Continuous distending pressure for respiratory distress in preterm infants (Review)

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TABLE OF CONTENTS

[Intervention Review]

Continuous distending pressure for respiratory distress in preterm infants

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ABSTRACT

Background

Respiratory distress syndrome (RDS) is the single most important cause of morbidity and mortality in preterm infants (Greenough 1998, Bancalari 1992). Intermittent positive pressure ventilation (IPPV) with surfactant is the standard treatment for the condition. The major difficulty with IPPV is that it is invasive, resulting in airway and lung injury and contributing to the development of chronic lung disease.

Objectives

To determine the effect of continuous distending pressure (CDP) on the need for IPPV and associated morbidity in spontaneously breathing preterm infants with respiratory distress.

Search strategy

The standard search strategy of the Neonatal Review Group was used. This included searches of the Oxford Database of Perinatal Trials, Cochrane Central Register of Controlled Trials (The Cochrane Library, Issue 2, 2008), MEDLINE (1966 - February, 2008), and EMBASE (1980 - February 2008), previous reviews including cross references, abstracts, conference and symposia proceedings, expert informants, journal hand searching mainly in the English language.

Selection criteria

All trials using random or quasi-random allocation of preterm infants with respiratory distress were eligible. Interventions were continuous distending pressure including continuous positive airway pressure (CPAP) by mask, nasal prong, nasopharyngeal tube, or endotracheal tube, or continuous negative pressure (CNP) via a chamber enclosing the thorax and lower body, compared with standard care.

Data collection and analysis

Standard methods of the Cochrane Collaboration and its Neonatal Review Group were used, including independent assessment of trial quality and extraction of data by each author.

Main results

CDP is associated with a lower rate of failed treatment (death or use of assisted ventilation) [summary RR 0.65 (95% CI 0.52, 0.81), RD -0.20 (95% CI -0.29, -0.10), NNT 5 (95% CI 4, 10)], overall mortality [summary RR 0.52 (95% CI 0.32, 0.87), RD -0.15 (95% CI -0.26, -0.04), NNT 7 (95% CI 4, 25)], and mortality in infants with birth weights above 1500 g [summary RR 0.24 (95% CI 0.07, 0.84), RD -0.28 (95% CI -0.48, -0.08), NNT 4 (95% CI 2, 13)]. The use of CDP is associated with an increased rate of pneumothorax [summary RR 2.64 (95% CI 1.39, 5.04), RD 0.10 (95% CI 0.04, 0.17), NNH 17 (95% CI 17, 25)].

Authors' conclusions

In preterm infants with respiratory distress the application of CDP either as CPAP or CNP is associated with reduced respiratory failure and reduced mortality. CDP is associated with an increased rate of pneumothorax. Four out of six of these trials were done in the 1970's. Therefore, the applicability of these results to current practice is difficult to assess. Where resources are limited, such as in developing countries, CPAP for RDS may have a clinical role. Further research is required to determine the best mode of administration and the role of CDP in modern intensive care settings

PLAIN LANGUAGE SUMMARY

Continuous distending pressure for respiratory distress in preterm infants

Some benefits found in using continuous distending pressure (CDP) for respiratory distress syndrome in preterm babies.

Respiratory distress syndrome (RDS) is the most common cause of disease and death in babies born before 34 weeks gestation. Intermittent positive pressure ventilation (IPPV) is the standard way of helping these babies breathe. A simpler method of assisting breathing is to provide a continuous lung distending pressure - either no continuous positive pressure to the airway or continuous negative pressure (partial vacuum). The review of trials found that continuous distending pressure (CDP) reduces the rate of death or the need for assisted ventilation and reduced the need for IPPV. The small and mostly dated trials also found that CDP can increase the rate of pneumothorax (air outside the lung in the chest cavity).

BACKGROUND

Respiratory failure due to pulmonary disease, particularly respiratory distress syndrome (RDS), is the most important cause of morbidity and mortality in preterm infants (Greenough 2004; Bancalari 1992). Most causes of respiratory distress present in a similar manner sometimes making precise diagnosis difficult. Intermittent positive pressure ventilation (IPPV) and surfactant treatment is the standard treatment for the condition. The major difficulty with IPPV is that it is invasive and contributes to airway and lung injury including the development of chronic lung disease. Surfactant has brought some amelioration to this problem (Soll 2004).

Continuous distending pressure (CDP) has been used for the prevention and treatment of RDS as well as the prevention of apnea, and in weaning from IPPV. Its use in the treatment of RDS might reduce the need for IPPV and hence its sequelae. Cost saving could occur if more expensive forms of treatment such as IPPV and use of surfactant were avoided.

CDP has been applied as a continuous positive airway pressure (CPAP) or as a continuous negative pressure (CNP). CPAP is applied via a face mask, nasopharyngeal tube, or nasal prongs, using a conventional ventilator, bubble circuit or CPAP driver. CNP is applied externally to the thorax using a negative pressure chamber with the seal around the neck; it produces lung distension as a result of negative intrathoracic pressure. Application of positive compared with negative pressure might have different results in terms of effectiveness and complications. Since use of CDP depends on the spontaneous respiratory efforts of the infant, those of very low birth weight, who would be expected to have reduced efforts and be more prone to apnea, might not respond as well.

A formal evaluation of the use of CDP is required to assess its role in preterm infants with established respiratory distress and to determine which methods of application are appropriate.

A systematic review on this subject has been previously published (Bancalari 1992).

OBJECTIVES

To determine the effect of CDP on the need for IPPV and associated morbidity in spontaneously breathing preterm infants with pulmonary respiratory failure.

Subgroup analyses were planned on the basis of birthweight (greater or less than 1000 or 1500 g), gestational age (groups divided at about 28 and 32 weeks), methods of application of CDP (i.e. CPAP and CNP), application early vs. late in the course of respiratory distress, high vs. low pressure CDP and application of CDP in tertiary compared with non-tertiary hospitals with sensitivity analysis by trial quality.

At the 2008 update, the objectives were modified to include preterm infants with respiratory failure.

METHODS

Criteria for considering studies for this review

Types of studies

Randomized or quasi-randomized studies

Types of participants

Preterm infants with respiratory failure.

Types of interventions

Continuous distending pressure (CDP) including CPAP by mask, nasal prong, nasopharyngeal tube, or endotracheal tube, or continuous negative pressure (CNP) via a chamber enclosing the thorax and lower body, compared with standard care.

Types of outcome measures

Primary

1. Treatment failure (death or respiratory failure as measured by use of any additional assisted ventilation, blood gas criteria or transfer to a neonatal intensive care unit)
2. Use of assisted ventilation
3. Respiratory failure by blood gas criteria
4. Transfer to a neonatal intensive care
5. Mortality at 28 days and at hospital discharge

At the 2008 update of the review, the definition for treatment failure was modified and the two additional outcomes, transfer to a neonatal intensive care unit and respiratory failure by blood gas criteria were added.

Secondary

1. Pulmonary morbidity as judged by pulmonary air leak (any air leak, gross air leak including pneumothorax), duration of oxygen therapy, chronic lung disease (respiratory support and/or oxygen therapy at 28 days and at 36 weeks postmenstrual age).
2. Use of surfactant
3. Other morbidities such as intraventricular hemorrhage, cystic brain lesions on ultrasound, retinopathy of prematurity, necrotizing enterocolitis, duration of hospital stay, neurodevelopment in childhood.

Search methods for identification of studies

The standard search strategy of the Neonatal Review Group was used. This included searches of the Oxford Database of Perinatal Trials, Cochrane Central Register of Controlled Trials (The Cochrane Library, Issue 2, 2008), previous reviews including cross references, abstracts, conference and symposia proceedings, expert informants, and journal hand searching. MEDLINE (1966 - February 2008) and EMBASE (1980 - February 2008) were searched using the terms newborn, neonate, respiratory distress syndrome, hyaline membrane disease, continuous distending airway pressure, continuous positive airway pressure, continuous positive transpulmonary pressure, continuous transpulmonary pressure, continuous inflating pressure, continuous negative distending pressure, continuous negative pressure or continuous airway pressure. Abstracts of the Society for Pediatric Research were hand searched for the years 1996 to 2007 inclusive and for the European Society for Pediatric Research for 2000 to 2007.

Data collection and analysis

The standard methods of the Cochrane Neonatal Review Group were used.

Selection of studies

All randomized and quasi-randomized controlled trials fulfilling the selection criteria described in the previous section were included. The authors reviewed the results of the search and separately selected the studies for inclusion. They resolved any disagreement by discussion.

Data extraction and management

Two review authors separately extracted, assessed and coded all data for each study. Any standard error of the mean was replaced by the corresponding standard deviation. Any disagreement was resolved by discussion. For each study, final data were entered into RevMan by one review author and then checked by a second review author.

Statistical analyses were performed using Review Manager (RevMan) software. Categorical data were analyzed using relative risk (RR), risk difference (RD) and the number needed to treat

(NNT). Continuous data were analyzed using weighted mean difference (WMD). The 95% confidence interval (CI) was reported on all estimates. A fixed effects model for meta-analysis was used.

Assessment of risk of bias in included studies

The standard methods of the Cochrane Neonatal Review Group were employed. The methodological quality of the studies was assessed using the following key criteria: allocation concealment (blinding of randomization), blinding of intervention, completeness of follow-up, and blinding of outcome measurement/assessment. For each criteria, assessment was yes, no, can't tell. The review authors separately assessed each study. They resolved any disagreement by discussion.

