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[Intervention Review]

Frequency of endotracheal suctioning for the prevention of respiratory morbidity in ventilated newborns

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ABSTRACT

Background

Endotracheal suctioning consists of the mechanical aspiration of pulmonary secretions from the endotracheal tube (ETT) to prevent obstruction. The optimal frequency of ETT suctioning has not been defined.

Objectives

To determine the effect of specific ordered frequency of ETT suctioning ('as scheduled') versus ETT suctioning only in case of indications ('as needed') and of more frequent ETT suctioning versus less frequent ETT suctioning on respiratory morbidity in ventilated newborns.

Search methods

We used the standard search strategy of the Cochrane Neonatal Review group to search the Cochrane Central Register of Controlled Trials (CENTRAL 2015, Issue 10), MEDLINE via PubMed (1966 to 31 October 2015), EMBASE (1980 to 31 October 2015), and CINAHL (1982 to 31 October 2015). We checked the reference lists of retrieved articles and contacted study authors to identify additional studies. We also searched clinical trials databases, conference proceedings, and the reference lists of retrieved articles for randomized controlled trials and quasi-randomized trials.

Selection criteria

Randomized, quasi-randomized, and cluster randomized controlled trials comparing different strategies regarding the frequency of ETT suctioning of newborn infants receiving ventilator support.

Data collection and analysis

We used the standard methods of the Cochrane Neonatal Review Group. Two review authors independently extracted data and assessed the risk of bias of trials. The primary outcome was bronchopulmonary dysplasia or chronic lung disease.

Frequency of endotracheal suctioning for the prevention of respiratory morbidity in ventilated newborns (Review)

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Main results

We identified one randomized controlled study recruiting 97 low birthweight infants that met the inclusion criteria. The study was conducted in the UK in 1987 and 1988. Randomized infants received ETT suctioning every six or 12 hours during the first three days of life. The quality of reporting was limited and we rated the trial at high risk of bias. Furthermore, the trial lacked adequate power. There were no statistically significant differences in any of reported outcomes: bronchopulmonary dysplasia (defined as oxygen at more than 30 days; risk ratio (RR) 0.49, 95% confidence interval (CI) 0.20 to 1.20); incidence of pneumothorax (RR 0.70, 95% CI 0.24 to 2.05); intraventricular hemorrhage (RR 1.12, 95% CI 0.44 to 2.85); neonatal death (RR 1.40, 95% CI 0.58 to 3.37); and time on ventilation (median time 39 hours in the 12-hourly group and 28 hours in the six-hourly group; RD not applicable for this outcome as mean and standard deviation were not reported). Tests for heterogeneity were not applicable as only one study was included.

Authors' conclusions

There was insufficient evidence to identify the ideal frequency of ETT suctioning in ventilated neonates. Future research should focus on the effects in the very preterm newborns, that is, the most vulnerable population as concerns the risk of both lung and brain damage. Assessment should include the cases of prolonged ventilation, when more abundant, dense secretions are common. Clinical trials might include comparisons between 'as-scheduled' versus 'as-needed' endotracheal suctioning, that is, based on specific indications, as well frequent versus less frequent suctioning schedules.

PLAIN LANGUAGE SUMMARY

Frequency of suctioning inside the tube that is used to ventilate newborn babies

Review question

We reviewed the evidence about the effects of different strategies in the frequency of suctioning of newborn babies that are on ventilators. Our main interest was prevention of lung damage.

Background

Newborns might need help with breathing as their lungs are still maturing. An airway catheter (tube) is inserted into the mouth or nose in order to maintain an open airway (patency) in newborns who are unable to breathe on their own. This procedure is called endotracheal intubation. Endotracheal tube suction is necessary to clear secretions and to maintain airway patency, therefore ensuring that the baby receives enough oxygen. The goal of endotracheal intubation suction should be remove as much of the secretions as possible with minimal side effects associated with the procedure. However, suctioning causes stress, pain, and inflammation (swelling) of the windpipe in newborns. The optimal frequency of suctioning has not been defined. Suctioning inside the airway tube might be performed 'as scheduled' by the specialist or only 'as needed'. Moreover, the 'as scheduled' approach might be more or less frequent. We explored the current evidence, up to October 2015, supporting one schedule or another.

Study characteristics

We searched medical databases for clinical studies comparing different strategies regarding the frequency of endotracheal tube suction in newborn babies on ventilators. We found only one study recruiting 97 newborns with bodyweights under 2.5 kg (these are called low birthweight infants). Suctioning was performed every six or 12 hours during the first three days of life.

Key results

There were no important differences on the time the babies were on the ventilator, occurrence of pneumothorax (collapsed lung), need for ventilation or oxygen at more than 30 days, bleeding in the brain, and death in the first month of life. In addition, the study reported no side effects.

Quality of the evidence

We only identified one study, which was conducted in 1987 and 1988 and had several shortcomings. We cannot advise health professionals and parents about the optimal frequency of suctioning when newborns are ventilated.

BACKGROUND

Endotracheal suctioning is commonly performed in intubated newborns. It consists of the mechanical aspiration of pulmonary secretions from the endotracheal tube (ETT) to prevent obstruction. Ideally, ETT suctioning should remove the secretions and avoid related complications (stress, pain, and detrimental physiological alterations). The optimal frequency of ETT suctioning has not been defined.

Description of the condition

Infants with respiratory insufficiency need endotracheal intubation and mechanical ventilation (MV) due to a variety of conditions, including respiratory distress syndrome, air leak, shock, congenital heart disease, and intraoperatively, if there is a need for general anesthesia. Many of these respiratory disorders may increase sputum volume and alter sputum rheology, which worsens secretion clearance, especially in the occurrence of lung inflammation or prolonged duration of MV.

In addition to the effects of the primary disease on the lung, ETT placement causes increased secretions due to tissue irritation and inhibition of ciliary action. The internal lumen of an ETT decreases substantially after a few days of intubation in ventilated adults with acute respiratory failure, due to the formation of biofilm (Shah 2004). Moreover, volume loss increases with increasing duration of tracheal intubation (Shah 2004). Consequently, the risk for ETT obstruction is inversely correlated to gestational age, due to the smaller ETT size and the higher probability for the need of a longer MV. Therefore, ETT suctioning in ventilated newborns is a routine practice to prevent tube obstruction, discomfort for the infant, and lobar collapse.

