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**Nasal continuous positive airway pressure (nCPAP) for term neonates with respiratory distress**

Jann P Foster, Adam Buckmaster, Lynn Sinclair, Sylvia Lees, Robert Guaran

1 School of Nursing and Midwifery, Western Sydney University, Penrith DC, Australia. 2 Sydney Nursing School/Central Clinical School, Discipline of Obstetrics, Gynaecology and Neonatology, Sydney Medical School, University of Sydney, Sydney, Australia. 3 Ingham Research Institute, Liverpool, Australia. 4 Department of Paediatrics, Gosford Hospital, Gosford, Australia. 5 NSW Pregnancy and newborn Services Network (PSN), Westmead, Australia. 6 Special Care Nursery, Wollongong Hospital, New South Wales, Australia

Contact address: Jann P Foster, School of Nursing and Midwifery, Western Sydney University, Penrith DC, Australia. j.foster@uws.edu.au. jann.foster@sydney.edu.au

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**ABSTRACT**

This is the protocol for a review and there is no abstract. The objectives are as follows:

To determine whether nCPAP as the primary modality of treatment is effective and safe for treating respiratory distress in the term neonate (≥ 37 weeks gestation).

We will explore potential sources of clinical heterogeneity through the following a priori subgroup analysis:

1. Age of infant at randomisation (< 6 hours, 6 to 12 hours, > 12 hours to 24 hours)
2. Setting (neonatal intensive care unit; non-tertiary special care nursery)
3. Level of continuing distending pressure used (≤ 5 cm H₂O; ≥ 6 cm H₂O)
4. Types of nCPAP (via continuous flow e.g. bubble nCPAP; variable flow nCPAP e.g. Infant Flow Driver)
5. Delivery system (nasal cannulae (short); nasal cannulae (long); nasal mask)
6. Method of oxygen delivery (ambient oxygen (crib, headbox); low-flow nasal cannulae; high-flow nasal cannulae)
7. Method of birth (caesarean section; vaginal delivery)
8. Reason for respiratory distress (e.g. hyaline membrane disease; transient tachypnoea of the newborn; bacterial pneumonia; meconium aspiration syndrome; persistent pulmonary hypertension).

**Sensitivity analysis**
BACKGROUND

Description of the condition

The most common cause of respiratory distress in preterm infants is transient surfactant deficiency leading to hyaline membrane disease (respiratory distress syndrome). This condition becomes less common as infants approach term gestation while other causes of respiratory distress become more common (Miall 2011). These include transient tachypnoea of the newborn; bacterial pneumonia; meconium aspiration; perinatal asphyxia leading to persistent pulmonary hypertension of the newborn; and pneumothorax, either spontaneous or secondary to one of the former conditions (Edwards 2013). The increasing number of term infants delivered by caesarean section is reported to have increased the incidence of respiratory distress in term infants (Edwards 2013). Each of these conditions has a different underlying aetiology but may initially present with the same set of physical signs making differentiation initially difficult. The range of possible respiratory support modalities that neonates with respiratory distress might require include ambient oxygen via a crib or headbox, low-flow nasal cannulae, high-flow nasal cannulae, continuous positive airway pressure and mechanical ventilation (Rodriguez 2003).

Description of the intervention

Continuous positive airway pressure (CPAP) refers to the application of heated and humidified positive pressure to the airway of a spontaneously breathing infant throughout the respiratory cycle (DiBlasi 2009). CPAP is seen as an alternative to intubation and mechanical ventilation of preterm infants. Mechanical ventilation can contribute to pulmonary growth arrest and the development of chronic lung disease, and CPAP has been shown to be less injurious to the lungs of newborn infants (DiBlasi 2009). CPAP is proposed as an effective and safe method of support for term neonates with respiratory distress. It is increasingly being introduced into non-tertiary special care nursery units worldwide (Buckmaster 2007; Roberts 2011, Australia; Donoghue 1998, New Zealand; Jónsson 1992, Scandinavia), and for use with larger, and term neonates. Similarly to its use in preterm infants, CPAP can be used for term infants as an alternative to mechanical ventilation. CPAP can provide additional respiratory support for neonates born in non-tertiary care centres to decrease the need for neonatal transfer to the higher-level tertiary NICU. The emotional distress to parents is substantial when a baby is transferred (Frischer 1992); and there are significant costs associated with transfer of an infant to a tertiary hospital (Buckmaster 2007). However, CPAP has been described as resource-and time-intensive, and caution has been advised with its use in units that are not well staffed or experienced in its use in infants (DiBlasi 2009). CPAP has been associated with adverse effects such as pneumothorax (Migliori 2003); and trauma of the nares of term and preterm infants (Jarana 2010; Robertson 1996).

