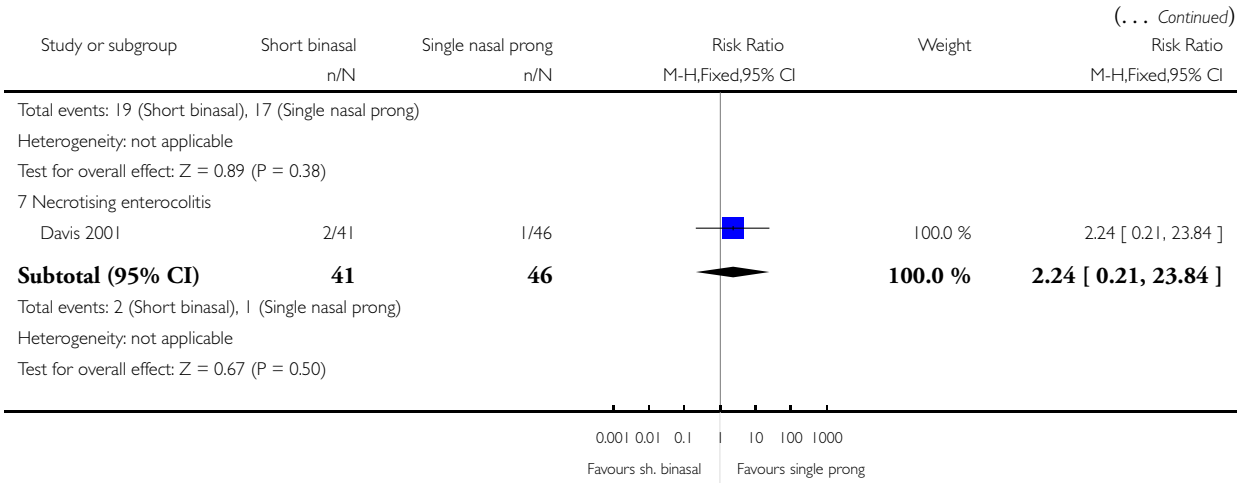
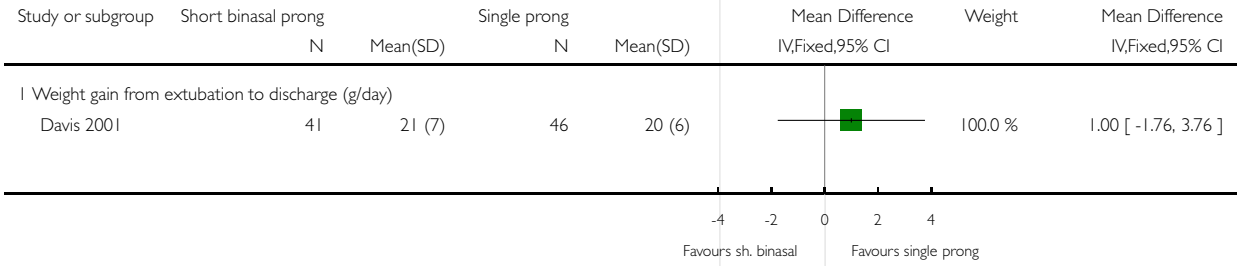


Analysis 4.5. Comparison 4 Short binasal prong vs single prong (nasal or nasopharyngeal) NCPAP to prevent extubation failure, Outcome 5 Weight gain.

Review: Devices and pressure sources for administration of nasal continuous positive airway pressure (NCPAP) in preterm neonates

Comparison: 4 Short binasal prong vs single prong (nasal or nasopharyngeal) NCPAP to prevent extubation failure

Outcome: 5 Weight gain



Analysis 4.6. Comparison 4 Short binasal prong vs single prong (nasal or nasopharyngeal) NCPAP to prevent extubation failure, Outcome 6 Days of respiratory support.