Description of the intervention

ETT suctioning consists of the placement of a catheter through the ETT and the application of negative pressure as the catheter is being withdrawn. Though it is hypothesized that normal saline instillation prior to suctioning may facilitate the removal of secretions, there is insufficient evidence to support this practice (AARC 2010). Large catheter size should be avoided as its use is associated with lower intratracheal pressure (Kiraly 2008). In-line suction catheters may be more effective than suctioning after disconnection from the ventilator (Taylor 2011).

Although it is essential to prevent airway obstruction, suctioning may cause adverse events, such as hypoxia, pneumothorax, mucosal trauma, atelectasis, and loss of ciliary function. Therefore, each procedure of ETT suctioning might impair respiratory function and increase the risk of bronchopulmonary dysplasia (BPD). However, delayed suctioning might damage the lungs and reduce alveolar recruitment. Therefore, it is difficult to predict the impact of procedure timing on lung injury and BPD pathogenesis. Other

potential complications of suctioning include impairment in cardiovascular effects (bradycardia, other cardiac arrhythmias, and increase in systemic blood pressure); neurologic sequelae (raised intracranial pressure, increase in cerebral blood volume, decrease in cerebral blood oxygen concentration, decreased cerebral oxygen availability, development of intraventricular hemorrhage (IVH), hypoxic-ischemic encephalopathy); nosocomial bacteremia (due to the introduction of pathogens by the suction catheter); and behavioral pain responses (Morrow 2008). In addition, ETT suctioning has been reported to enhance catecholamine response in preterm infants, though without impairment in blood pressure (Greisen 1985). Among the most serious adverse effects, tracheal suctioning has been associated with prolonged disturbances of cerebral hemodynamics in very low birthweight infants (Kaiser 2008). A lower frequency of ETT suctioning might be particularly important during the first days of life when the risk of developing IVH is very high in extremely preterm infants. However, one retrospective study showed an inverse relationship between the incidence of IVH and the number of suction procedures performed during the first 24 hours of life (Linder 2003).

How the intervention might work

Protocols for ETT care vary widely between institutions in relation to most items, including suctioning frequency. Schedules of frequency of ETT suctioning may refer to either specific ordered frequency of suctioning ('as scheduled') or suctioning only in case of indications ('as needed'). Of note, mixed types are possible, that is, the scheduled frequency of suctioning is supplemented 'as needed'. Moreover, an ideal time interval between suctionings has not been identified in the as-scheduled approach.

The American Association for Respiratory Care (AARC) recommends that suctioning should be performed only when clinically indicated in order to maintain the ETT patency (AARC 2010). According to these guidelines, the need to remove accumulated pulmonary secretions would be evidenced by one of the following markers: "sawtooth pattern on the flow-volume loop; on the monitor screen of the ventilator and/or the presence of coarse crackles over the trachea are strong indicators of retained pulmonary secretions; increased peak inspiratory pressure during volume-controlled MV or decreased tidal volume during pressure-controlled ventilation; deterioration of oxygen saturation and/or arterial blood gas values; visible secretions in the airway; patient's inability to generate an effective spontaneous cough; acute respiratory distress; suspected aspiration of gastric or upper-airway secretions" (AARC 2010). However, these indications are considerably broad and subjective: the need for suctioning is a complex issue. Moreover, other causes than ETT obstruction might result in the same clinical signs, thus leading to unnecessary suctioning events (Thomas 2005). Of note, it has been suggested that ETT occlusion might be detected by acoustic reflectometry (Durbin 2004).

Negative effects on suboptimal ventilation and instability for the infant need to be evaluated.

Why it is important to do this review

There are Cochrane reviews focusing on the need for preoxygenation (Pritchard 2001), use of disconnection (Taylor 2011), and depth of ETT suctioning (Gillies 2011), but the frequency of this procedure has not been addressed. This systematic review may help in identifying the optimal frequency and timing of ETT suctioning, avoiding both inopportune and unnecessary suctionings. It has been recommended that ETT suctioning should be performed only when secretions are present, and not routinely (AARC 2010; Morrow 2008; Trevisanuto 2009). However, specific recommendations about optimal suctioning may have an important impact on neonatal health and long-term outcomes for the newborn infant.

OBJECTIVES

To determine the effect of specific ordered frequency of ETT suctioning ('as scheduled') versus ETT suctioning only in case of indications ('as needed') and of more frequent ETT suctioning versus less frequent ETT suctioning on respiratory morbidity in ventilated newborns.

METHODS

Criteria for considering studies for this review

Types of studies

Randomized controlled clinical trials, quasi-randomized controlled trials, and cluster randomized controlled trials.

Types of participants

All newborn infants (of any postnatal age) receiving ventilator support via an ETT.

Types of interventions

We compared different strategies regarding the frequency of ETT suctioning:

1. Suctioning protocols that specified the time between suctioning procedures ('as scheduled') versus protocols that mandated suctioning when certain criteria were met ('as needed'/'as indicated'). For example, we included a trial if it compared a

group with ETT suctioning every six hours versus the other group with ETT suctioning as needed. We accepted the criteria for determining suctioning in the 'as needed' group as defined by the trial authors: we considered trials with different selection of the indications for suctioning in any case in the 'as needed' group.

2. Schedules of more frequent (interval between suctioning episodes six hours or less) versus less frequent (greater than six hours) suctioning. For example, we excluded a trial if the interventions was every hour versus every three hours, as both interventions would be in the 'more frequent' suctioning group. Similarly, we excluded a trial if the interventions were every eight versus every 12 hours, as both interventions would be in the 'less frequent' suctioning group. However, we considered post hoc analysis if we identified multiple trials within each of the previously stated groups.

We described specific subgroup analyses that we would have performed for each comparison in the [Subgroup analysis and investigation of heterogeneity](#) section: less frequent and more frequent suctioning versus suctioning as needed for 'as scheduled' versus 'as needed' (comparison one); and schedules of more frequent (interval between suctioning episodes six hours or less) versus less frequent (greater than six hours) suctioning for more frequent versus less frequent (comparison two).

Types of outcome measures

Primary outcomes

Bronchopulmonary dysplasia/chronic lung disease, defined as:

1. Respiratory support or oxygen, or both, at 28 days of life (NIH 1979).
2. Treatment with oxygen greater than 21% for at least 28 days, with grade of severity scored at 36 weeks of postmenstrual age (PMA) (Jobe 2001).
3. Physiologic definition (measured at 36 weeks' PMA) (Walsh 2004).

We considered 'Need for supplemental oxygen at more than 30 days of age' sufficiently similar to our primary outcome. Acknowledging this as a partial deviation from our protocol, we added it to our primary outcomes.