There have been a number of Cochrane reviews investigating the effectiveness of CPAP for preterm infants. Davis 2003 evaluated the use of nasal CPAP after extubation for preventing morbidity and found nasal CPAP to be effective in preventing failure of extubation in preterm infants following a period of endotracheal intubation and intermittent positive pressure ventilation (IPPV). Davis 2001 compared extubation from low-rate intermittent positive airway pressure versus extubation after a trial of endotracheal CPAP and recommended that preterm infants no longer requiring endotracheal intubation and IPPV should be directly extubated without a trial of endotracheal CPAP. Ho 2002 examined the effect of continuous distending pressure (CDP, continuous positive airway pressure or continuous negative pressure) for respiratory distress in preterm infants and concluded that CDP reduces mortality, or the need for assisted ventilation and reduces the need for IPPV. Subramaniam 2005 explored prophylactic (early) nasal CPAP for preventing morbidity and mortality in very preterm infants but found insufficient information to evaluate its effectiveness in reducing the use of IPPV.

The pressure sources of CPAP can be broadly grouped into variable and continuous flow systems (Yagui 2011). Variable flow devices such as the Infant Flow Driver generate CPAP pressure by varying the inspiratory flow. For example, a flow adjusted to 8L/min results in an approximate nCPAP level of 5 cm H2O (DiBlasi 2009). Continuous flow variable pressure systems such as ‘bubble’ CPAP vary the CPAP pressure by a mechanism other than inspiratory flow variation (Yagui 2011). The level of bubble CPAP pressure is determined by the distance the distal end of the expiratory limb of the tubing is placed into a water filled chamber: for example, 5 cm below surface = 5 cm H2O (DiBlasi 2009) and as the gas exits the tube, it creates bubbles. The inspiratory flow may also be adjusted with bubble CPAP to maintain the required level of CPAP (Yagui 2011). Higher CPAP pressures may be needed in order to recruit lungs with low compliance. CPAP pressures from 5 cm H2O up to 12 cm H2O have been used in the neonatal population (DiBlasi 2009). CPAP can be used either as a primary modality of respiratory support (with escalation of support if CPAP fails), or as a ‘step-down’ method from a higher level of respiratory support. CPAP as the primary modality can be instituted prophylactically (e.g. immediately after birth) or after clinical manifestations have occurred. The interest of this systematic review is CPAP that is delivered nasally (nCPAP). The most commonly used devices for nCPAP delivery are short or long nasal prongs, and nasal masks (DiBlasi 2009). nCPAP is contraindicated in infants with upper airway abnormalities (i.e. cleft palate, choanal atresia, tracheoesophageal fistula), unrepaired diaphragmatic hernia, severe cardiovascular instability, recurrent apneic episodes, and in patients with...
severe ventilatory impairment (pH 7.25, and PaCO\textsubscript{2} 60 mm Hg) \citep{AmericanAssociationforRespiratoryCare2004}.

**How the intervention might work**

CPAP works by delivering a constant positive pressure to the spontaneously breathing infant’s airway. CPAP is most commonly delivered to the nasal airway opening using bi-nasal short prongs or a nasal mask, and pressure is generated using a variety of devices. CPAP pressure is maintained in the lungs due to the anatomic seal that forms between the infant’s tongue and the soft palate \citep{DiBlasi2009}. CPAP’s mechanism of action is complex and only partially understood but is believed to decrease the work of breathing by increasing oxygenation through the stabilisation and recruitment of collapsed alveoli \citep{Thompson2006}. The functional residual capacity is increased resulting in an increased alveolar surface area for gas exchange and a decrease in intrapulmonary shunt and endogenous surfactant is conserved. The breathing pattern regularises with stabilisation of the rib cage, reducing recession and increasing efficiency of the diaphragm \citep{Thompson2006}. It had been proposed that pressure oscillations during bubble CPAP improve gas exchange \citep{Lee1998}; however, this postulation was not supported in a more recent study \citep{Morley2005}.