Review: Devices and pressure sources for administration of nasal continuous positive airway pressure (NCPAP) in preterm neonates

Comparison: 4 Short binasal prong vs single prong (nasal or nasopharyngeal) NCPAP to prevent extubation failure

Outcome: 6 Days of respiratory support

Study or subgroup	Short binasal prong N	Mean(SD)	Single prong N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Total days on NCPAP							
Davis 2001	41	26.7 (16.59)	46	30.89 (19.34)		100.0 %	-4.19 [-11.74, 3.36]
Subtotal (95% CI)	**41**		**46**			**100.0 %**	**-4.19 [-11.74, 3.36]**
Heterogeneity: not applicable							
Test for overall effect: Z = 1.09 (P = 0.28)							
2 Total days intubated							
Davis 2001	41	13.85 (14.82)	46	17.24 (17.69)		100.0 %	-3.39 [-10.22, 3.44]
Subtotal (95% CI)	**41**		**46**			**100.0 %**	**-3.39 [-10.22, 3.44]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.97 (P = 0.33)							
3 Total days of respiratory support (NCPAP and intubation)							
Davis 2001	41	39.93 (24.68)	46	46.28 (25.91)		100.0 %	-6.35 [-16.99, 4.29]
Subtotal (95% CI)	**41**		**46**			**100.0 %**	**-6.35 [-16.99, 4.29]**
Heterogeneity: not applicable							
Test for overall effect: Z = 1.17 (P = 0.24)							
Test for subgroup differences: Chi^2 = 0.21, df = 2 (P = 0.90), I^2 =0.0%							

Analysis 4.7. Comparison 4 Short binasal prong vs single prong (nasal or nasopharyngeal) NCPAP to prevent extubation failure, Outcome 7 Resource utilisation.

Review: Devices and pressure sources for administration of nasal continuous positive airway pressure (NCPAP) in preterm neonates

Comparison: 4 Short binasal prong vs single prong (nasal or nasopharyngeal) NCPAP to prevent extubation failure

Outcome: 7 Resource utilisation

Study or subgroup	Short binasal prong N	Mean(SD)	Single prong N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Total days in level III hospital							
Davis 2001	41	77.1 (35.5)	46	81.72 (53.2)		100.0 %	-4.62 [-23.45, 14.21]

Analysis 5.1. Comparison 5 Infant Flow Driver (short binasal) vs INCA prong (short binasal) to prevent extubation failure, Outcome 1 Endotracheal intubation within 7 days post-extubation.

Review: Devices and pressure sources for administration of nasal continuous positive airway pressure (NCPAP) in preterm neonates

Comparison: 5 Infant Flow Driver (short binasal) vs INCA prong (short binasal) to prevent extubation failure

Outcome: 1 Endotracheal intubation within 7 days post-extubation

Study or subgroup	Infant Flow Driver n/N	INCA prongs n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Stefanescu 2003	30/78	32/84		100.0 %	1.01 [0.68, 1.49]
Total (95% CI)	**78**	**84**		**100.0 %**	**1.01 [0.68, 1.49]**

Total events: 30 (Infant Flow Driver), 32 (INCA prongs)

Heterogeneity: not applicable

Test for overall effect: Z = 0.05 (P = 0.96)

Analysis 5.2. Comparison 5 Infant Flow Driver (short binasal) vs INCA prong (short binasal) to prevent extubation failure, Outcome 2 Death.

Review: Devices and pressure sources for administration of nasal continuous positive airway pressure (NCPAP) in preterm neonates

Comparison: 5 Infant Flow Driver (short binasal) vs INCA prong (short binasal) to prevent extubation failure

Outcome: 2 Death

Study or subgroup	Infant Flow Driver n/N	INCA prongs n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Stefanescu 2003	8/78	3/84		100.0 %	2.87 [0.79, 10.44]
Total (95% CI)	**78**	**84**		**100.0 %**	**2.87 [0.79, 10.44]**

Total events: 8 (Infant Flow Driver), 3 (INCA prongs)