Secondary outcomes

1. Mortality.
2. Mortality during hospitalization.
3. Mortality to latest follow-up (maximum 12 months).
4. Episodes of oxygen desaturation, defined as a spontaneous fall in oxygen saturation of 85% for 10 seconds or longer in duration, during suctioning or immediately following suctioning.
5. Episodes of bradycardia, defined as a fall in heart rate of more than 30% below the baseline or less than 100 beats per

minute for 10 seconds or longer, during suctioning or immediately following suctioning.

6. Concentration of inflammatory markers in bronchoalveolar lavage, for example, interleukins (IL) and tumor necrosis factor (TNF)- α levels (measured at any time points while the infant was intubated).

7. Number of re-intubations (for suspected or actual blockage of the ETT) while the infant was intubated.

8. Number of unplanned/accidental extubations (dislodgement of the ETT, i.e. the presence of the tube either in a bronchus (on chest x-ray) or above the glottis).

9. Pneumonia (yes/no).

10. Bloodstream infection (blood culture positive, or however defined in individual trials) during hospitalization.

11. Atelectasis (yes/no): lung collapse on chest x-ray during hospitalization.

12. Pneumothorax (yes/no): pneumothorax on chest x-ray during hospitalization.

13. Time on ventilation (hours).

14. Length of stay in neonatal intensive care unit (NICU) (days).

15. Any IVH, and severe IVH (grade 3 or 4 IVH according to Papile classification) (Papile 1978).

16. Cystic periventricular leukomalacia.

17. Major neurodevelopmental disability (cerebral palsy, developmental delay (Bayley or Griffith assessment more than two standard deviations (SD) below the mean) or intellectual impairment (IQ more than two SD below mean), blindness (vision less than 6/60 in both eyes), sensorineural deafness requiring amplification). We evaluated each component of major neurodevelopmental disability:

i) cerebral palsy on physician assessment (yes/no);

ii) developmental delay or intellectual impairment:

Bayley or Griffith assessment more than two SD below the mean or intellectual impairment (IQ more than two SD below mean); neuromotor development (Bayley Scales of Infant Development - Psychomotor Development Index (BSID PDI)) assessed in survivors; mental development (Bayley Scales of Infant Development - Mental Development Index (BSID MDI)) assessed in survivors;

iii) blindness vision (less than 6/60 in both eyes);

iv) sensorineural deafness requiring amplification. We reported these components of long-term outcome for all

included trials that evaluated children after 18 months' chronological age. We performed separate analyses for children aged 18 to 24 months and aged three to five years (Jacobs 2013).

18. Sedation/agitation/pain scale: Premature Infant Pain Profile (PIPP); Neonatal Infant Pain Scale (NIPS); CRIES score (C - crying; R - requires increased oxygen administration; I - increased vital signs; E - expression; S - sleeplessness); Neonatal Pain, Agitation, and Sedation Scale (NPASS). We accepted any time points reported by the authors of the primary studies; in other words, we did not prespecify precise time points.

Search methods for identification of studies

Electronic searches

We used the criteria and standard methods of Cochrane and the Cochrane Neonatal Review Group. We completed a comprehensive search including:

1. the Cochrane Neonatal Group Specialized Register (see [the Cochrane Neonatal Group search strategy for specialized register](#));

2. the Cochrane Central Register of Controlled Trials (CENTRAL), 2015 Issue 10;

3. MEDLINE (from January 1980 to October 2015);

4. EMBASE (from January 1980 to October 2015);

5. CINAHL (from 1982 to October 2015);

6. Abstracts of the Pediatric Academic Societies (PAS) from 2000 to October 2015, electronically through the PAS website ([abstractsonline](#));

7. Perinatal Society of Australia and New Zealand (PSANZ). [Appendix 1](#) shows the full search strategies for each database.

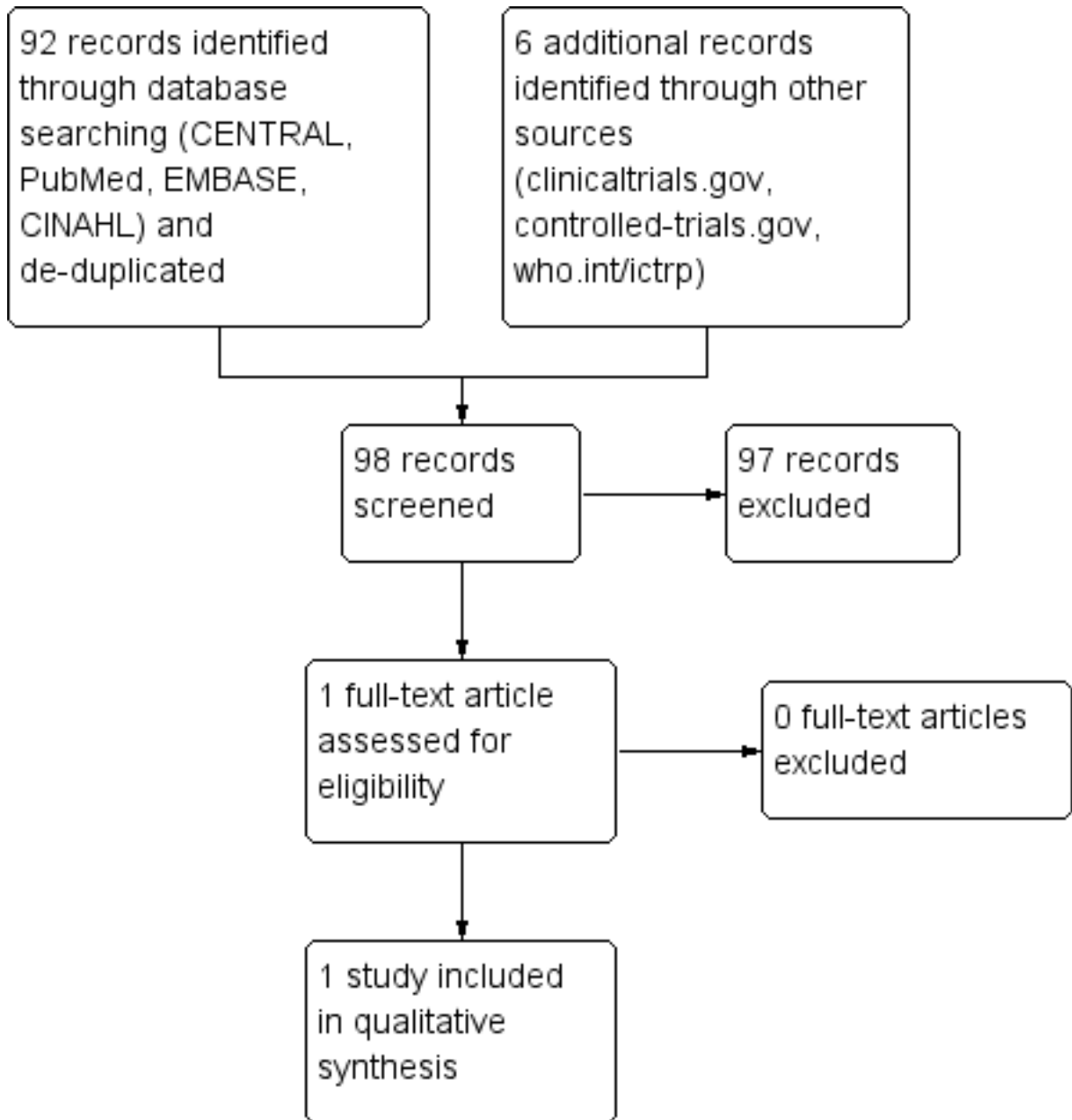
We did not apply any language restrictions and we searched the reference lists of any cited articles.