**Why it is important to do this review**

The use of nCPAP in the preterm population is now widely used but its efficacy and safety for the term population has not been determined \citep{Roberts2011}. It is also important for the long-term outcomes for preterm and term neonates who receive nCPAP outside tertiary care centres to be examined \citep{Roberts2011}. We were unable to identify any systematic reviews that have assessed the efficacy and safety of nCPAP in the term infant population. Thus, the interest of this review is to determine whether nCPAP is a safe and effective treatment (including most effective pressure) in the term neonate.

**OBJECTIVES**

To determine whether nCPAP as the primary modality of treatment is effective and safe for treating respiratory distress in the term neonate (≥ 37 weeks gestation).

We will explore potential sources of clinical heterogeneity through the following a priori subgroup analysis:

1. Age of infant at randomisation (< 6 hours, 6 to 12 hours, > 12 hours to 24 hours)
2. Setting (neonatal intensive care unit; non-tertiary special care nursery)
3. Level of continuing distending pressure used (≤ 5 cm H\textsubscript{2}O; ≥ 6 cm H\textsubscript{2}O)
4. Types of nCPAP (via continuous flow e.g. bubble nCPAP; variable flow nCPAP e.g. Infant Flow Driver)
5. Delivery system (nasal cannulae (short); nasal cannulae (long); nasal mask)
6. Method of oxygen delivery (ambient oxygen (crib, headbox); low-flow nasal cannulae; high-flow nasal cannulae)
7. Method of birth (caesarean section; vaginal delivery)
8. Reason for respiratory distress (e.g. hyaline membrane disease; transient tachypnoea of the newborn; bacterial pneumonia; meconium aspiration syndrome; persistent pulmonary hypertension).

**Sensitivity analysis**

**METHODS**

**Criteria for considering studies for this review**

**Types of studies**

Randomised controlled trials and quasi-randomised trials assessing nCPAP as a primary modality of respiratory support. Cluster trials will be accepted. Cross-over trials will be excluded.

**Types of participants**

Newborn infants (≥ 37 weeks gestation) with respiratory distress requiring oxygen therapy and up to 28 days postnatal age. Infants must be randomised within 24 hours post birth. Infants with a cleft palate, choanal atresia, or tracheoesophageal fistula will be excluded from the review.

**Types of interventions**

Nasal continuous positive airway pressure (nCPAP) versus ambient oxygen (via crib, headbox);
Nasal continuous positive airway pressure (nCPAP) versus low-flow nasal cannulae; and
Nasal continuous positive airway pressure (nCPAP) versus high-flow nasal cannulae.

Studies comparing CPAP versus intubation and assisted mechanical ventilation will not be included in this review.
Types of outcome measures

Primary outcomes
Mortality prior to hospital discharge;
Mortality following hospital discharge (up to one year post discharge)

Secondary outcomes
Need for increased level of respiratory support (e.g., escalation of respiratory support from nCPAP, ambient oxygen, low-flow nasal cannulae or high-flow nasal cannulae);
Incidence of pneumothorax (defined as presence of air between the visceral and parietal pleura, and lung collapse, Lim 2011) diagnosed by X-ray during treatment with intervention;
Length of total hospitalisation (days-at all hospitals);
Duration receiving oxygen therapy (days);
Weight at discharge home (grams);
Neurodevelopmental disability (after at least 18 months postnatal age) defined as neurological abnormality including cerebral palsy on clinical examination, developmental delay more than 2 standard deviations (SDs) below population mean on a standardised test of development, or blindness (visual acuity < 6/60), or deafness (any hearing impairment requiring amplification);
Duration of ventilation (for infants requiring escalation from nCPAP);
Duration of CPAP (for infants requiring escalation from oxygen);
Nasal trauma (as described by authors) during treatment with nCPAP;
Parental stress - measured using a validated scale (e.g. Parental Stressor Scale: NICU (PSS: NICU, Miles 1993) (during treatment with intervention);
Nurses’ workload - measured using a validated scale (e.g. Professional Assessment of Optimal Nursing Care Intensity Level (PAONCIL, Fagerstrom 2000); and
Any adverse effects not predetermined but reported by the authors (during treatment with intervention).

Search methods for identification of studies
We will use the standard search strategy of The Cochrane Neonatal Review Group (CNRG) as documented in The Cochrane Library. See the CNRG search strategy.