Heterogeneity: not applicable

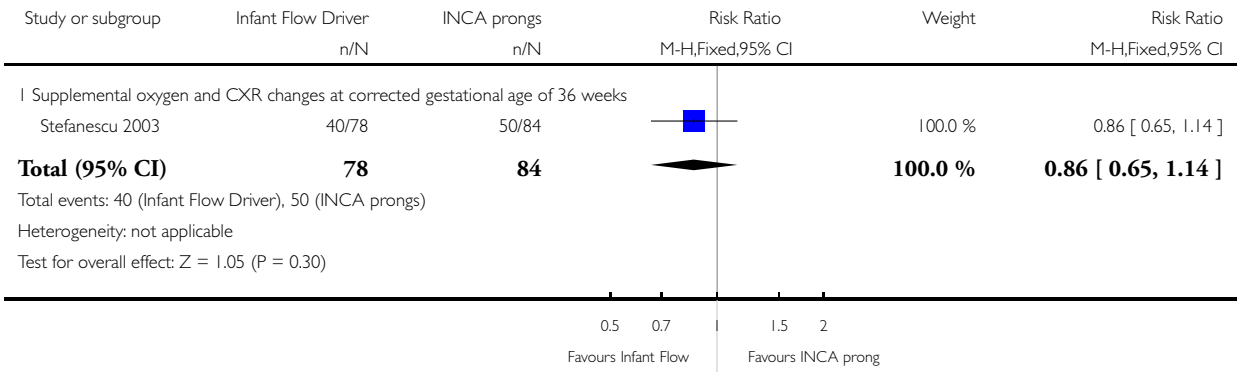
Test for overall effect: Z = 1.60 (P = 0.11)

Analysis 5.3. Comparison 5 Infant Flow Driver (short binasal) vs INCA prong (short binasal) to prevent extubation failure, Outcome 3 Chronic lung disease.

Review: Devices and pressure sources for administration of nasal continuous positive airway pressure (NCPAP) in preterm neonates

Comparison: 5 Infant Flow Driver (short binasal) vs INCA prong (short binasal) to prevent extubation failure

Outcome: 3 Chronic lung disease

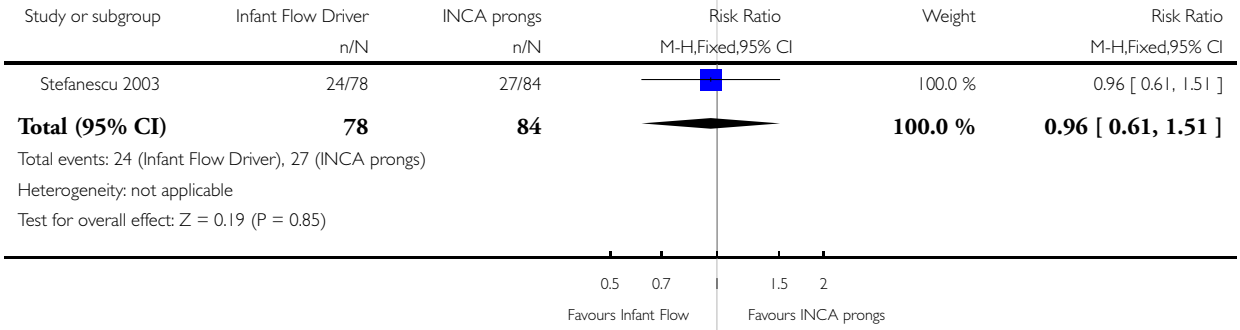


Analysis 5.4. Comparison 5 Infant Flow Driver (short binasal) vs INCA prong (short binasal) to prevent extubation failure, Outcome 4 PIE and gross air leak.

Review: Devices and pressure sources for administration of nasal continuous positive airway pressure (NCPAP) in preterm neonates

Comparison: 5 Infant Flow Driver (short binasal) vs INCA prong (short binasal) to prevent extubation failure

Outcome: 4 PIE and gross air leak



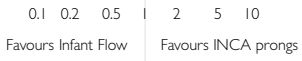
Analysis 5.5. Comparison 5 Infant Flow Driver (short binasal) vs INCA prong (short binasal) to prevent extubation failure, Outcome 5 Non-pulmonary outcomes.