Two review authors (SZ, MB) independently screened all titles and abstracts to assess which studies met the inclusion criteria. We retrieved full-text copies of all papers that were potentially relevant. We resolved any disagreements by discussion.

Searching other resources

We searched clinical trials registries for ongoing or recently completed trials ([clinicaltrials.gov](#); [controlled-trials.com](#); [who.int/ictcp](#)). See [Figure 1](#).

Figure 1. Study flow diagram.



Data collection and analysis

We used the standard methods of the Cochrane Neonatal Review Group. Each review author independently performed assessments of methodology and extraction of data with comparison and resolution of any differences found at each stage. We assessed the risk of bias regarding blinding of randomization, intervention, and outcome measurements, as well as completeness of follow-up. Where necessary, we asked the trial authors to provide unpublished outcome data.

Selection of studies

Two review authors (SZ, MB) independently searched and identified eligible trials that meet the inclusion criteria. The review authors screened the titles and abstracts to identify potentially relevant citations. We retrieved the full texts of all potentially relevant articles and independently assessed trial eligibility by completing eligibility forms designed in accordance with the specified inclusion criteria. We reviewed studies for relevance based on study design, types of participants, interventions, and outcome measures. We resolved any disagreements by discussion and, if necessary, by consulting a third review author (MGC).

Data extraction and management

Two review authors (SZ, MB) independently extracted, assessed, and coded all available data for each included study using a specially designed data extraction form. We extracted information regarding:

1. study setting (e.g. country and settings);
2. study intervention;
3. sample size;
4. randomization procedure;
5. risk of different biases (see [Assessment of risk of bias in included studies](#) section);
6. outcomes (as listed under [Primary outcomes](#); [Secondary outcomes](#)).

We contacted the trial authors to request additional information and clarification of published data. One review author (MGC) used Review Manager 5 to enter all data ([RevMan 2014](#)).

Assessment of risk of bias in included studies

Two review authors (SZ, MB) independently assessed the risk of bias of all included trials, using Cochrane's 'Risk of bias' tool ([Higgins 2011](#)).

Sequence generation (selection bias)

For each included trial, we categorized the risk of selection bias as:

1. low risk - adequate (any truly random process, e.g. random number table; computer random number generator);
2. high risk - inadequate (any nonrandom process, e.g. odd or even date of birth; hospital or clinic record number);
3. unclear risk - no or unclear information provided.

Allocation sequence concealment (selection bias)

For each included trial, we categorized the risk of bias regarding allocation concealment as:

1. low risk - adequate (e.g. telephone or central randomization; consecutively numbered sealed opaque envelopes);
2. high risk - inadequate (open random allocation; unsealed or nonopaque envelopes, alternation; date of birth);
3. unclear risk - no or unclear information provided.

Blinding (performance bias)

For each included trial, we categorized the methods used to blind study personnel from knowledge of which intervention a participant received.

Blinding (detection bias)

For each included trial, we categorized the methods used to blind outcome assessors from knowledge of which intervention a participant received. We assessed blinding separately for different outcomes or classes of outcomes.

Incomplete outcome data (attrition bias)

For each included trial and for each outcome, we described the completeness of data including attrition and exclusions from the analysis. We noted whether attrition and exclusions were reported, the numbers included in the analysis at each stage (compared with the total randomized participants), reasons for attrition or exclusion where reported, and whether missing data were balanced across groups or related to outcomes. In order to reduce bias from trials with high loss to follow-up, we planned to perform a sensitivity analysis only including data that reported follow-up data for at least 80% of the randomized sample.

Selective outcome reporting (reporting bias)

For each included trial, we described how we investigated the risk of selective outcome reporting bias and what we found. We assessed the methods as:

1. low risk - adequate (where it was clear that all of the study's prespecified outcomes and all expected outcomes of interest to the review were reported);

2. high risk - inadequate (where not all the study's prespecified outcomes were reported; one or more reported primary outcomes were not prespecified; outcomes of interest were reported incompletely and so could not be used; study failed to include results of a key outcome that would have been expected to have been reported);

3. unclear risk - no or unclear information provided (the study protocol was not available).

Other potential sources of bias (other bias)

For each included trial, we described any important concerns we had about other possible sources of bias (e.g. whether there was a potential source of bias related to the specific study design or whether the trial was stopped early due to some data-dependent process). We assessed whether each trial was free of other problems that could put it at risk of bias as:

1. low risk - no concerns of other bias raised;

2. high risk - concerns raised about multiple looks at the data with the results made known to the investigators, difference in number of participants enrolled in abstract and final publications of the paper;

3. unclear - concerns raised about potential sources of bias that could not be verified by contacting the study authors.

We summarized the risk of bias for the primary outcomes within and across trials. We used a 'Risk of bias' graph to illustrate risk across studies. We resolved any disagreements by consensus and, if necessary, by adjudication with a third review author (MGC).

Measures of treatment effect

We used the standard methods of the Cochrane Neonatal Review Group to synthesize the data. We extracted categorical data for each intervention group, and calculated risk ratio (RR), relative risk reduction, and absolute risk difference (RD). We obtained mean and SD values for continuous data. We performed analysis using the mean difference (MD) value. For each measure of effect, we gave the 95% confidence intervals (CI). We presented the number needed to treat for an additional beneficial outcome (NNTB) and number needed to treat for an additional harmful outcome (NNTH), as appropriate.