Electronic searches
Two review authors will perform the electronic database searches independently. The standard search strategy of CNRG as described in The Cochrane Library will be used. Randomised controlled trials will be identified from databases-the Cochrane Central Register of Controlled Trials (Issue 4, 2013), PubMed (from 1966 to current), EMBASE (from 1988 to current) and CINAHL (from 1982 to current)-using the following subject headings (MeSH) and text words: (infant-newborn OR infant*, OR Neonat*, AND [continuous positive airway pressure OR continuous distending pressure OR CPAP OR CDP]). We will search clinical trials registries for ongoing or recently completed trials (www.clinicaltrials.gov, www.controlled-trials.com and www.who.int/ictrp). We will attempt to identify all relevant studies regardless of language or publication status (published, unpublished and in press).

Data collection and analysis
We will use Cochrane’s standard systematic review methods as documented in the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2011); and CNRG.

Selection of studies
Review authors will independently assess for inclusion all the potential studies identified as a result of the search strategy. We will resolve any disagreement through discussion or, if required, we will consult a Cochrane review arbiter.
Specifically, we will:
1. Merge search results using reference management software and remove duplicate records of the same report;
2. Examine titles and abstracts to remove irrelevant reports;
3. Retrieve the full text of the potentially relevant reports;
4. Link together multiple reports of the same study;
5. Examine full text reports for compliance of studies with eligibility criteria;
6. Correspond with investigators, when appropriate, to clarify study eligibility;
7. At all stages, note reasons for inclusion and exclusion of articles; and resolve disagreements through consensus, or refer for arbitration to the editorial base of CNRG if needed;
8. Make final decisions on study inclusion and proceed to data collection;

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9. Resolve all discrepancies through a consensus process.

Data extraction and management
We will design a form to extract data. For eligible studies, review authors will extract the data using the agreed form. We will resolve discrepancies through discussion or, if required, we will consult a review arbiter. We will enter data using Review Manager 5 software and check for accuracy (RevMan 2012). When information regarding any of the above is unclear, we will attempt to contact authors of the original reports to provide further details.

Assessment of risk of bias in included studies
Review authors will independently assess risk of bias for each study using the criteria outlined in the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2011). We will resolve any disagreement by discussion or by involving a review arbiter.

(1) Random sequence generation (checking for possible selection bias)
We will describe for each included study the method used to generate the allocation sequence in sufficient detail to allow an assessment of whether it should produce comparable groups. We will assess the method as:
- low risk (any truly random process, e.g. random number table; computer random number generator);
- high risk (any non-random process, e.g. odd or even date of birth; hospital or clinic record number); or
- unclear risk.

(2) Allocation concealment (checking for possible selection bias)
We will describe for each included study the method used to conceal the allocation sequence in sufficient detail and determine whether intervention allocation could have been foreseen in advance of, or during, recruitment or changed after assignment. We will assess the methods as:
- low risk (e.g. telephone or central randomisation; consecutively numbered sealed opaque envelopes);
- high risk (open random allocation; unsealed or non-opaque envelopes, alternation; date of birth); or
- unclear risk.

(3) Blinding (checking for possible performance bias)
We will describe for each included study the methods used, if any, to blind study participants and personnel from knowledge of which intervention a participant received. We will judge studies to be at low risk of bias if they were blinded or if we judge that the lack of blinding could not have affected the results. We will assess blinding separately for different outcomes or class of outcomes. We will assess the risk of bias methods as:
- low risk, high risk or unclear risk for participants;
- low risk, high risk or unclear risk for personnel; or
- low risk, high risk or unclear risk for outcome assessors.

(4) Incomplete outcome data (checking for possible attrition bias through withdrawals, dropouts, protocol deviations)
We will describe for each included study, and for each outcome or class of outcomes, the completeness of data including attrition and exclusions from the analysis. We will state whether attrition and exclusions were reported, the numbers included in the analysis at each stage (compared with the total randomised participants), reasons for attrition or exclusion where reported and whether missing data were balanced across groups or were related to outcomes. Where sufficient information is reported, or can be supplied by the trial authors, we will re-include missing data in the analyses which we undertake. We will assess the risk of bias methods as:
- low risk (less than 20% missing data); high risk; or unclear risk.

(5) Selective reporting bias
We will describe for each included study how we investigated the possibility of selective outcome reporting bias and what we found. We will assess the methods as:
- low risk (where it is clear that all of the study’s prespecified outcomes and all expected outcomes of interest to the review have been reported);
- high risk (where not all the study’s pre-specified outcomes have been reported; one or more reported primary outcomes were not pre-specified; outcomes of interest are reported incompletely and so cannot be used; study fails to include results of a key outcome that would have been expected to have been reported);
- unclear risk.