Subgroup analysis and investigation of heterogeneity

The treatment effects of individual trials and heterogeneity between trials was examined by inspecting the forest plots and quantifying the impact of heterogeneity using the I^2 statistic. If statistical heterogeneity was detected, the possible causes (for example, differences in study quality, participants, intervention regimens, or outcome assessments) were explored using post-hoc subgroup analyses.
Specific subgroup analyses were performed according to the 'Objectives' section of this review.

RESULTS

Description of studies

See: Characteristics of included studies; Characteristics of excluded studies; Characteristics of studies awaiting classification.
Six studies were included. Details of these studies are shown in the Table of Included Studies. The entry criteria for participants were based on a clinical diagnosis of respiratory failure and spontaneous breathing in an FiO_2 which ranged from 0.3 - 0.95. In Samuels 1996, the included infants had respiratory distress not due to infection, meconium aspiration or congenital heart disease and all were in respiratory failure thought to be due to RDS but without radiological confirmation.The study population was randomized within strata which were formed according to gestation and whether intubated or not. Only preterm infants breathing spontaneously at trial entry were included in this review; individual patient data on this group of patients were supplied by the authors. Buckmaster 2007 included neonates with respiratory distress not due to cardiac disease. Data for preterm infants were supplied by the authors. These infants all had respiratory failure thought to due to RDS but it is not possible to exclude other conditions, in particular, meconium aspiration in eight infants with meconium stained amniotic fluid. The study was performed in non-tertiary hospitals.
Antenatal steroids were administered to less than 20% of participants in Samuels 1996, and 35% in Buckmaster 2007. The other studies did not mentioned their use. Samuels 1996 was the only trial where surfactant use was reported. Some of the participants in Buckmaster 2007 may have received surfactant after transfer to a neonatal intensive care unit but this was not recorded.

The source of distending pressure was a negative pressure chamber in two studies (Fanaroff 1973; Samuels 1996), face mask CPAP in two studies (Rhodes 1973; Belenky 1976) and nasal CPAP in one study (Buckmaster 2007). The other study used negative pressure for less severe illness and endotracheal CPAP when more severe (Durbin 1976).
Two studies did a subgroup analysis of mortality for very low birthweight infants (Rhodes 1973; Belenky 1976). Buckmaster 2007 stratified for gestations of 31 - 33 and 34 - 36 weeks.
The study by Belenky 1976 included both spontaneously breathing infants on facemask CPAP and ventilated infants on face mask or endotracheal IPPV with PEEP. Only those infants who were spontaneously breathing at trial entry were eligible for this review. The published report of this study describes, in infants spontaneously breathing at trial entry, only the subsequent use of IPPV; information on other outcomes in such infants was obtained from the author.
In one study (Samuels 1996) neurodevelopmental assessment was done at 9 - 15 years of age (Telford 2006). This follow-up study is waiting further assessment.
Three studies were excluded. Details are given in the Table of Excluded Studies. One study (Tooley 2003) included infants of 25 to 28 weeks gestation who were all intubated at birth, given a single dose of surfactant then randomised at about one hour of age to extubation to nasal CPAP or to continued conventional IPPV. No criteria for the diagnosis of RDS were given. The second study (Swyer 1973) was a randomized comparison of three continuous distending pressure methods but no control (standard) treatment group was included. The Pieper study was performed in a developing country. Subjects were extremely low birth weight babies 750 - 1000 g or 26 - 28 weeks gestation who had no access to intensive care. This study was not randomised (Pieper 2003).

Risk of bias in included studies

Five studies used random allocation (Fanaroff 1973; Durbin 1976; Belenky 1976; Samuels 1996; Buckmaster 2007), one used an off-site computer generated random sequence and allocation (Buckmaster 2007), three used sealed envelopes (Fanaroff 1973; Durbin 1976; Samuels 1996) and in three the method of generation of a random sequence was not mentioned. One study (Rhodes 1973) used alternate allocation. Blinding of treatment or outcome assessment was not feasible. Three studies (Durbin 1976; Samuels

1996; Buckmaster 2007) stated how many were randomized. In all three studies more than 90% were analyzed. Three studies (Fanaroff 1973; Rhodes 1973; Belenky 1976) only state the numbers analyzed and it is not possible to tell how many exclusions there were after randomization.

Effects of interventions

Six trials (Rhodes 1973; Fanaroff 1973; Durbin 1976; Belenky 1976; Samuels 1996; Buckmaster 2007), which included a total of 355 infants, met eligibility criteria.

Continuous distending pressure vs. standard care (Comparison 1):

Treatment failure (death or respiratory failure measured by use of additional ventilation, blood gas criteria or transfer to a NICU) (Outcome 1.1):

All trials reported treatment failure as death or respiratory failure defined by the need for additional ventilation, one trial measured treatment failure as death or respiratory failure by blood gas criteria (Buckmaster 2007), and one trial as death or transfer to a NICU (Buckmaster 2007). In three trials (Fanaroff 1973; Rhodes 1973; Buckmaster 2007), failure defined by use of mechanical ventilation was significantly reduced in the CDP group. The meta-analysis of all six trials supports a significant reduction in the treatment failure in the CDP compared with the control group [summary RR 0.65 (95% CI 0.52, 0.81), RD -0.20 (95% CI -0.29, -0.10), NNT 5 (95% CI 4, 10)]. Treatment failure defined by blood gas criteria was significantly reduced in the one trial that measured this, [RR 0.53 (95% CI 0.32, 0.90), RD -0.18 (95% CI -0.32, -0.04), NNT 6(95% CI 4, 25)]. Treatment failure defined by transfer to a NICU was significantly reduced in the one trial measuring this, [RR 0.49 (95% CI 0.30, 0.78) , RD -0.24 (95% CI -0.38, -0.10), NNT 5(95% CI 3, 10)].

Death or respiratory failure by blood gas criteria (Outcome 1.1.2):

Respiratory failure by blood gas criteria was significantly reduced in the one study reporting this outcome (Buckmaster 2007), [RR 0.53 (95% CI 0.32, 0.90), RD -0.18 (95% CI -0.32, -0.04), NNT 6 (95% CI 4, 25)].

Use of additional ventilatory assistance (Outcome 1.2):

One trial (Buckmaster 2007) showed a difference in the use of IPPV and four trials did not (Fanaroff 1973; Durbin 1976; Belenky 1976; Samuels 1996). The meta-analysis showed reduced use of IPPV in the CDP group [summary RR 0.72 (95% CI 0.56, 0.91, RD-0.15 (95% CI -0.25, -0.05), NNT 7 (95% CI 5, 22)].

Transfer to a NICU (Outcome 1.3):

Buckmaster reported transfer to a NICU. This was significantly reduced in the CDP group, [RR 0.49 (95% CI 0.30, 0.78), RD -0.24 (95% CI -0.38, -0.10), NNT 5 (95% CI 3 ,10)]

Mortality (Outcome 1.4 - 1.6):

Six trials reported effect on mortality, but only Belenky (1976) found a significant reduction [RR 0.38 (95% CI 0.14, 0.99)]. The meta-analysis of all six trials supports a reduction in mortality [summary RR 0.52 (95% CI 0.32, 0.87), RD -0.15 (95% CI -0.26, -0.04), NNT 7 (95% CI 4, 25)]. Two trials (Rhodes 1973; Belenky 1976) reported mortality by birth weight less than or greater than 1500 g. For infants over 1500 g birth weight mortality was reduced in the CDP group [summary RR 0.24 (95% CI 0.07, 0.84), RD -0.28 (95% CI -0.48, -0.08), NNT 4 (95% CI 2, 13)]. For infants with birth weights of 1500 g or less there was a nonsignificant trend towards a lower mortality in the CDP group.

Pulmonary morbidity (Outcomes 1.7 - 1.11):

Six trials reported the rate of pneumothorax at any time. Although no individual trial showed a significant increase, overall there is an increase in the CDP group [summary RR 2.64 (95% CI 1.39, 5.04)), RD 0.10 (95% CI 0.04, 0.17), NNH 10 (95% CI 6, 25)]. SIx trials reported the presence of pneumothorax occurring after trial entry and overall there is a similar increase in the CDP group, [summary RR 2.42 (95% CI 1.26, 4.65), RD 0.09 (95% CI 0.03, 0.15), NNT 11 (95% CI 7, 33)]. There is no evidence of difference between the treatment and control groups in the duration of oxygen therapy (two trials, Durbin 1976; Samuels 1996), or rates of CLD at 28 days (three trials Belenky 1976; Samuels 1996; Buckmaster 2007). 'Minimal bronchopulmonary dysplasia' (not defined) at discharge in survivors was reported in one trial (Fanaroff 1973), 0/11 in the CDP group and 2/8 in the control group.

Use of surfactant (Outcome 1.10):

One trial (Samuels 1996) reported that fewer infants received surfactant in the CNP group (3/26) than in the control group (7/26) but this difference is not significant.

Intraventricular hemorrhage and cystic brain lesions:

One trial (Samuels 1996) reported outcomes for parenchymal hemorrhage and periventricular leukomalacia or cysts. There were no cases in either group.

Necrotizing enterocolitis:

One trial (Samuels 1996) reported necrotizing enterocolitis and there were no cases in either group.

Retinopathy of prematurity:

Fanaroff 1973 reported retrolental fibroplasia in survivors and found only one case with mild proliferative changes in the control group. Samuels 1996 reported retinopathy of prematurity and found grade I changes in two of 15 babies examined in the CNP group and one of 13 babies examined in the control group.

