

## **Cover sheet**

### **Title**

TREATMENT: Intervention or intervention contrast, I; Disease, D; Population, P. Thus, I for D in P.

PREVENTION: Intervention, I; Primary outcome, O; Population, P. Thus, I for prevention of O in P

### **Reviewers**

Bell JC, Henderson-Smart D

### **Dates**

Date edited: 23/03/2004

Date of last substantive update: 19/02/2004

Date of last minor update: 20/02/2004

Date next stage expected: / /

Protocol first published:

Review first published:

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### **Internal sources of support**

Add the name of the institution where you work, then choose your country from the list of countries displayed, e.g., AUSTRALIA

## **External sources of support**

Add name of any grant /funding you receive which is allowing you to do this review, then choose the country from the list of countries displayed, e.g., AUSTRALIA

## **Contribution of reviewers**

Add what each reviewer has contributed to the protocol or the review.

FOR EXAMPLE:

Reviewer A - wrote protocol, searched for studies, extracted data, analysed data, wrote review

Reviewer B - wrote protocol, searched for studies, edited review

Reviewer C - extracted data, edited review

## **Acknowledgements**

Add people or institutions who have contributed to your review. This excludes authors of the review as authorship acknowledges this. It might include people who have provided extra data for some of the studies or people who have helped edit the review.

Thank you to the reviewers who allowed sections of their reviews to be used as examples in this teaching review.

Information included in this review outline has been taken from:

- Organization of a Systematic Review for the Neonatal Review Group. Guidelines for Reviewers and Editors (<http://hiru.mcmaster.ca/cochrane/centres/canadian/neonatal/checklist.pdf>)
- Cochrane Reviewers' Handbook: Clarke M, Oxman AD, editors. Cochrane Reviewers' Handbook 4.2.0 [updated March 2003]. <http://www.cochrane.dk/cochrane/handbook/handbook.htm>
- Docherty M, Smith R. The case for structuring the discussion of scientific papers. *British Medical Journal* 1999; 318: 1224-5.
- Moher D, Cook DJ, Eastwood S, Olkin I, Rennie D, Stroup DF for the QUORUM Group. Improving the quality of reports of meta-analyses of randomised controlled trials: the QUORUM statement. *Lancet* 1999; 354:1896-900.

## **Potential conflict of interest**

Cochrane reviews should be free of any real or perceived bias introduced by the receipt of any benefit in cash or kind, any hospitality, or any subsidy derived from any source that may have or be perceived to have an interest in the outcome of the review. It is a matter of Cochrane Collaboration policy that direct funding from a single source with a vested interest in the results of the review is not acceptable.

Reviewers should report any conflict of interest capable of influencing their judgements, including personal, political, academic and other possible conflicts, as well as financial conflicts. Any secondary interest (such as personal conflicts) that might unduly influence judgements made in a review (concerning, for example, the inclusion or exclusion of studies, assessments of the validity of included studies or the interpretation of results) should be reported.

EXAMPLE 1: The authors were the investigators responsible for one study included in this review

(REFERENCE ID). The authors are currently investigating the effect of drug I for treatment of disease D in preterm infants in a large randomised controlled trial.

EXAMPLE 2: None

EXAMPLE 3: One reviewer has received lecture honoraria from [drug company] which manufactures [drug], one of the therapies considered in this review.

## **What's new**

The What's New section of a review is to be completed only for an update of an existing review. The following should be stated (typically 2-3 sentences):

1. This is an update of ...(state title of review, issue/year of publication)
2. Search was updated to ...(date) and n additional eligible studies were detected and added.
3. The conclusions of the review did, did not change as a result of adding the new studies.

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### "Dates"

When you click on the "Dates" tab on this same screen, RevMan asks for many dates to be completed on the Cover Sheet and in the What's New section of a review. The following clarifies what is expected to be completed at the time you submit your review to the editorial office.

**Date edited:** User cannot edit this date. This date is changed automatically by the program with any edit.

**Date next stage expected:** When submitting your protocol, this date must be filled in. The date to be inserted here is the date that you plan to submit your completed review. The Neonatal Review Group asks for reviews to be submitted within nine months of that module submission - i.e. if a protocol is included with a November submission to The Cochrane Library, the completed review is expected the following August. When submitting completed review, leave blank as it is not applicable.