Assessment of heterogeneity

We planned to assess clinical heterogeneity by comparing the distribution of important participant factors between trials (e.g. age) and trial factors (randomization concealment, blinding of outcome assessment, losses to follow-up, treatment type, and co-interventions). We planned to assess statistical heterogeneity by examining the I^2 statistic (Higgins 2011), a quantity that describes the

proportion of variation in point estimates that is due to variability across trials rather than sampling error. We intended to interpret the I^2 statistic as described by Higgins 2003:

1. less than 25% no (none) heterogeneity;

2. 25% to 49% low heterogeneity;

3. 50% to 74% moderate heterogeneity;

4. 75% or greater high heterogeneity.

In addition, we planned to employ a χ^2 test of homogeneity to determine the presence of heterogeneity. We intended to explore clinical variation across trials by comparing the distribution of important participant factors among trials (e.g. age) and trial factors (randomization concealment, blinding of outcome assessment, losses to follow-up, treatment type, and co-interventions).

Assessment of reporting biases

We planned to assess reporting and publication bias by examining the degree of asymmetry of a funnel plot in Review Manager 5 (RevMan 2014), if at least 10 trials had met our inclusion criteria (Egger 1997; Higgins 2011). However, this was not feasible as we identified only one trial.

Data synthesis

We performed statistical analysis using Review Manager 5 (RevMan 2014), using the standard methods of the Cochrane Neonatal Review Group. We used RR, relative risk reduction, and RD values for categorical data. We planned to obtain mean and SD values for continuous data and perform analyses using MD when appropriate. We planned to calculate 95% CIs, and present the NNTB and NNTH values, as appropriate. For each comparison reviewed, meta-analysis was feasible if we identified more than one eligible trial and there was sufficient homogeneity among the studies with respect to participants and interventions. We planned to combine the trials using the fixed-effect model, regardless of statistical evidence for heterogeneity effect sizes. For estimates of typical RR and RD, we used the Mantel-Haenszel method.

Subgroup analysis and investigation of heterogeneity

We planned to conduct subgroup analyses for each comparison as follows.

Comparison one: 'as scheduled' versus 'as needed' suctioning in ventilated newborns)

1. Less frequent and more frequent suctioning versus suctioning as needed.

2. Gestational age: less than 30 weeks, 30 weeks or greater.

3. ETT size (with two subgroups: diameter less than 3 mm and 3 mm or greater).

4. Duration of tube placement (with two subgroups, less than 48 hours or 48 hours or greater).

Comparison two: more frequent (six hours or less) versus less frequent (greater than six hours) suctioning in ventilated newborns)

1. With and without suctioning as needed.
2. Gestational age: less than 30 weeks, 30 weeks or greater.
3. ETT size (with two subgroups: diameter less than 3 mm and 3 mm or greater).
4. Duration of tube placement (with two subgroups, less than 48 hours or 48 hours or greater).

RESULTS

Description of studies

Results of the search

The literature search run in February 2015 identified 95 references. An updated search in October 2015 found three additional references. After screening, we considered only one study as potentially eligible (Wilson 1991) (see Figure 1).

Included studies

One study recruiting 97 infants met the inclusion criteria (Wilson 1991). Details of the study are described in Characteristics of

included studies table. This study was conducted in 1987 and 1988 in Cambridge, UK and enrolled 97 low birthweight (less than 2.5 kg) infants admitted to the NICU who were ventilated from birth for respiratory support. Infants were randomized to receive ETT suctioning every six or 12 hours during the first three days of life. Birthweight and gestational age were similar in the two groups (i.e. 1274 g with six hours versus 1311 g with 12 hours; 29.2 weeks with six hours versus 28.7 weeks with 12 hours). One infant was withdrawn from the analysis: the authors did not specify whether the analysis followed an intention-to-treat approach. Sample size calculations and power were not reported. The study reported time on ventilation, incidence of pneumothorax, need for oxygen for more than 30 days, IVH, and death in the first month of life.

Excluded studies

We considered none of the other 94 identified studies eligible. We found no relevant studies on the clinical trials registries for ongoing or recently completed trials.

Risk of bias in included studies

The Characteristics of included studies table, Figure 2, and Figure 3 report details of the methodological quality of the study. The study did not describe the generation of the random sequence. The study groups seemed to be well balanced.

Figure 2. Risk of bias graph: review authors' judgments about each risk of bias item presented as percentages across all included studies.