Review: Devices and pressure sources for administration of nasal continuous positive airway pressure (NCPAP) in preterm neonates

Comparison: 5 Infant Flow Driver (short binasal) vs INCA prong (short binasal) to prevent extubation failure

Outcome: 5 Non-pulmonary outcomes

Study or subgroup	Infant Flow Driver n/N	INCA prongs n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
1 Necrotising enterocolitis				
Stefanescu 2003	18/78	15/84		1.29 [0.70, 2.38]
2 Sepsis: culture positive and suspected combined				
Stefanescu 2003	66/78	70/84		1.02 [0.89, 1.16]
3 Intraventricular haemorrhage: grade 3 and 4				
Stefanescu 2003	11/78	14/84		0.85 [0.41, 1.75]
4 Periventricular leukomalacia				
Stefanescu 2003	3/78	5/84		0.65 [0.16, 2.61]
5 Retinopathy of prematurity: all grades				
Stefanescu 2003	60/78	72/84		0.90 [0.77, 1.04]



Analysis 5.6. Comparison 5 Infant Flow Driver (short binasal) vs INCA prong (short binasal) to prevent extubation failure, Outcome 6 Total days of NCPAP.

Review: Devices and pressure sources for administration of nasal continuous positive airway pressure (NCPAP) in preterm neonates

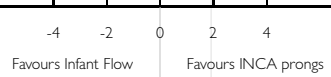
Comparison: 5 Infant Flow Driver (short binasal) vs INCA prong (short binasal) to prevent extubation failure

Outcome: 6 Total days of NCPAP

Study or subgroup	Infant Flow Driver N	Mean(SD)	INCA prongs N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Stefanescu 2003	78	8.74 (8.04)	84	10.17 (8.53)		100.0 %	-1.43 [-3.98, 1.12]
Total (95% CI)	**78**		**84**			**100.0 %**	**-1.43 [-3.98, 1.12]**

Heterogeneity: not applicable

Test for overall effect: Z = 1.10 (P = 0.27)



Analysis 5.7. Comparison 5 Infant Flow Driver (short binasal) vs INCA prong (short binasal) to prevent extubation failure, Outcome 7 Days in oxygen.

Review: Devices and pressure sources for administration of nasal continuous positive airway pressure (NCPAP) in preterm neonates

Comparison: 5 Infant Flow Driver (short binasal) vs INCA prong (short binasal) to prevent extubation failure

Outcome: 7 Days in oxygen

Study or subgroup	Infant Flow Driver N	Mean(SD)	INCA prong N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Stefanescu 2003	78	65.7 (31.4)	84	77.2 (35.1)		100.0 %	-11.50 [-21.74, -1.26]
Total (95% CI)	**78**		**84**			**100.0 %**	**-11.50 [-21.74, -1.26]**

Heterogeneity: not applicable

Test for overall effect: Z = 2.20 (P = 0.028)

Analysis 5.8. Comparison 5 Infant Flow Driver (short binasal) vs INCA prong (short binasal) to prevent extubation failure, Outcome 8 Resource utilisation.

Review: Devices and pressure sources for administration of nasal continuous positive airway pressure (NCPAP) in preterm neonates

Comparison: 5 Infant Flow Driver (short binasal) vs INCA prong (short binasal) to prevent extubation failure

Outcome: 8 Resource utilisation

Study or subgroup	Infant Flow Driver N	Mean(SD)	INCA prongs N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Total days in hospital							
Stefanescu 2003	78	73.7 (28.7)	84	86.3 (37.34)		100.0 %	-12.60 [-22.81, -2.39]
Total (95% CI)	**78**		**84**			**100.0 %**	**-12.60 [-22.81, -2.39]**