Only one study reported long term follow-up (Samuels 1996). This was reported in Telford 2006. This study is awaiting further assessment.

Subgroup analyses by type and by early use of CDP (CPAP or CNP) resulted in small numbers in the meta-analyses and allowing for this, the results are not substantially different from the overall analysis **(Comparisons 2 - 6)**. The reduction in failure rate in the CDP group reached statistical significance in both the CNP

[summary RR 0.61 (95% CI 0.41, 0.90)] and CPAP [summary RR 0.61 (95% CI 0.45, 0.81)] subgroups.
Sensitivity analyses, which excluded the study using quasi-random patient allocation (Rhodes 1973) and excluded the study whose only infants eligible for inclusion in this review were those who were breathing spontaneously at trial entry (Belenky 1976) did not yield substantially different results.

DISCUSSION

These data should be interpreted with caution since in the studies reviewed the numbers of infants were small, blinding of the treatment was not possible, and blinding of the outcome assessment was not reported, thus possibly introducing bias. Furthermore, four of these six trials were carried out in the 1970s when standard care was principally based on oxygen administration and correction of metabolic acidosis, with use of IPPV when severe respiratory failure occurred.

Inclusion of the subgroup of spontaneously breathing infants from the Belenky 1976 trial could be criticised as the group allocation to CDP or control was not stratified by this characteristic and this could lead to imbalance. That there is imbalance is suggested by the greater birthweight of the group allocated to CPAP. Removal of this trial as part of a sensitivity analysis did not substantially alter the results.

There are a number of reasons why the results of this review, which included trials which were carried out in the 1970's, have limited application to current neonatal care. In the 1970's antenatal corticosteroid use was uncommon and surfactant treatment was not available. The mean birth weight of the patients in the studies reviewed was between 1700 and 2000g, with three trials (Fanaroff 1973; Belenky 1976, Durbin 1976) excluding infants below 1000g. CPAP was applied by mask in both trials of CPAP (Belenky 1976; Rhodes 1973) and this route has been reported to be associated with adverse effects (Pape 1976). Currently the nasal route is the standard way of delivering CPAP (Davis 2004) and differences in efficacy have been shown between devices delivering nasal CPAP (De Paoli 2004). The intervention in the early trials was initiated later than would currently be practiced (Tooley 2003; Narendran 2003), with the mean age at entry being more than 10 hours in four studies and 28 hours in the fifth. Buckmaster 2007 initiated CPAP at a mean of 3 hours. Earlier CPAP is more effective at preventing intubation for IPPV than later CPAP in infants with RDS (Ho 2004).

The conditions existing today in developing countries have certain dissimilarities to those of the studies from the 1970s included in this review. Developing countries today have some availability, even if it is limited, of antenatal steroids, surfactant and ventilators. CDP is an inexpensive therapy and therefore randomised trials in developing countries where resources are scarce seem appropriate. However, the reduced mortality seen in our meta-analysis makes randomisation to headbox oxygen (compared to CDP) difficult. This problem is well illustrated by the trial of Pieper et al (Pieper 2003). Loss of equipoise by the clinical staff at participating South African centres led to cessation of randomisation and allocation of infants to CPAP on the basis of availability of this form of care.

AUTHORS' CONCLUSIONS

Implications for practice

In preterm infants with respiratory distress, the application of CDP either as CPAP or CNP is associated with reduced respiratory failure and reduced mortality. CDP is associated with an increased rate of pneumothorax. The applicability of these results to current practice is difficult to assess, given the intensive care setting of the 1970s in which four of these trials were done. The contribution of the two studies done in the post-surfactant era does not alter the overall results. Where resources are limited, such as in developing countries, CPAP for respiratory distress may have a clinical role.

Implications for research

Further trials of CDP (preferably using low cost nasal CPAP) vs. standard care for preterm infants with RDS could be carried out in developing countries to assess the relative benefits and harms in such settings. In other settings further studies are required to evaluate the use of early nasal CPAP with or without prior temporary tracheal intubation for surfactant administration (Verder 1999). More studies are required on the optimum level (pressure) and mode of delivery of CPAP.

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Dr Belenky kindly provided additional information on infants in his trial. Dr Southall provided individual patient data on infants in the Samuels 1996 trial. Dr Buckmaster provided additional details for the preterm infants in his trial.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

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

Belenky 1976

Methods	Concealment of allocation unclear. Drawing of cards. Not stated whether in envelopes. No blinding of treatment or outcome assessment. Completeness of follow up not clear.
Participants	51 preterm infants (22 CPAP, 29 control) who were spontaneously breathing at trial entry Clinical and xray evidence of RDS, absence of infection and congenital abnormalities. PaO2 50 mm Hg or less on FiO2 of 0.6. Outborns meeting eligibility criteria for less than 6 hours included. Stratified for weight, 1000-1500 g, 1501-2000 g, > 2000 g. Infants < 1000 g excluded. Age at trial entry for weight stratified groups between 10 hours(SD=6) and 17 hours (SD=13).
Interventions	Face mask CPAP or PEEP (6-14 cm water) vs oxygen or IPPV without PEEP. Endotracheal IPPV initiated in those on facemask IPPV with gastric distension or inadequate ventilation.
Outcomes	IPPV in group spontaneously breathing at trial entry. Mortality, mortality by weight, pneumothorax, and chronic lung disease.
Notes	From a total of 71 trial participants 20 were excluded on the grounds that they were not spontaneously breathing at trial entry. Additional information was supplied by the authors on the outcomes for 51 included infants. Of these the birthweight in the group who were allocated to CPAP is significantly higher.

Risk of bias

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

Buckmaster 2007

Methods	Random sequence generation and allocation concealed using off-site computer. Stratified by gestation 31-33 and 34-36 weeks and hospital. All infants randomised were included in the analysis. 12 infants withdrawn before primary outcome measurement were not excluded from the analysis.
Participants	Infants in non tertiary hospitals >=31 and < 37 weeks weighing > 1200g, < 24 hours of age with respiratory distress as defined by recession, grunt, nasal flare, and/or tachypnoea who required > 30% oxygen in a headbox to maintain oxygen saturation levels >= 94% for 30 minutes. For multiples only the first sibling to meet the inclusion criteria was included.
Interventions	Nasal CPAP using Hudson prong and bubble delivery circuit compared with headbox oxygen

Buckmaster 2007 (*Continued*)

Outcomes	Treatment failure or transfer to a neonatal intensive care unit. Transfer to a neonatal intensive care unit, pneumothorax,
Notes	300 infants were randomised and of these 158 who were preterms with respiratory distress without cardiac disease were included in this review. Data was supplied by the authors. It not possible to exclude meconium aspiration as the cause of respiratory distress in 8 infants with reported meconium staining of amniotic fluid. IVH was not reported as not all infants had a cranial ultrasound examination. Surfactant not used prior to transfer. Antenatal steroids used for 35% of infants.

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	Off site computer

Durbin 1976

Methods	Concealment of allocation adequate (sealed envelope). No blinding of treatment or outcome assessment. Completeness of follow up adequate.
Participants	24 infants (12 CNP, 12 control) with severe RDS, > 1000 g, PaO2 < 60 mm Hg in FiO2 > 0.95 for 15 mins. Mean age (hrs) for control group 30.3(SD=6.1), and treatment group 28.2(SD=3.7).
Interventions	8-12 cm water CNP for less severe illness and endotracheal CPAP for more severe vs oxygen. IPPV started if PaO2 < 35 mm Hg.
Outcomes	IPPV, mortality, duration of O2, duration on FiO2 > 0.5, and > 0.6, any pneumothorax, pneumothorax after randomization.
Notes	Infants with pneumothorax before randomization were excluded from the analysis of pneumothorax after randomisation.

Risk of bias

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

Fanaroff 1973

Methods	Concealment of allocation adequate (sealed envelope). Sequential analysis. No concealment of treatment or outcome assessment. Completeness of follow up uncertain.
Participants	29 preterm infants (15 CNP, 14 control) > 1000g, free from congenital abnormality, with RDS with PO2 < 60 mm Hg in FiO2 0.7. Total participants, 19. Infants matched at allocation for age (<24 and >24hrs) and weight group (1000-1499, 1500 - 1999, and > 2000 g).
Interventions	CNP chamber (6-14 cm water negative pressure) vs oxygen hood. Study group failures received mechanical ventilation and control group failures either CPAP or mechanical ventilation.
Outcomes	Any further respiratory assistance, mortality, BPD, RLF.
Notes	Rate of pneumothorax taken from Bancalari 1992, who obtained information from authors.

Risk of bias

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

Rhodes 1973

Methods	Concealment inadequate. Alternate allocation to treatment or control group by 500 g birthweight groups. No blinding of treatment or outcome assessment. Completeness of followup uncertain.
Participants	41 preterm infants (22 CPAP, 19 control) with clinical and xray features of RDS and PaO2 < 60 mm Hg in FiO2 0.5, stratified by 500 g birthweight groups from < 1500 g to > 2500 g. Mean age (hrs) for intervention group 10.1 (SD=1.8) and 12.4 (SD=2.0).
Interventions	Tight fitting mask CPAP (8-10 cm water) vs head box oxygen. CPAP used on control patients failing headbox treatment. Assisted ventilation given for apnoea requiring bag and mask ventilation, PaO2 < 40 mm Hg in FiO2 1.0, or PCO2 > 80 mm Hg.
Outcomes	Mortality, mortality in < 1500 g, mortality in 1500 g or more, assisted ventilation, pneumothorax after randomization, any pneumothorax.
Notes	Infants with pneumothorax before randomization were excluded from the analysis of pneumothorax after randomisation.