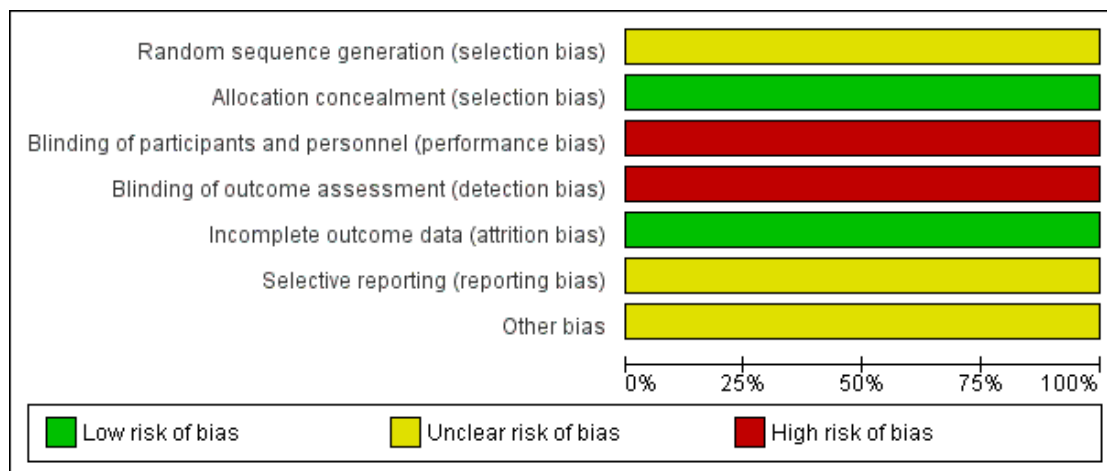
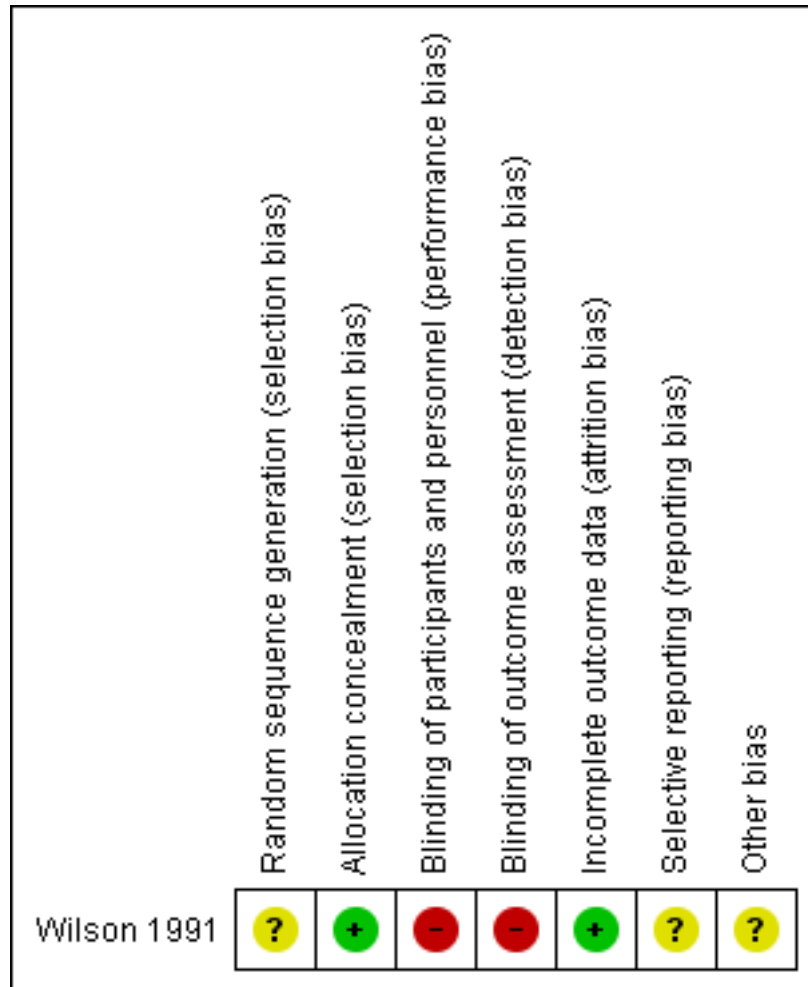


Figure 3. Risk of bias summary: review authors' judgments about each risk of bias item for each included study.



Effects of interventions

Comparison one: 'as scheduled' versus 'as needed' suctioning in ventilated newborns

We found no trials comparing 'as scheduled' versus 'as needed' suctioning.

Comparison two: more frequent (six hours or less) versus less frequent (greater than six hours) suctioning in ventilated newborns

We identified one trial (Wilson 1991). Tests for heterogeneity were not applicable for any of the analyses as we included only one study.

Primary outcome

Bronchopulmonary dysplasia/chronic lung disease

The included study reported on a slightly different definition of BPD (i.e. need for supplemental oxygen at greater than 30 days of age) from that proposed in the present review.

Wilson 1991 reported no significant differences between the groups in the proportion of infants with BPD (RR 0.49, 95% CI 0.20 to 1.20; RD -0.13, 95% CI -0.28 to 0.03) (Analysis 1.1).

Secondary outcomes

Mortality (Outcome 1.2)

Wilson 1991 reported no significant differences on neonatal death (RR 1.40, 95% CI 0.58 to 3.37; RD 0.06, 95% CI -0.09 to 0.21) (Analysis 1.2). In the included study, there were 10 deaths in the less frequent group and seven in the more frequent group.

Pneumothorax (yes/no): pneumothorax on chest x-ray during hospitalization (Outcome 1.3)

Wilson 1991 reported no significant differences between more frequent versus less frequent suctioning in ventilated newborns (RR 0.70, 95% CI 0.24 to 2.05; RD -0.04, 95% CI -0.17 to 0.09) (Analysis 1.3). There were five infants with pneumothoraces in the less frequent group and seven in the more frequent group.

Time on ventilation (Outcome 1.5)

Time on ventilation was reported as median and not as mean and SD; we were unable to analyze this outcome. Medians for time on ventilation were 39 hours in the less frequent group and 28 hours in the more frequent group.

Any IVH, and severe IVH (grade 3 or 4 IVH according to Papile classification) (Outcome 1.4)

Wilson 1991 reported no significant differences between more frequent versus less frequent suctioning in ventilated newborns (RR 1.12, 95% CI 0.44 to 2.85; RD 0.02, 95% CI -0.13 to 0.16) (Analysis 1.4). There were eight infants with IVH in the less frequent group and seven in the more frequent group.

Other secondary outcomes

The study did not report mortality during hospitalization or to latest follow-up, episodes of oxygen desaturation, episodes of bradycardia, concentration of inflammatory markers in bronchoalveolar lavage, number of re-intubations, number of unplanned/accidental extubations, pneumonia, bloodstream infection, atelectasis, length of stay in NICU, cystic periventricular leukomalacia, major neurodevelopmental disability, or sedation/agitation/pain scale.

Subgroup analysis

We were unable to conduct any subgroup or publication bias analysis because we included only one trial (Wilson 1991).

DISCUSSION

Summary of main results

The review included only one study enrolling 97 newborns (Wilson 1991). Timing of ETT suctioning was based on fixed intervals, that is, 12-hourly versus six-hourly. There were no statistically significant differences in any outcome between the two groups. Of note, assessment was limited to the first three days of life: the limited size and length of the intervention were likely to have decreased the power of the study. We cannot exclude even large differences. Thus, we have not evaluated the effects on neonates undergoing prolonged ventilation. We identified no studies comparing 'as scheduled' with 'as needed' strategies. Nearly three decades after the first trial about the optimal time of suctioning was published, research has not progressed. More frequent suctioning may be useful, not useful, or detrimental. Our systematic review does not exclude any of these possibilities.

Overall completeness and applicability of evidence

The included trial reported few of the outcomes of this review, and assessed no long-term outcomes. It was not possible to perform a priori subgroup analyses (gestational age, ETT size, duration of tube placement, with or without preoxygenation, with or without increased MV, with or without disconnection from the ventilator). However, other neonatal reviews addressed some of these issues regarding suctioning, for example preoxygenation (Pritchard 2001), disconnection from the ventilator (Taylor 2011), and depth of suction (Gillies 2011).