Heterogeneity: not applicable

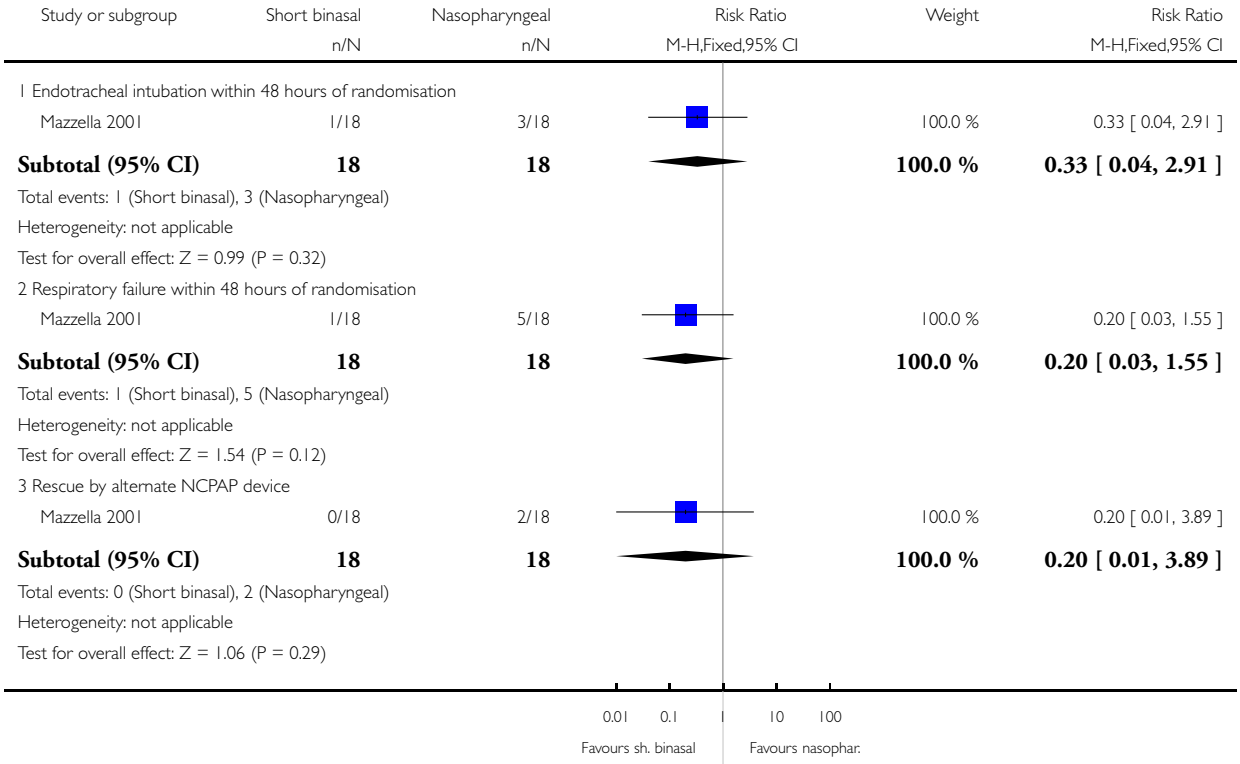
Test for overall effect: Z = 2.42 (P = 0.016)

Analysis 6.1. Comparison 6 Short binasal prong vs nasopharyngeal (single tube) CPAP for early respiratory distress, Outcome 1 Treatment failure.