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	No	C - Inadequate

Samuels 1996

Methods	Concealment of allocation adequate. Sealed envelopes randomized in sequentially matched pairs. Stratified for gestation, oxygen requirement and whether intubated. No blinding of intervention or outcomes. Follow up complete.
Participants	In two centres, 52 preterm infants with respiratory failure not due to infection or congenital heart disease spontaneously breathing at 4 hours in FiO2 0.4 or > to maintain PO2 above 60 mm Hg (subgroup of trial). Mean (SD) gestational age at birth 32.5 (1.8) v 31.0 (1.9) weeks, range 30-36 v 29-36. Prenatal corticosteroids 5/26 v 4/26; C/S 22/26 v 23/26; labour 19/26 v 21/26; maternal hypertension 11/26 v 10/26; SGA 5/26 v 7/26; Mean (SD) FiO2 at entry 0.55 (0.1) v 0.51(0.09).
Interventions	CNP chamber 4-6 cm water vs head box oxygen.
Outcomes	Mortality at 28 days and at discharge, failure (required IPPV), pneumothorax, BPD, parenchymal intracranial hemorrhage, PVL, NEC, ROP
Notes	244 patients were randomized. Of these the 52 who were preterms with respiratory failure and spontaneously breathing at trial entry were included in this review. Individual patient data on these infants was supplied by the authors. Only 17% of the mothers of the 52 infants received prenatal corticosteroids (similar in each group).

Risk of bias

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

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

Pieper 2003	First 4 of 21 babies allocated randomly but remaining babies allocated according to availability of CPAP system. If CPAP system occupied baby used as a control.
Swyer 1973	Randomized comparison of three continuous distending pressure methods but no control (standard) treatment group was included.
Tooley 2003	The study included infants of 25 to 28 weeks gestation who were all intubated at birth, given a single dose of surfactant and positive pressure ventilation then randomised at about one hour of age to extubation to nasal CPAP or to continued conventional IPPV. No criteria for the diagnosis of RDS were given.

Characteristics of studies awaiting assessment *[ordered by study ID]*

Telford 2006

Methods	See Samuels 1996
Participants	See Samuels 1996
Interventions	See Samuels 1996
Outcomes	9-15 year neurodevelopmental outcomes
Notes	9-15 year outcomes of Samuels 1996

DATA AND ANALYSES

Comparison 1. CDP vs standard care

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Treatment failure (by death and use of additional ventilatory assistance, by blood gas criteria or transfer to a neonatal intensive care unit)	6		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 Death or use of additional ventilatory support	6	355	Risk Ratio (M-H, Fixed, 95% CI)	0.65 [0.52, 0.81]
1.2 Death or respiratory failure by blood gas criteria	1	158	Risk Ratio (M-H, Fixed, 95% CI)	0.53 [0.32, 0.90]
1.3 Death or transfer to a neonatal intensive care unit	1	158	Risk Ratio (M-H, Fixed, 95% CI)	0.49 [0.30, 0.78]
2 Use of additional ventilatory assistance	5	314	Risk Ratio (M-H, Fixed, 95% CI)	0.72 [0.56, 0.91]
3 Transfer to a neonatal intensive care unit	1	158	Risk Ratio (M-H, Fixed, 95% CI)	0.47 [0.30, 0.75]
4 Mortality	6	355	Risk Ratio (M-H, Fixed, 95% CI)	0.52 [0.32, 0.87]
5 Mortality 1500 g or less	2	32	Risk Ratio (M-H, Fixed, 95% CI)	0.67 [0.38, 1.20]
6 Mortality above 1500 g	2	60	Risk Ratio (M-H, Fixed, 95% CI)	0.24 [0.07, 0.84]
7 Duration of supplemental oxygen (days)	2	76	Mean Difference (IV, Fixed, 95% CI)	0.65 [-1.86, 3.15]
8 Any pneumothorax	6	355	Risk Ratio (M-H, Fixed, 95% CI)	2.64 [1.39, 5.04]
9 Pneumothorax occurring after allocation	6	351	Risk Ratio (M-H, Fixed, 95% CI)	2.42 [1.26, 4.65]
10 Use of surfactant	1	52	Risk Ratio (M-H, Fixed, 95% CI)	0.43 [0.12, 1.48]
11 Chronic lung disease at 28 days in survivors	3	260	Risk Ratio (M-H, Fixed, 95% CI)	1.22 [0.44, 3.39]

Comparison 2. CNP vs standard care

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Failure (death or use of additional ventilatory assistance)	2	81	Risk Ratio (M-H, Fixed, 95% CI)	0.61 [0.41, 0.90]
2 Use of additional ventilatory assistance	2	81	Risk Ratio (M-H, Fixed, 95% CI)	0.71 [0.46, 1.07]
3 Mortality	2	81	Risk Ratio (M-H, Fixed, 95% CI)	0.80 [0.31, 2.09]
4 Pneumothorax after allocation	2	81	Risk Ratio (M-H, Fixed, 95% CI)	2.26 [0.63, 8.12]

5 Chronic lung disease at 28 days in survivors	1	52	Risk Ratio (M-H, Fixed, 95% CI)	3.0 [0.13, 70.42]

Comparison 3. CPAP vs standard care

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Treatment Failure (by death or use of additional ventilatory assistance)	3		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 Death or the use of additional ventilation	3	250	Risk Ratio (M-H, Fixed, 95% CI)	0.61 [0.45, 0.81]
1.2 Death or failure by blood gas criteria	1	158	Risk Ratio (M-H, Fixed, 95% CI)	0.53 [0.32, 0.90]
1.3 Death or transfer to a neonatal intensive care unit	1	158	Risk Ratio (M-H, Fixed, 95% CI)	0.49 [0.30, 0.78]
2 Use of additional ventilatory assistance	2	209	Risk Ratio (M-H, Fixed, 95% CI)	0.65 [0.47, 0.89]
3 Mortality	2	199	Risk Ratio (M-H, Fixed, 95% CI)	0.52 [0.23, 1.16]
4 Mortality 1500 g or less	1	18	Risk Ratio (M-H, Fixed, 95% CI)	1.0 [0.52, 1.92]
5 Mortality above 1500 g	1	24	Risk Ratio (M-H, Fixed, 95% CI)	0.10 [0.01, 1.59]
6 Any pneumothorax	1	41	Risk Ratio (M-H, Fixed, 95% CI)	2.59 [0.29, 22.88]
7 Pneumothorax occurring after allocation	1	41	Risk Ratio (M-H, Fixed, 95% CI)	0.86 [0.06, 12.89]

Comparison 4. Early application of CDP vs standard care

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Failure (death or use of additional ventilatory assistance)	3	121	Risk Ratio (M-H, Fixed, 95% CI)	0.59 [0.44, 0.79]
2 Mortality	2	70	Risk Ratio (M-H, Fixed, 95% CI)	0.56 [0.29, 1.05]

Comparison 5. CDP versus standard care - excluding Rhodes (quasi-random)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Failure (death or use of additional ventilatory assistance)	5	314	Risk Ratio (M-H, Fixed, 95% CI)	0.68 [0.54, 0.86]
2 Mortality	4	263	Risk Ratio (M-H, Fixed, 95% CI)	0.64 [0.26, 1.56]

Comparison 6. CDP versus standard care - excluding Belenky (low quality)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Failure (death or use of additional ventilatory assistance)	5	304	Risk Ratio (M-H, Fixed, 95% CI)	0.61 [0.47, 0.80]
2 Mortality	5	304	Risk Ratio (M-H, Fixed, 95% CI)	0.61 [0.34, 1.11]

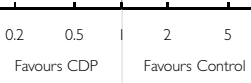
Analysis 1.1. Comparison 1 CDP vs standard care, Outcome 1 Treatment failure (by death and use of additional ventilatory assistance, by blood gas criteria or transfer to a neonatal intensive care unit).

Review: Continuous distending pressure for respiratory distress in preterm infants

Comparison: 1 CDP vs standard care

Outcome: 1 Treatment failure (by death and use of additional ventilatory assistance, by blood gas criteria or transfer to a neonatal intensive care unit)

Study or subgroup	CDP n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 Death or use of additional ventilatory support					
Belenky 1976	15/22	25/29		21.8 %	0.79 [0.57, 1.09]
Buckmaster 2007	15/79	28/79		28.3 %	0.54 [0.31, 0.92]
Durbin 1976	8/12	6/12		6.1 %	1.33 [0.67, 2.67]
Fanaroff 1973	5/15	12/14		12.5 %	0.39 [0.18, 0.82]
Rhodes 1973	7/22	13/19		14.1 %	0.47 [0.23, 0.92]
Samuels 1996	13/26	17/26		17.2 %	0.76 [0.48, 1.23]
Subtotal (95% CI)	**176**	**179**		**100.0 %**	**0.65 [0.52, 0.81]**
Total events: 63 (CDP), 101 (Control)					
Heterogeneity: Chi^2 = 9.23, df = 5 (P = 0.10); I^2 =46%					
Test for overall effect: Z = 3.81 (P = 0.00014)					
2 Death or respiratory failure by blood gas criteria					
Buckmaster 2007	16/79	30/79		100.0 %	0.53 [0.32, 0.90]
Subtotal (95% CI)	**79**	**79**		**100.0 %**	**0.53 [0.32, 0.90]**
Total events: 16 (CDP), 30 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.37 (P = 0.018)					
3 Death or transfer to a neonatal intensive care unit					
Buckmaster 2007	18/79	37/79		100.0 %	0.49 [0.30, 0.78]
Subtotal (95% CI)	**79**	**79**		**100.0 %**	**0.49 [0.30, 0.78]**
Total events: 18 (CDP), 37 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 3.01 (P = 0.0026)					



Analysis 1.2. Comparison 1 CDP vs standard care, Outcome 2 Use of additional ventilatory assistance.