Quality of the evidence

The included trial was conducted in the late 1980s and it showed some limitations. Nature of intensive care and respiratory support has dramatically changed, for example, gas conditioning equipment. Studies in this field are not easy and face a number of practical difficulties. The study by Wilson et al. should be welcomed as a pioneering, important work in relation to this question (Wilson 1991).

Potential biases in the review process

As the study was conducted in the late 1980s, study authors were unable to provide additional data on the outcomes that were not reported in the original manuscript.

Agreements and disagreements with other studies or reviews

The ideal frequency of ETT suctioning has been investigated in few studies. The most relevant was a retrospective study conducted

in 180 very low birthweight infants who were suctioned either every four or every eight hours (Cordero 2001). There were no differences between the two groups. Interestingly, duration of MV longer than seven days was an inclusion criterion. Thus, the population differs substantially from the newborns investigated in the included trial (Wilson 1991), in which assessment focused on the first three days of life. Duration of MV is likely to affect amount and density of secretions, and, therefore, the need for suctioning (Shah 2004). An acoustic secretion detector might be a useful tool to support the clinician and nurse in the timing of suctioning the ETT, anticipating clinical deterioration, and reducing unnecessary aspirations (Lucchini 2011). However, this device has not been validated in infants.

Though no controlled trials have compared 'as needed' versus 'as scheduled' endotracheal suctioning, recommendations suggest that suction should be performed only when clinically indicated (AARC 2010; Gardner 2009; Morrow 2008).

AUTHORS' CONCLUSIONS

Implications for practice

There is insufficient evidence to identify the ideal frequency of endotracheal tube (ETT) suctioning in ventilated neonates. We were unable to provide any answer of interest to the basic questions posed by all health professionals caring for intubated newborns: "How often should ETT suctioning be performed? Is

more frequent suction better?" Concerns about generalizability and methodological quality of the included study prohibit implications for practice for the most frequently performed invasive procedure in intubated newborns in neonatal intensive care units.

Implications for research

Future research should focus on the effects in very preterm newborns, that is, the most vulnerable population as concerns the risk of lung inflammation and intraventricular hemorrhage. Assessment should include the cases of prolonged ventilation, when more abundant, dense secretions are common. To this regard, validation of acoustic secretion detectors in the neonatal population might add useful data to optimize timing of suctioning and to avoid unnecessary procedures. Moreover, clinical trials might include the comparison between 'as-scheduled' versus 'as-needed' endotracheal suctioning, that is, based on specific indications.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

Wilson 1991

Methods	Randomized controlled trial
Participants	97 newborns. All low birthweight newborns (< 2.5 kg) ventilated for respiratory distress syndrome during a period of 14 months Birthweights (SD): 1311 g (408) in 12-hourly group and 1274 g (477) in 6-hourly group Inclusion criteria: all babies with birthweight < 2.5 kg ventilated from birth for respiratory distress syndrome Exclusion criteria: neonates ventilated for meconium aspiration, birth asphyxia, pneumonia, or those with lethal malformations
Interventions	Intervention: endotracheal suction 12-hourly (less frequently) Control: endotracheal suction 6-hourly (more frequently)
Outcomes	Primary outcome: effect of reducing endotracheal lavage to 12 hourly on time on ventilation and incidence of pneumothorax or blocked endotracheal tubes in uncomplicated cases of respiratory distress syndrome Secondary outcomes: mortality, intraventricular hemorrhage (all grade)
Notes	Clinical outcomes were reported for all randomized infants

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No information provided
Allocation concealment (selection bias)	Low risk	Sealed envelopes used
Blinding of participants and personnel (performance bias) All outcomes	High risk	Unblinded intervention
Blinding of outcome assessment (detection bias) All outcomes	High risk	No mention of any procedure to blind the researchers assessing study endpoints
Incomplete outcome data (attrition bias) All outcomes	Low risk	1 infant removed from 1 of the trial groups
Selective reporting (reporting bias)	Unclear risk	The trial was not registered in a trial registry and we could not ascertain if there were deviations from the original protocol in the final publication

Wilson 1991 (Continued)

Other bias	Unclear risk	No prior calculations of sample size were made due to absence of preliminary data. Lack of statistical power
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DATA AND ANALYSES

Comparison 1. More frequent (six hours or less) versus less frequent (greater than six hours) suctioning

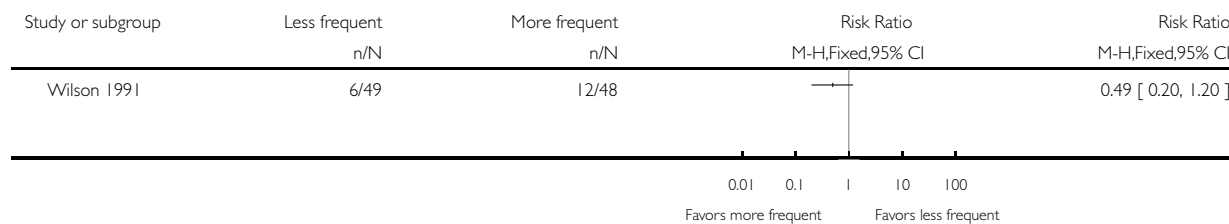
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Need for supplemental oxygen at > 30 days of age	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
2 Neonatal death	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
3 Pneumothorax	1		Risk Difference (M-H, Fixed, 95% CI)	Totals not selected
4 Intraventricular hemorrhage (all grades)	1		Risk Difference (M-H, Fixed, 95% CI)	Totals not selected

Analysis 1.1. Comparison 1 More frequent (six hours or less) versus less frequent (greater than six hours) suctioning, Outcome 1 Need for supplemental oxygen at > 30 days of age.

Review: Frequency of endotracheal suctioning for the prevention of respiratory morbidity in ventilated newborns

Comparison: 1 More frequent (six hours or less) versus less frequent (greater than six hours) suctioning

Outcome: 1 Need for supplemental oxygen at > 30 days of age

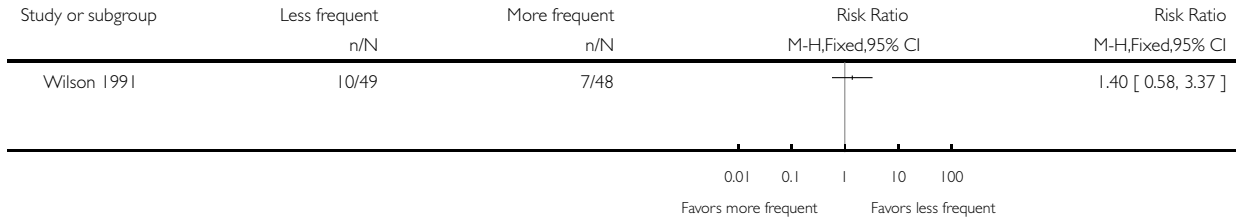


Analysis 1.2. Comparison 1 More frequent (six hours or less) versus less frequent (greater than six hours) suctioning, Outcome 2 Neonatal death.