Review: Devices and pressure sources for administration of nasal continuous positive airway pressure (NCPAP) in preterm neonates

Comparison: 6 Short binasal prong vs nasopharyngeal (single tube) CPAP for early respiratory distress

Outcome: 1 Treatment failure

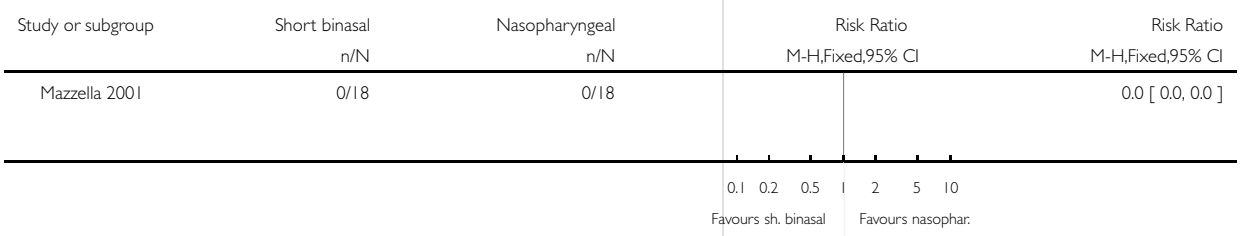


Analysis 6.2. Comparison 6 Short binasal prong vs nasopharyngeal (single tube) CPAP for early respiratory distress, Outcome 2 Death.

Review: Devices and pressure sources for administration of nasal continuous positive airway pressure (NCPAP) in preterm neonates

Comparison: 6 Short binasal prong vs nasopharyngeal (single tube) CPAP for early respiratory distress

Outcome: 2 Death



Analysis 6.3. Comparison 6 Short binasal prong vs nasopharyngeal (single tube) CPAP for early respiratory distress, Outcome 3 Pulmonary outcomes.

Review: Devices and pressure sources for administration of nasal continuous positive airway pressure (NCPAP) in preterm neonates

Comparison: 6 Short binasal prong vs nasopharyngeal (single tube) CPAP for early respiratory distress

Outcome: 3 Pulmonary outcomes

Study or subgroup	Short binasal n/N	Nasopharyngeal n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
1 Chronic lung disease (supplemental oxygen at 28 days)				
Mazzella 2001	0/18	0/18		0.0 [0.0, 0.0]
Subtotal (95% CI)	**18**	**18**		**0.0 [0.0, 0.0]**
Total events: 0 (Short binasal), 0 (Nasopharyngeal)				
Heterogeneity: not applicable				
Test for overall effect: Z = 0.0 (P < 0.00001)				
2 Pneumothorax				
Mazzella 2001	1/18	0/18		3.00 [0.13, 69.09]
Subtotal (95% CI)	**18**	**18**		**3.00 [0.13, 69.09]**
Total events: 1 (Short binasal), 0 (Nasopharyngeal)				
Heterogeneity: not applicable				
Test for overall effect: Z = 0.69 (P = 0.49)				

Analysis 6.4. Comparison 6 Short binasal prong vs nasopharyngeal (single tube) CPAP for early respiratory distress, Outcome 4 Non-pulmonary outcomes.

Review: Devices and pressure sources for administration of nasal continuous positive airway pressure (NCPAP) in preterm neonates

Comparison: 6 Short binasal prong vs nasopharyngeal (single tube) CPAP for early respiratory distress

Outcome: 4 Non-pulmonary outcomes

Study or subgroup	Short binasal n/N	Nasopharyngeal n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
1 Intraventricular haemorrhage				
Mazzella 2001	0/18	0/18		0.0 [0.0, 0.0]
Subtotal (95% CI)	**18**	**18**		**0.0 [0.0, 0.0]**
Total events: 0 (Short binasal), 0 (Nasopharyngeal)				
Heterogeneity: not applicable				
Test for overall effect: Z = 0.0 (P < 0.00001)				
2 Nasal trauma				
Mazzella 2001	4/18	0/18		9.00 [0.52, 155.86]
Subtotal (95% CI)	**18**	**18**		**9.00 [0.52, 155.86]**
Total events: 4 (Short binasal), 0 (Nasopharyngeal)				
Heterogeneity: not applicable				
Test for overall effect: Z = 1.51 (P = 0.13)				

Analysis 6.5. Comparison 6 Short binasal prong vs nasopharyngeal (single tube) CPAP for early respiratory distress, Outcome 5 Total days of respiratory support.