Review: Continuous distending pressure for respiratory distress in preterm infants

Comparison: 1 CDP vs standard care

Outcome: 2 Use of additional ventilatory assistance

Study or subgroup	CDP n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Belenky 1976	15/22	25/29		26.7 %	0.79 [0.57, 1.09]
Buckmaster 2007	15/79	28/79		34.6 %	0.54 [0.31, 0.92]
Durbin 1976	8/12	6/12		7.4 %	1.33 [0.67, 2.67]
Fanaroff 1973	5/15	8/14		10.2 %	0.58 [0.25, 1.36]
Samuels 1996	13/26	17/26		21.0 %	0.76 [0.48, 1.23]
Total (95% CI)	**154**	**160**		**100.0 %**	**0.72 [0.56, 0.91]**
Total events: 56 (CDP), 84 (Control)					
Heterogeneity: Chi^2 = 4.85, df = 4 (P = 0.30); I^2 =18%					
Test for overall effect: Z = 2.76 (P = 0.0058)					

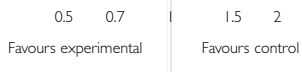
Analysis 1.3. Comparison 1 CDP vs standard care, Outcome 3 Transfer to a neonatal intensive care unit.

Review: Continuous distending pressure for respiratory distress in preterm infants

Comparison: 1 CDP vs standard care

Outcome: 3 Transfer to a neonatal intensive care unit

Study or subgroup	CPAP n/N	Headbox n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Buckmaster 2007	18/79	38/79		100.0 %	0.47 [0.30, 0.75]
Total (95% CI)	**79**	**79**		**100.0 %**	**0.47 [0.30, 0.75]**
Total events: 18 (CPAP), 38 (Headbox)					
Heterogeneity: not applicable					
Test for overall effect: Z = 3.14 (P = 0.0017)					

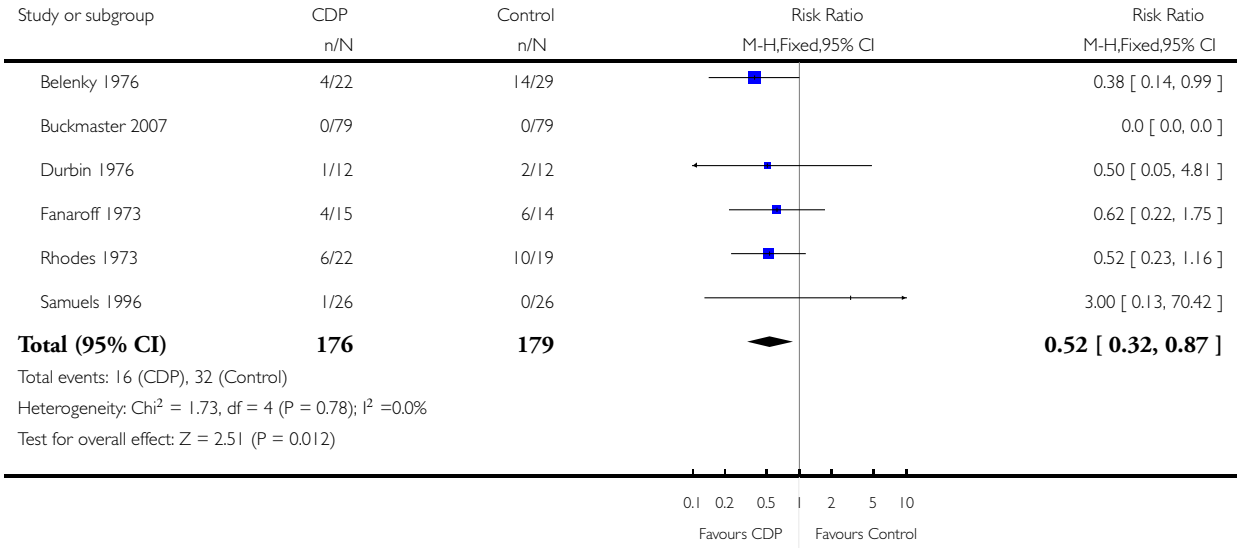


Analysis 1.4. Comparison 1 CDP vs standard care, Outcome 4 Mortality.

Review: Continuous distending pressure for respiratory distress in preterm infants

Comparison: 1 CDP vs standard care

Outcome: 4 Mortality

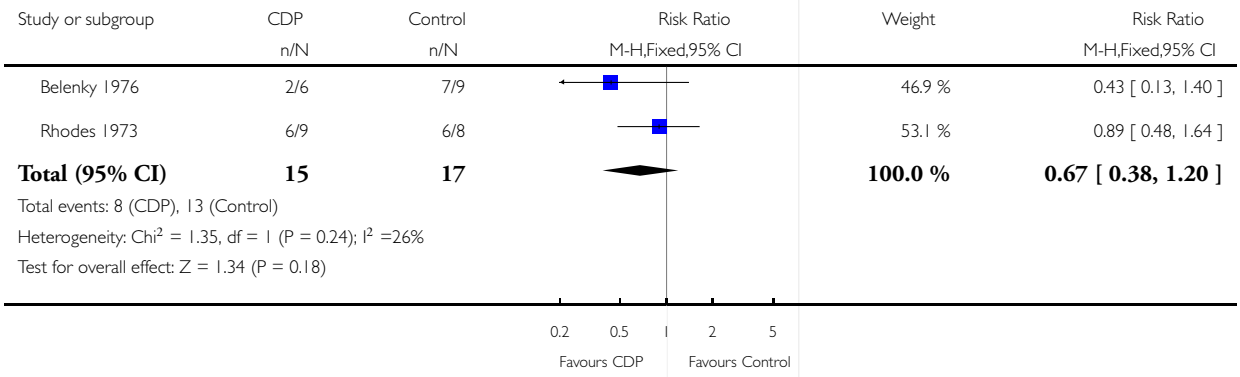


Analysis 1.5. Comparison 1 CDP vs standard care, Outcome 5 Mortality 1500 g or less.

Review: Continuous distending pressure for respiratory distress in preterm infants

Comparison: 1 CDP vs standard care

Outcome: 5 Mortality 1500 g or less



Analysis 1.6. Comparison 1 CDP vs standard care, Outcome 6 Mortality above 1500 g.

Review: Continuous distending pressure for respiratory distress in preterm infants

Comparison: 1 CDP vs standard care

Outcome: 6 Mortality above 1500 g

Study or subgroup	CDP n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Belenky 1976	2/16	7/20		56.2 %	0.36 [0.09, 1.49]
Rhodes 1973	0/13	4/11		43.8 %	0.10 [0.01, 1.59]
Total (95% CI)	**29**	**31**		**100.0 %**	**0.24 [0.07, 0.84]**

Total events: 2 (CDP), 11 (Control)

Heterogeneity: $Chi^2 = 0.71$, df = 1 (P = 0.40); $I^2 = 0.0\%$

Test for overall effect: Z = 2.23 (P = 0.026)

Analysis 1.7. Comparison 1 CDP vs standard care, Outcome 7 Duration of supplemental oxygen (days).

Review: Continuous distending pressure for respiratory distress in preterm infants

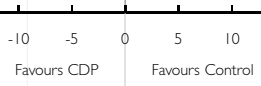
Comparison: 1 CDP vs standard care

Outcome: 7 Duration of supplemental oxygen (days)

Study or subgroup	CDP N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Durbin 1976	12	9.5 (3.8)	12	9.3 (2.8)		87.9 %	0.20 [-2.47, 2.87]
Samuels 1996	26	9.85 (18.59)	26	5.96 (2.27)		12.1 %	3.89 [-3.31, 11.09]
Total (95% CI)	**38**		**38**			**100.0 %**	**0.65 [-1.86, 3.15]**

Heterogeneity: $Chi^2 = 0.89$, df = 1 (P = 0.35); $I^2 = 0.0\%$

Test for overall effect: Z = 0.51 (P = 0.61)



Analysis 1.8. Comparison 1 CDP vs standard care, Outcome 8 Any pneumothorax.

Review: Continuous distending pressure for respiratory distress in preterm infants

Comparison: 1 CDP vs standard care

Outcome: 8 Any pneumothorax

Study or subgroup	CDP n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Belenky 1976	8/22	4/29		31.1 %	2.64 [0.91, 7.64]
Buckmaster 2007	8/79	3/79		27.0 %	2.67 [0.73, 9.68]
Durbin 1976	2/12	0/12		4.5 %	5.00 [0.27, 94.34]
Fanaroff 1973	2/15	2/14		18.7 %	0.93 [0.15, 5.76]
Rhodes 1973	3/22	1/19		9.7 %	2.59 [0.29, 22.88]
Samuels 1996	5/26	1/26		9.0 %	5.00 [0.63, 39.91]
Total (95% CI)	**176**	**179**		**100.0 %**	**2.64 [1.39, 5.04]**

Total events: 28 (CDP), 11 (Control)

Heterogeneity: Chi^2 = 1.80, df = 5 (P = 0.88); I^2 =0.0%

Test for overall effect: Z = 2.95 (P = 0.0032)

Analysis 1.9. Comparison 1 CDP vs standard care, Outcome 9 Pneumothorax occurring after allocation.