Review: Frequency of endotracheal suctioning for the prevention of respiratory morbidity in ventilated newborns

Comparison: 1 More frequent (six hours or less) versus less frequent (greater than six hours) suctioning

Outcome: 2 Neonatal death

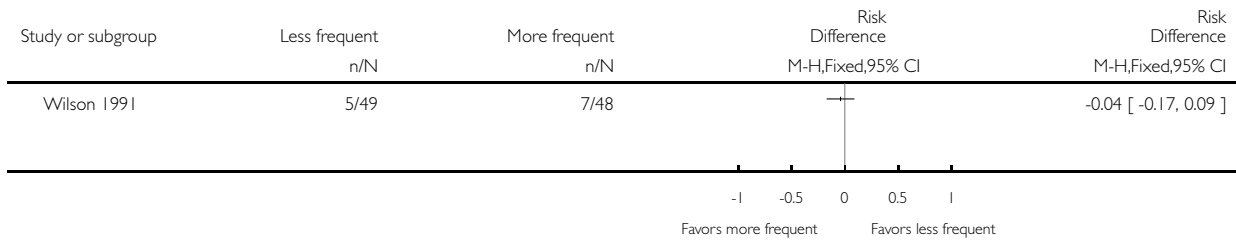


Analysis 1.3. Comparison 1 More frequent (six hours or less) versus less frequent (greater than six hours) suctioning, Outcome 3 Pneumothorax.

Review: Frequency of endotracheal suctioning for the prevention of respiratory morbidity in ventilated newborns

Comparison: 1 More frequent (six hours or less) versus less frequent (greater than six hours) suctioning

Outcome: 3 Pneumothorax

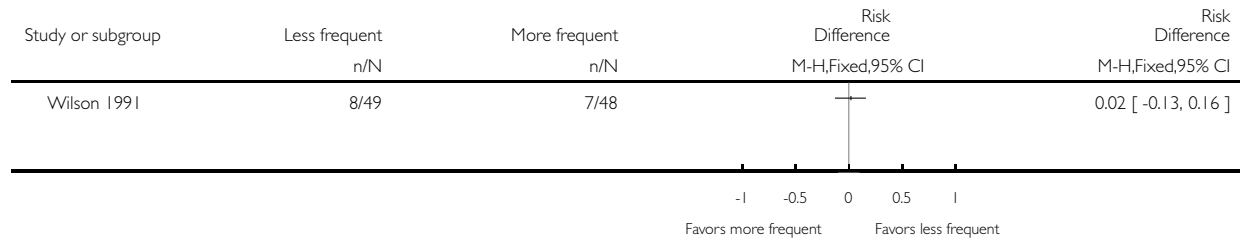


Analysis 1.4. Comparison 1 More frequent (six hours or less) versus less frequent (greater than six hours) suctioning, Outcome 4 Intraventricular hemorrhage (all grades).

Review: Frequency of endotracheal suctioning for the prevention of respiratory morbidity in ventilated newborns

Comparison: 1 More frequent (six hours or less) versus less frequent (greater than six hours) suctioning

Outcome: 4 Intraventricular hemorrhage (all grades)



APPENDICES

Appendix I. Search strategy

1. The Cochrane Neonatal Group Specialized Register (see [the Cochrane Neonatal Group search strategy for specialized register](#)).
2. The Cochrane Central Register of Controlled Trials (CENTRAL) in *The Cochrane Library* using text words “Infant, Newborn” and “endotracheal suctioning”.
3. MEDLINE (from January 1980 to October 2015): “Respiration, Artificial”[Mesh] AND endotracheal[All Fields] AND “suction”[MeSH Terms] AND “infant, newborn”[MeSH Terms] AND (randomized controlled trial [pt] OR controlled clinical trial [pt] OR randomized [tiab] OR randomly [tiab] OR trial [tiab] OR groups [tiab]).
4. EMBASE (from January 1980 to October 2015) using the limits Randomized Clinical Trial and newborn and the Emtree terms “endotracheal” AND “suction*”.
5. CINAHL (from 1982 to October 2015) using text words and subject headings for endotracheal suctioning and limiting the search to: human; neonate; and clinical trial.
6. Abstracts of the Pediatric Academic Societies (PAS) from 2000 to October 2015, electronically through the PAS website ([abstractsonline](#)) using the following key words: “endotracheal suctioning” AND “clinical trial”.
7. Perinatal Society of Australia and New Zealand (PSANZ).

WHAT'S NEW

Last assessed as up-to-date: 31 October 2015.

Date	Event	Description
9 May 2016	Amended	Author affiliations updated

CONTRIBUTIONS OF AUTHORS

MB conceived the idea, reviewed the literature and drafted the protocol and the final manuscript.

SZ and MGC performed the literature search, extracted and analyzed the data.

MB, SZ, MGC, and LM commented on and reviewed the protocol and the final manuscript.

DECLARATIONS OF INTEREST

All review authors declared to have neither competing financial nor any other conflicts of interest.

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Internal sources

- Institute for Clinical Sciences, Lund University, Lund, Sweden.
to MB
- Istituto Giannina Gaslini, Genoa, Italy.
to SZ and MGC

External sources

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We used the search terms we listed in the protocol, with one exception: for PubMed, we searched (endotracheal AND suction*) plus the neonatal search terms.

We included 'Need for supplemental oxygen at greater than 30 days of age' as a primary outcome and 'Neonatal death' as a secondary outcome.

We corrected the definition of bronchopulmonary dysplasia, as in [Jobe 2001](#).

INDEX TERMS

Medical Subject Headings (MeSH)

*Catheter Obstruction; *Intubation, Intratracheal; *Respiration, Artificial; Infant, Low Birth Weight; Lung [secretion]; Randomized Controlled Trials as Topic; Suction [*methods]; Time Factors

MeSH check words

Humans; Infant, Newborn