(6) Other sources of bias
We will describe for each included study any important concerns we have about other possible sources of bias (e.g. early termination of trial due to data-dependant process, extreme baseline imbalance, etc.). We will assess whether each study was free of other problems that could put it at risk of bias. We will assess other sources of bias as: low risk; high risk; or unclear risk. We will make explicit judgements about whether studies are at high risk of bias, according to the criteria given in the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2011). With reference to the above, we will assess the likely magnitude and direction of the bias and whether we consider it likely to impact on the findings. We will explore the impact of the level of bias through undertaking sensitivity analyses (see Sensitivity analysis). We will try to obtain the study protocols of all included studies.
Each criterion will be judged as being at ‘low risk’ of bias, ‘high risk’ of bias, or ‘unclear risk’ of bias (for either lack of information or uncertainty over the potential for bias).

Quality of evidence
We will assess the quality of evidence for the main comparison at the outcome level using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach (Guyatt 2011a). This methodological approach considers evidence from randomised controlled trials as high quality that may be downgraded based on consideration of any of five areas: design (risk of bias), consistency across studies, directness of the evidence, precision of estimates, and presence of publication bias (Guyatt 2011a). The GRADE approach results in an assessment of the quality of a body of evidence in one of four grades: 1) High: we are very confident that the true effect lies close to that of the estimate of the effect; 2) Moderate: we are moderately confident in the effect estimate-the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different; 3) Low: our confidence in the effect estimate is limited-the true effect may be substantially different from the estimate of the effect; 4) Very Low: we have very little confidence in the effect estimate-the true effect is likely to be substantially different from the estimate of effect (Schünemann 2013).

The review authors will independently assess the quality of the evidence found for the following outcomes identified as critical or important for clinical decision making: mortality prior to hospital discharge; mortality following hospital discharge (up to one year post discharge); need for increased level of respiratory support (e.g. escalation of respiratory support from nCPAP, ambient oxygen, low-flow nasal cannulae or high-flow nasal cannulae); incidence of pneumothorax; length of total hospitalisation; duration receiving oxygen therapy; neurodevelopmental disability.

In cases where we consider the risk of bias arising from inadequacies regarding concealment of allocation, randomised assignment, complete follow-up or blinded outcome assessment to reduce our confidence in the effect estimates, we will downgrade the quality of evidence accordingly (Guyatt 2011b). Consistency will be evaluated by similarity of point estimates, extent of overlap of confidence intervals and statistical criteria including measurement of heterogeneity (I²). The quality of evidence will be downgraded when inconsistency across study results is large and unexplained (i.e. some studies suggest important benefit and others no effect or harm without a clinical explanation; Guyatt 2011d). Precision will be assessed accordingly with the 95% confidence interval around the pooled estimation (Guyatt 2011c). When trials were conducted in populations other than the target population, we will downgrade the quality of evidence because of indirectness (Guyatt 2011e).

Data (i.e. pooled estimates of the effects and corresponding 95% confidence Interval) and explicit judgements for each of the above aspects assessed will be entered into the Guideline Development Tool, the software used to create ‘Summary of findings’ tables (GRADEpro 2008). All judgements involving the assessment of the study characteristics described above will be explained in footnotes or comments in the ‘Summary of findings’ table.

Measures of treatment effect
The results of the studies will be analysed using the statistical package Review Manager 5 (RevMan 2012). Data will be summarised in a meta-analysis if they are sufficiently homogeneous, both clinically and statistically.

Dichotomous data
We will present results as risk ratios (RR) and risk differences (RD) with 95% confidence intervals (CI) for dichotomous data. We will calculate the number needed to treat for an additional beneficial outcome (NNTB), or number needed to treat for an additional harmful outcome (NNTH), and associated 95% CIs if there is a statistically significant reduction (or increase) in RD.

Continuous data
For continuous data, we will use the mean difference (MD) if outcomes are measured in the same way between trials.

Unit of analysis issues
The unit of analysis is the participating infant in individually randomised trials and the neonatal unit (or sub-unit) for cluster randomised trials. Cross-over trials will be excluded.