Review: Continuous distending pressure for respiratory distress in preterm infants

Comparison: 1 CDP vs standard care

Outcome: 9 Pneumothorax occurring after allocation

Study or subgroup	CDP n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Rhodes 1973	1/20	1/19		9.3 %	0.95 [0.06, 14.13]
Fanaroff 1973	2/15	2/14		18.8 %	0.93 [0.15, 5.76]
Belenky 1976	8/22	4/29		31.4 %	2.64 [0.91, 7.64]
Durbin 1976	1/10	0/12		4.2 %	3.55 [0.16, 78.56]
Samuels 1996	5/26	1/26		9.1 %	5.00 [0.63, 39.91]
Buckmaster 2007	8/79	3/79		27.3 %	2.67 [0.73, 9.68]
Total (95% CI)	**172**	**179**		**100.0 %**	**2.42 [1.26, 4.65]**
Total events: 25 (CDP), 11 (Control)					
Heterogeneity: Chi^2 = 2.09, df = 5 (P = 0.84); I^2 =0.0%					
Test for overall effect: Z = 2.65 (P = 0.0079)					

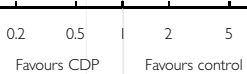
Analysis 1.10. Comparison 1 CDP vs standard care, Outcome 10 Use of surfactant.

Review: Continuous distending pressure for respiratory distress in preterm infants

Comparison: 1 CDP vs standard care

Outcome: 10 Use of surfactant

Study or subgroup	Favors CDP n/N	Favors Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Samuels 1996	3/26	7/26		100.0 %	0.43 [0.12, 1.48]
Total (95% CI)	**26**	**26**		**100.0 %**	**0.43 [0.12, 1.48]**
Total events: 3 (Favors CDP), 7 (Favors Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.34 (P = 0.18)					



Analysis 1.11. Comparison 1 CDP vs standard care, Outcome 11 Chronic lung disease at 28 days in survivors.

Review: Continuous distending pressure for respiratory distress in preterm infants

Comparison: 1 CDP vs standard care

Outcome: 11 Chronic lung disease at 28 days in survivors

Study or subgroup	CDP n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Belenky 1976	4/22	5/29		74.3 %	1.05 [0.32, 3.47]
Buckmaster 2007	1/79	1/79		17.2 %	1.00 [0.06, 15.71]
Samuels 1996	1/25	0/26		8.5 %	3.12 [0.13, 73.06]
Total (95% CI)	**126**	**134**		**100.0 %**	**1.22 [0.44, 3.39]**

Total events: 6 (CDP), 6 (Control)

Heterogeneity: $Chi^2 = 0.42$, df = 2 (P = 0.81); $I^2 = 0.0\%$

Test for overall effect: Z = 0.38 (P = 0.70)

Analysis 2.1. Comparison 2 CNP vs standard care, Outcome 1 Failure (death or use of additional ventilatory assistance).

Review: Continuous distending pressure for respiratory distress in preterm infants

Comparison: 2 CNP vs standard care

Outcome: 1 Failure (death or use of additional ventilatory assistance)

Study or subgroup	CNP n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Fanaroff 1973	5/15	12/14		42.2 %	0.39 [0.18, 0.82]
Samuels 1996	13/26	17/26		57.8 %	0.76 [0.48, 1.23]
Total (95% CI)	**41**	**40**		**100.0 %**	**0.61 [0.41, 0.90]**

Total events: 18 (CNP), 29 (Control)

Heterogeneity: $Chi^2 = 2.27$, df = 1 (P = 0.13); $I^2 = 56\%$

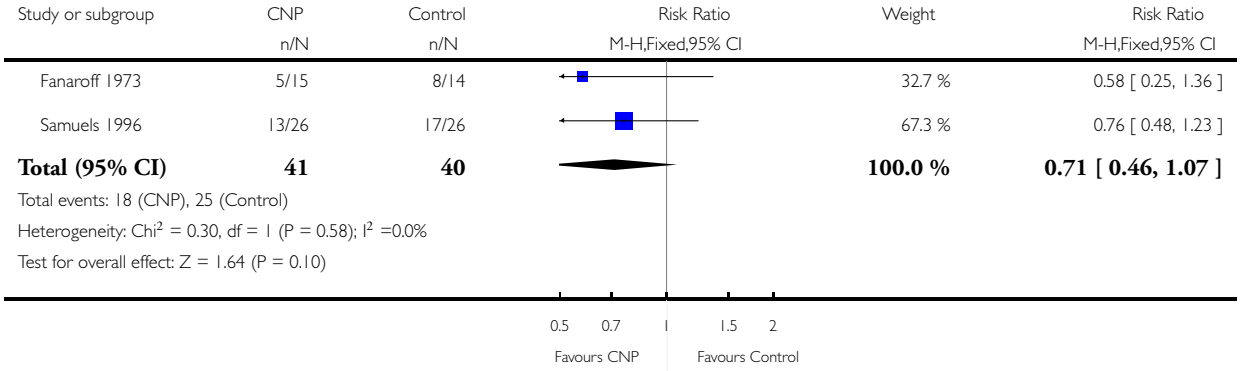
Test for overall effect: Z = 2.46 (P = 0.014)

Analysis 2.2. Comparison 2 CNP vs standard care, Outcome 2 Use of additional ventilatory assistance.

Review: Continuous distending pressure for respiratory distress in preterm infants

Comparison: 2 CNP vs standard care

Outcome: 2 Use of additional ventilatory assistance

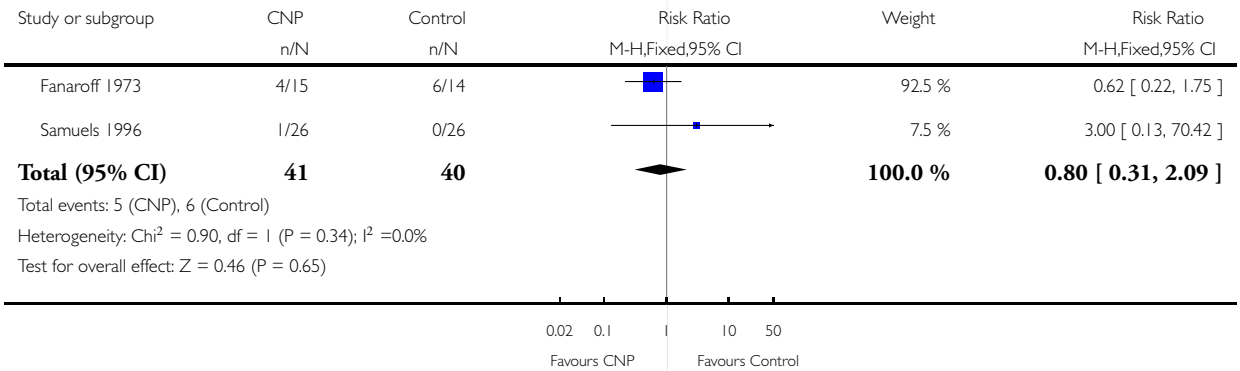


Analysis 2.3. Comparison 2 CNP vs standard care, Outcome 3 Mortality.

Review: Continuous distending pressure for respiratory distress in preterm infants

Comparison: 2 CNP vs standard care

Outcome: 3 Mortality

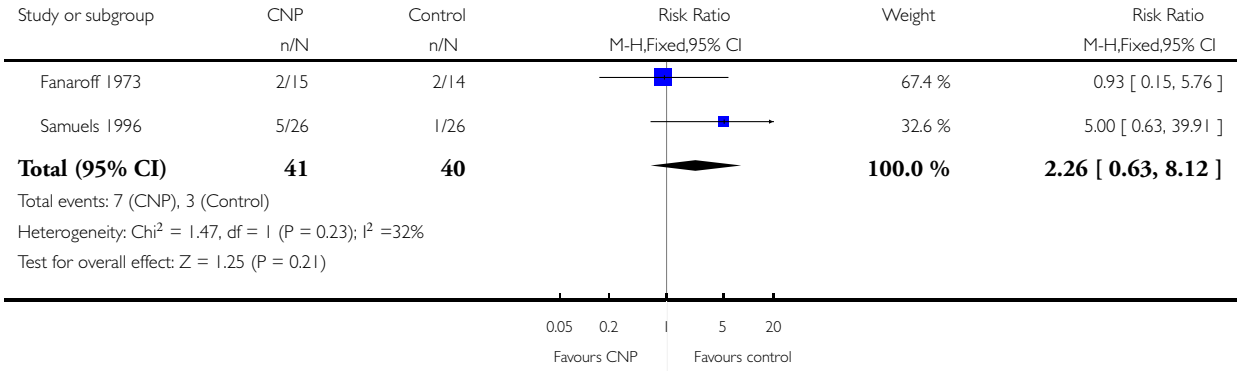


Analysis 2.4. Comparison 2 CNP vs standard care, Outcome 4 Pneumothorax after allocation.