Review: Devices and pressure sources for administration of nasal continuous positive airway pressure (NCPAP) in preterm neonates

Comparison: 6 Short binasal prong vs nasopharyngeal (single tube) CPAP for early respiratory distress

Outcome: 5 Total days of respiratory support

Study or subgroup	Short binasal N	Mean(SD)	Nasopharyngeal N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
Mazzella 2001	18	2.1 (1.3)	18	2.3 (1.2)		-0.20 [-1.02, 0.62]

Analysis 7.1. Comparison 7 Hudson prong (short binasal) vs Argyle prong (short binasal) CPAP in preterm infants: broad inclusion criteria, Outcome 1 Nasal hyperaemia.

Review: Devices and pressure sources for administration of nasal continuous positive airway pressure (NCPAP) in preterm neonates

Comparison: 7 Hudson prong (short binasal) vs Argyle prong (short binasal) CPAP in preterm infants: broad inclusion criteria

Outcome: 1 Nasal hyperaemia

Study or subgroup	Hudson prong n/N	Argyle prong n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Rego 2002	10/50	22/46		100.0 %	0.42 [0.22, 0.79]
Total (95% CI)	**50**	**46**		**100.0 %**	**0.42 [0.22, 0.79]**
Total events: 10 (Hudson prong), 22 (Argyle prong)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.71 (P = 0.0068)					

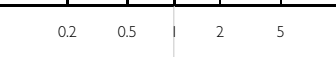
Analysis 7.2. Comparison 7 Hudson prong (short binasal) vs Argyle prong (short binasal) CPAP in preterm infants: broad inclusion criteria, Outcome 2 Nasal bleeding.

Review: Devices and pressure sources for administration of nasal continuous positive airway pressure (NCPAP) in preterm neonates

Comparison: 7 Hudson prong (short binasal) vs Argyle prong (short binasal) CPAP in preterm infants: broad inclusion criteria

Outcome: 2 Nasal bleeding

Study or subgroup	Hudson prong n/N	Argyle prong n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Rego 2002	16/50	11/46		100.0 %	1.34 [0.70, 2.58]
Total (95% CI)	**50**	**46**		**100.0 %**	**1.34 [0.70, 2.58]**
Total events: 16 (Hudson prong), 11 (Argyle prong)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.87 (P = 0.38)					



WHAT'S NEW

Last assessed as up-to-date: 30 August 2007.

30 May 2008	Amended	Converted to new review format.

HISTORY

Protocol first published: Issue 1, 2001

Review first published: Issue 4, 2002

31 August 2007	New search has been performed	This updates the review "Devices and pressure sources for administration of nasal continuous positive airway pressure (NCPAP) in preterm neonates" published in The Cochrane Library, Issue 4, 2002 (De Paoli 2002). An updated search identified three new trials for inclusion in this update (Stefanescu 2003; Rego 2002; Buettiker 2004). Several additional trials were identified, but not eligible for inclusion and have been added to the Excluded Studies reference list.

CONTRIBUTIONS OF AUTHORS

The authors De Paoli, Davis and Faber developed the protocol, performed the literature search, data collection and analysis. Professor Morley acted as a content expert throughout the writing of the review.

DECLARATIONS OF INTEREST

Dr Peter Davis and Brenda Faber are authors of one of the trials included in this review.

SOURCES OF SUPPORT

Internal sources

- Royal Women's Hospital Foundation, Melbourne, Australia.
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- University of Melbourne, Australia.

External sources

- No sources of support supplied

INDEX TERMS

Medical Subject Headings (MeSH)

Continuous Positive Airway Pressure [instrumentation; *methods]; Infant, Newborn; Infant, Premature; Randomized Controlled Trials as Topic; Respiratory Distress Syndrome, Newborn [*therapy]; Respiratory Insufficiency [*therapy]; Ventilator Weaning

MeSH check words

Humans