Cluster randomised trials:
We will include cluster randomised trials in the analyses along with individually randomised trials. We will analyse them using the methods described in the Cochrane Handbook for Systematic Reviews of Interventions using an estimate of the intracluster correlation coefficient (ICC) derived from the trial (if possible) or from another source (Higgins 2011). If ICCs from other sources are used, we will report this and conduct sensitivity analyses to investigate the effect of variation in the ICC. If we identify both cluster randomised trials and individually randomised trials, we plan to synthesise the relevant information. We will consider it reasonable to combine the results from both if there is little heterogeneity between the study designs and the interaction between the effect of intervention and the choice of randomisation unit is considered to be unlikely. We will also acknowledge heterogeneity in the randomisation unit and perform a separate meta-analysis.
Dealing with missing data

For all included studies, we will note levels of attrition. If data from the trial reports are insufficient, unclear or missing, we will attempt to contact the trial authors for additional information. We will explore the impact of including studies with high levels of missing data in the overall assessment of treatment effect by using sensitivity analysis. For all outcomes we will carry out analyses, as far as possible, on an intention-to-treat (ITT) basis, i.e. we will attempt to include all participants randomised to each group in the analyses and we will analyse all participants in the group to which they were allocated, regardless of whether they received the allocated intervention. The denominator for each outcome in each trial will be the number randomised minus any participants whose outcomes are known to be missing.

Assessment of heterogeneity

Statistical heterogeneity will be assessed by visual inspection of forest plots, the I² statistic, and Chi² test. We will use the following cut-offs as recommended by the CNRG for the reporting of heterogeneity: less than 25%, no heterogeneity; 25% to 49%, low heterogeneity; 50% to 74%, moderate heterogeneity; and 75% or higher, high heterogeneity. In cases of moderate or high heterogeneity, we will explore the possible causes in terms of the population, intervention, comparison and outcome assessment, and determine whether a meta-analysis is appropriate.

Assessment of reporting biases

We will try to obtain the study protocols of all included studies and we will compare outcomes reported in the protocol to those reported in the findings for each of the included studies. We will investigate reporting and publication bias by examining the degree of asymmetry of a funnel plot if there are at least 10 studies reporting on the same outcome and included in the meta-analysis. Where we suspect reporting bias (see ‘(5) Selective reporting bias’ in Assessment of risk of bias in included studies above), we will attempt to contact study authors asking them to provide missing outcome data. Where this is not possible and the missing data are thought to introduce serious bias, we will explore the impact of including such studies in the overall assessment of results by a sensitivity analysis.

Data synthesis

We will use the fixed-effect model in Review Manager 5 (RevMan 2012) for meta-analyses. For dichotomous data we will use typical RR, RD, and NNTB or NNTH if there is a statistically significant reduction (or increase) in RD; and for continuous data we will use typical MD or standard MD as measures of treatment effect. We will use the generic inverse variance strategy to combine cluster trials.

Subgroup analysis and investigation of heterogeneity

1. Age of infant at randomisation (< 6 hours, 6 to 12 hours, > 12 hours to 24 hours)
2. Setting (neonatal intensive care unit; non-tertiary special care nursery)
3. Level of continuing distending pressure used (≤ 5 cm H₂O; ≥ 6 cm H₂O)
4. Types of CPAP (via continuous flow e.g. bubble nCPAP; variable flow nCPAP e.g. Infant Flow Driver)
5. Delivery system (nasal cannulae (short), nasal cannulae (long), nasal mask)
6. Method of oxygen delivery (ambient oxygen (crib, headbox), low-flow nasal cannulae, high-flow nasal cannulae)
7. Method of birth (caesarean section vs. vaginal delivery)
8. Reason for respiratory distress (e.g. hyaline membrane disease; transient tachypnoea of the newborn; bacterial pneumonia; meconium aspiration syndrome; persistent pulmonary hypertension).

Sensitivity analysis

We will explore methodological heterogeneity through the use of sensitivity analysis. We will assess studies at low risk of bias as those with adequate sequence generation, allocation concealment, and less than 10% losses with ITT analysis.

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14651858.CD001078]

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Donoghue 1998

Edwards 2013

Fagerstrom 2000

Frischer 1992

GRADEpro 2008 [Computer program]

Guyatt 2011a

Guyatt 2011b

Guyatt 2011c

Guyatt 2011d

Guyatt 2011e

Higgins 2011

Ho 2002

Jatana 2010

Jönsson 1992

Lee 1998

Lim 2011

Miall 2011

Migliori 2003

Miles 1993
CONTRIBUTIONS OF AUTHORS

JF and AB wrote the protocol. All other authors provided feedback on the draft protocol.

DECLARATIONS OF INTEREST

JF, AB and SL were involved in an RCT on the use of CPAP in non-tertiary care centres.

SOURCES OF SUPPORT

Internal sources

• No sources of support supplied

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