Review: Continuous distending pressure for respiratory distress in preterm infants

Comparison: 2 CNP vs standard care

Outcome: 4 Pneumothorax after allocation

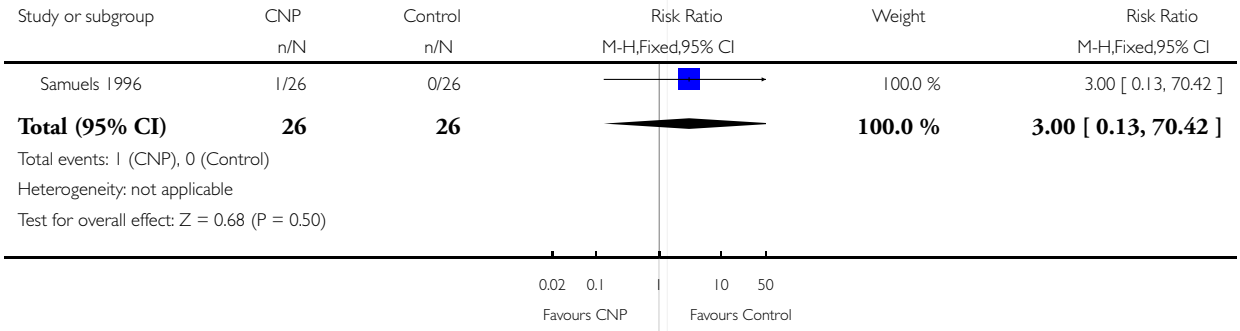


Analysis 2.5. Comparison 2 CNP vs standard care, Outcome 5 Chronic lung disease at 28 days in survivors.

Review: Continuous distending pressure for respiratory distress in preterm infants

Comparison: 2 CNP vs standard care

Outcome: 5 Chronic lung disease at 28 days in survivors



Analysis 3.1. Comparison 3 CPAP vs standard care, Outcome 1 Treatment Failure (by death or use of additional ventilatory assistance).

Review: Continuous distending pressure for respiratory distress in preterm infants

Comparison: 3 CPAP vs standard care

Outcome: 1 Treatment Failure (by death or use of additional ventilatory assistance)

Study or subgroup	CPAP n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 Death or the use of additional ventilation					
Belenky 1976	15/22	25/29		34.0 %	0.79 [0.57, 1.09]
Buckmaster 2007	15/79	28/79		44.1 %	0.54 [0.31, 0.92]
Rhodes 1973	7/22	13/19		22.0 %	0.47 [0.23, 0.92]
Subtotal (95% CI)	**123**	**127**		**100.0 %**	**0.61 [0.45, 0.81]**
Total events: 37 (CPAP), 66 (Control)					
Heterogeneity: Chi^2 = 3.41, df = 2 (P = 0.18); I^2 =41%					
Test for overall effect: Z = 3.39 (P = 0.00070)					
2 Death or failure by blood gas criteria					
Buckmaster 2007	16/79	30/79		100.0 %	0.53 [0.32, 0.90]
Subtotal (95% CI)	**79**	**79**		**100.0 %**	**0.53 [0.32, 0.90]**
Total events: 16 (CPAP), 30 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.37 (P = 0.018)					
3 Death or transfer to a neonatal intensive care unit					
Buckmaster 2007	18/79	37/79		100.0 %	0.49 [0.30, 0.78]
Subtotal (95% CI)	**79**	**79**		**100.0 %**	**0.49 [0.30, 0.78]**
Total events: 18 (CPAP), 37 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 3.01 (P = 0.0026)					

Analysis 3.2. Comparison 3 CPAP vs standard care, Outcome 2 Use of additional ventilatory assistance.

Review: Continuous distending pressure for respiratory distress in preterm infants

Comparison: 3 CPAP vs standard care

Outcome: 2 Use of additional ventilatory assistance

Study or subgroup	CPAP n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Belenky 1976	15/22	25/29		43.5 %	0.79 [0.57, 1.09]
Buckmaster 2007	15/79	28/79		56.5 %	0.54 [0.31, 0.92]
Total (95% CI)	**101**	**108**		**100.0 %**	**0.65 [0.47, 0.89]**
Total events: 30 (CPAP), 53 (Control)					
Heterogeneity: Chi^2 = 1.98, df = 1 (P = 0.16); I^2 =49%					
Test for overall effect: Z = 2.67 (P = 0.0075)					

Analysis 3.3. Comparison 3 CPAP vs standard care, Outcome 3 Mortality.

Review: Continuous distending pressure for respiratory distress in preterm infants

Comparison: 3 CPAP vs standard care

Outcome: 3 Mortality

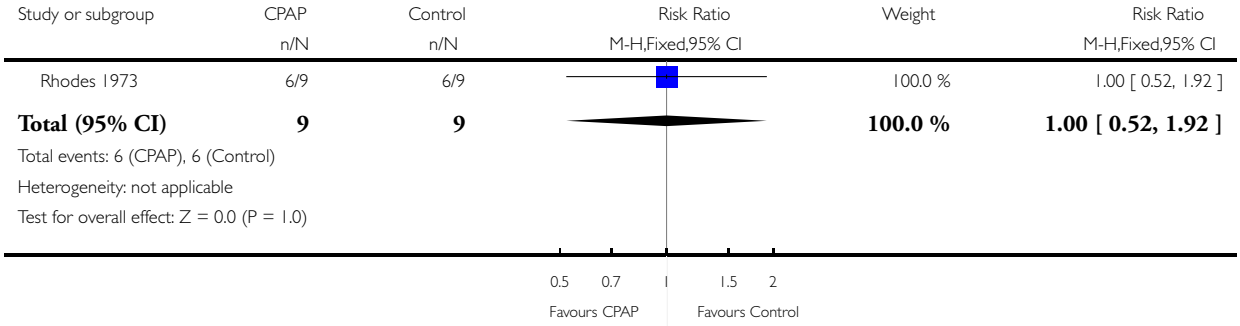
Study or subgroup	CPAP n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Buckmaster 2007	0/79	0/79		0.0 [0.0, 0.0]
Rhodes 1973	6/22	10/19		0.52 [0.23, 1.16]
Total (95% CI)	**101**	**98**		**0.52 [0.23, 1.16]**
Total events: 6 (CPAP), 10 (Control)				
Heterogeneity: Chi^2 = 0.0, df = 0 (P = 1.00); I^2 =0.0%				
Test for overall effect: Z = 1.60 (P = 0.11)				

Analysis 3.4. Comparison 3 CPAP vs standard care, Outcome 4 Mortality 1500 g or less.

Review: Continuous distending pressure for respiratory distress in preterm infants

Comparison: 3 CPAP vs standard care

Outcome: 4 Mortality 1500 g or less

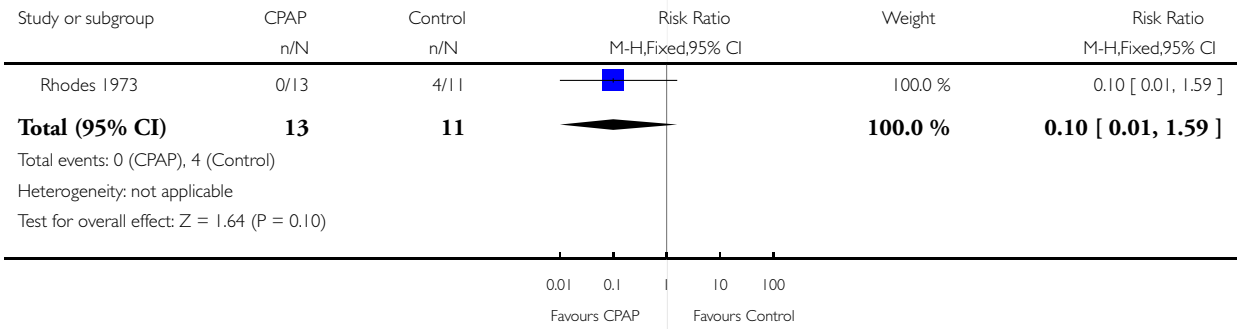


Analysis 3.5. Comparison 3 CPAP vs standard care, Outcome 5 Mortality above 1500 g.

Review: Continuous distending pressure for respiratory distress in preterm infants

Comparison: 3 CPAP vs standard care

Outcome: 5 Mortality above 1500 g



Analysis 3.6. Comparison 3 CPAP vs standard care, Outcome 6 Any pneumothorax.

Review: Continuous distending pressure for respiratory distress in preterm infants

Comparison: 3 CPAP vs standard care

Outcome: 6 Any pneumothorax

Study or subgroup	CPAP n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Rhodes 1973	3/22	1/19		100.0 %	2.59 [0.29, 22.88]
Total (95% CI)	**22**	**19**		**100.0 %**	**2.59 [0.29, 22.88]**
Total events: 3 (CPAP), 1 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.86 (P = 0.39)					

Analysis 3.7. Comparison 3 CPAP vs standard care, Outcome 7 Pneumothorax occurring after allocation.

Review: Continuous distending pressure for respiratory distress in preterm infants

Comparison: 3 CPAP vs standard care

Outcome: 7 Pneumothorax occurring after allocation

Study or subgroup	CPAP n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Rhodes 1973	1/22	1/19		100.0 %	0.86 [0.06, 12.89]
Total (95% CI)	**22**	**19**		**100.0 %**	**0.86 [0.06, 12.89]**
Total events: 1 (CPAP), 1 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.11 (P = 0.92)					

Analysis 4.1. Comparison 4 Early application of CDP vs standard care, Outcome 1 Failure (death or use of additional ventilatory assistance).

Review: Continuous distending pressure for respiratory distress in preterm infants

Comparison: 4 Early application of CDP vs standard care

Outcome: 1 Failure (death or use of additional ventilatory assistance)

Study or subgroup	Early CDP n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Belenky 1976	15/22	25/29		45.0 %	0.79 [0.57, 1.09]
Fanaroff 1973	5/15	12/14		25.9 %	0.39 [0.18, 0.82]
Rhodes 1973	7/22	13/19		29.1 %	0.47 [0.23, 0.92]
Total (95% CI)	**59**	**62**		**100.0 %**	**0.59 [0.44, 0.79]**
Total events: 27 (Early CDP), 50 (Control)					
Heterogeneity: Chi^2 = 4.84, df = 2 (P = 0.09); I^2 =59%					
Test for overall effect: Z = 3.56 (P = 0.00038)					

Analysis 4.2. Comparison 4 Early application of CDP vs standard care, Outcome 2 Mortality.

Review: Continuous distending pressure for respiratory distress in preterm infants

Comparison: 4 Early application of CDP vs standard care

Outcome: 2 Mortality

Study or subgroup	Early CDP n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Fanaroff 1973	4/15	6/14		36.6 %	0.62 [0.22, 1.75]
Rhodes 1973	6/22	10/19		63.4 %	0.52 [0.23, 1.16]
Total (95% CI)	**37**	**33**		**100.0 %**	**0.56 [0.29, 1.05]**
Total events: 10 (Early CDP), 16 (Control)					
Heterogeneity: Chi^2 = 0.07, df = 1 (P = 0.78); I^2 =0.0%					
Test for overall effect: Z = 1.81 (P = 0.070)					

Analysis 5.1. Comparison 5 CDP versus standard care - excluding Rhodes (quasi-random), Outcome 1 Failure (death or use of additional ventilatory assistance).

Review: Continuous distending pressure for respiratory distress in preterm infants

Comparison: 5 CDP versus standard care - excluding Rhodes (quasi-random)

Outcome: 1 Failure (death or use of additional ventilatory assistance)

Study or subgroup	CDP n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Belenky 1976	15/22	25/29		25.4 %	0.79 [0.57, 1.09]
Buckmaster 2007	15/79	28/79		32.9 %	0.54 [0.31, 0.92]
Durbin 1976	8/12	6/12		7.1 %	1.33 [0.67, 2.67]
Fanaroff 1973	5/15	12/14		14.6 %	0.39 [0.18, 0.82]
Samuels 1996	13/26	17/26		20.0 %	0.76 [0.48, 1.23]
Total (95% CI)	**154**	**160**		**100.0 %**	**0.68 [0.54, 0.86]**

Total events: 56 (CDP), 88 (Control)

Heterogeneity: Chi^2 = 7.58, df = 4 (P = 0.11); I^2 =47%

Test for overall effect: Z = 3.22 (P = 0.0013)

Analysis 5.2. Comparison 5 CDP versus standard care - excluding Rhodes (quasi-random), Outcome 2 Mortality.

Review: Continuous distending pressure for respiratory distress in preterm infants

Comparison: 5 CDP versus standard care - excluding Rhodes (quasi-random)

Outcome: 2 Mortality

Study or subgroup	CDP n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Buckmaster 2007	0/79	0/79		0.0 [0.0, 0.0]
Durbin 1976	1/12	2/12		0.50 [0.05, 4.81]
Fanaroff 1973	4/15	6/14		0.62 [0.22, 1.75]
Samuels 1996	1/26	1/26		1.00 [0.07, 15.15]
Total (95% CI)	**132**	**131**		**0.64 [0.26, 1.56]**

Total events: 6 (CDP), 9 (Control)

Heterogeneity: Chi^2 = 0.15, df = 2 (P = 0.93); I^2 =0.0%

Test for overall effect: Z = 0.99 (P = 0.32)

Analysis 6.1. Comparison 6 CDP versus standard care - excluding Belenky (low quality), Outcome 1 Failure (death or use of additional ventilatory assistance).

Review: Continuous distending pressure for respiratory distress in preterm infants

Comparison: 6 CDP versus standard care - excluding Belenky (low quality)

Outcome: 1 Failure (death or use of additional ventilatory assistance)

Study or subgroup	CDP n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Buckmaster 2007	15/79	28/79		36.2 %	0.54 [0.31, 0.92]
Durbin 1976	8/12	6/12		7.8 %	1.33 [0.67, 2.67]
Fanaroff 1973	5/15	12/14		16.0 %	0.39 [0.18, 0.82]
Rhodes 1973	7/22	13/19		18.0 %	0.47 [0.23, 0.92]
Samuels 1996	13/26	17/26		22.0 %	0.76 [0.48, 1.23]
Total (95% CI)	**154**	**150**		**100.0 %**	**0.61 [0.47, 0.80]**

Total events: 48 (CDP), 76 (Control)

Heterogeneity: Chi^2 = 7.96, df = 4 (P = 0.09); I^2 =50%

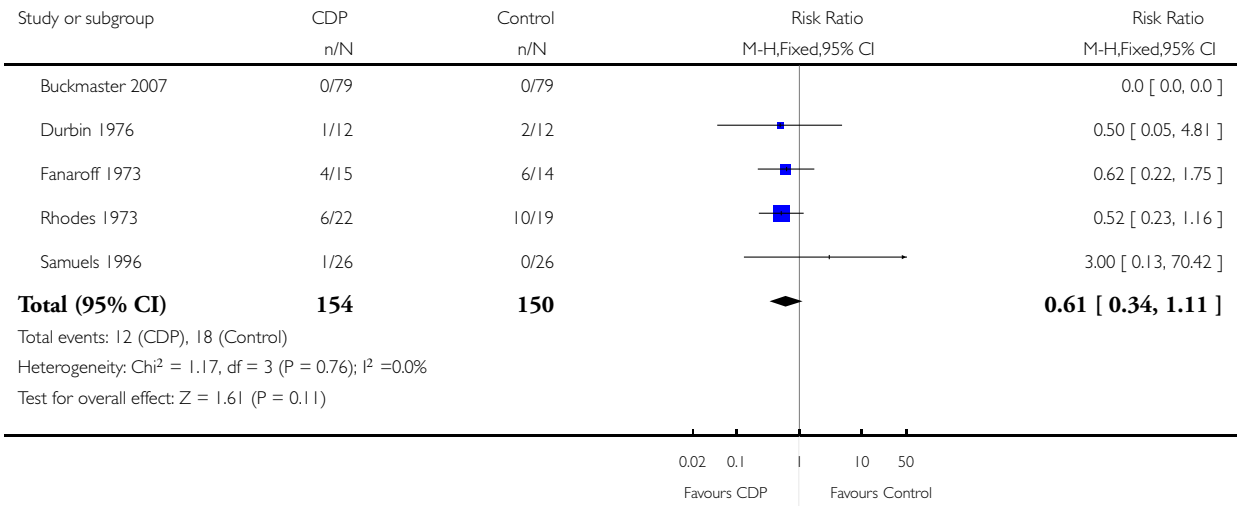
Test for overall effect: Z = 3.53 (P = 0.00042)

Analysis 6.2. Comparison 6 CDP versus standard care - excluding Belenky (low quality), Outcome 2 Mortality.

Review: Continuous distending pressure for respiratory distress in preterm infants

Comparison: 6 CDP versus standard care - excluding Belenky (low quality)

Outcome: 2 Mortality



WHAT'S NEW

Last assessed as up-to-date: 23 May 2008.

24 May 2008	New search has been performed	This updates the review "Continuous distending pressure for respiratory distress syndrome in preterm infants" published in the Cochrane Database of Systematic Reviews, Issue 1, 2004. The title has been modified slightly to read "Continuous distending pressure for respiratory distress in preterm infants". The primary outcome has been modified and additional outcomes included. The search was repeated and one new trial has been included. There was no change to the conclusions.
10 April 2008	Amended	Converted to new review format.

HISTORY

Protocol first published: Issue 3, 2000

Review first published: Issue 3, 2000

27 August 2004	New search has been performed	This review updates the previous version of review of "Continuous distending pressure for respiratory distress syndrome in preterm infants" last updated The Cochrane Library, Issue 2, 2002 (Ho 2002). The literature search was repeated and no further trials eligible for inclusion were found. There are no changes to the overall conclusions.
7 February 2002	New citation required and conclusions have changed	Substantive amendment

CONTRIBUTIONS OF AUTHORS

Search: JJH with contribution by DHS

Data extraction: JJH, PXS, DHS

Writing of text: JJH with contributions by DHS and PGD

DECLARATIONS OF INTEREST

None

SOURCES OF SUPPORT

Internal sources

- Penang Medical College, Malaysia.
- Centre for Perinatal Health Services Research, University of Sydney, Australia.
- Royal Womens Hospital, Melbourne, Australia.
- Wanganui Hospital, New Zealand, Malaysia.
- Neonatal Unit, Royal Prince Alfred Hospital, Sydney, Australia.

External sources

- No sources of support supplied

INDEX TERMS

Medical Subject Headings (MeSH)

*Infant, Premature; Infant, Newborn; Intermittent Positive-Pressure Ventilation [adverse effects]; Outcome Assessment (Health Care); Positive-Pressure Respiration [*methods]; Randomized Controlled Trials as Topic; Respiratory Distress Syndrome, Newborn [*therapy]

MeSH check words

Humans