**Date of last substantive update:** Edit this date if you have made any substantive change/update to your review. Examples of substantive changes include the addition of one or more included studies (whether or not they change the conclusions of the review), re-categorization of studies previously designated as awaiting appraisal or ongoing, and the completion date of a new search for eligible studies (whether or not any were identified). If your updated search has not identified any new studies, this date should not be changed.

**Protocol first published:** Do not fill in. Review Group Coordinator will insert this date when the protocol is accepted for publication.

**Review first published:** Do not fill in. Review Group Coordinator will insert this date when the review is accepted for publication.

**Date of last minor update:** Enter this date if any minor update or edit was done. Examples of a minor update would be search repeated for an update, but no new trials identified, adding the synopsis, or minor edits that do not affect the results but have altered the text of the review slightly.

**Dates**

Protocol first published:

Review first published:

Date of last substantive update: 19/02/2004

Date of last minor update: 20/02/2004

Date review re-formatted: / /

Date new studies sought but none found: / /

Date new studies found but not yet included/excluded: / /

Date new studies found and included or excluded: / /

Date reviewers' conclusions section amended: / /

Date comment/criticism added: / /

Date response to comment/criticism added: / /

## Synopsis

The synopsis is a brief summary of a review's results in plain, non-technical language for consumers and non-specialist readers. The synopsis is written when the review is completed - it does not form part of the protocol.

Reviewers have the option of writing this synopsis themselves or it can be left blank and the editorial office will forward the review to the Australasian Cochrane Centre where the Consumer Group will prepare the synopsis. Any synopses prepared by this group are returned to the editorial office and reviewer for approval. If you choose to prepare your own synopsis, Guidelines can be found in the Reviewer's Handbook, Appendix 2a.2 <http://www.cochrane.dk/Cochrane/handbook/handbook.htm>. It might also help you to look at existing synopses in the Cochrane Library to see how they are worded.

### EXAMPLE 1:

Using methylxanthines to help wean babies from mechanical ventilation might help some babies. Methylxanthines are drugs (such as caffeine) that can help improve breathing in preterm babies (babies born early). They can be given to preterm babies when weaning from machine-assisted breathing (extubation from mechanical ventilation) is planned. The review of trials found that they might be helpful for some babies. There is evidence to suggest they might be beneficial for those babies born at less than 1000g, and being taken off the ventilator during the first week after birth. However, they may not help in other situations.

### EXAMPLE 2:

There is not enough evidence to show the best way to wean premature babies off oxygen supplementation.

Babies born either prematurely (before 37 weeks) or with a low birthweight often have breathing problems and need extra oxygen. Accurate oxygen levels are important as damage to the eyes or lungs can result if levels are wrong. The decision to stop giving oxygen gradually or abruptly can also affect the health of the baby. The review of trials found that gradual rather than abrupt weaning from oxygen supplementation reduces the risk of eye damage but could not conclude which is the best method of weaning. More research is needed.

## **Abstract**

### **Background**

### **Objectives**

### **Search strategy**

### **Selection criteria**

### **Data collection & analysis**

### **Main results**

### **Reviewers' conclusions**

#### **ABSTRACT GUIDELINES**

The abstract is written when the review is finished. It is not part of the protocol stage.

The abstract should be brief (not more than 400 words) and should be organised using the above headings (i.e. Background, Objectives, Methods, Results and Conclusions). It should be understandable on its own, without the need to access the full review. Guidelines can be found in the CNRG Guidelines for Reviewers and Editors (<http://hiru.mcmaster.ca/cochrane/centres/canadian/neonatal/checklist.pdf>) and in the Reviewer's Handbook, Appendix 2a.3 <http://www.cochrane.dk/Cochrane/handbook/handbook.htm>

Information to include under each abstract heading:

**Background:** include a very brief background that introduces the major issues regarding the review.

**Objectives:** brief statement of the primary objectives of the review.

**Search strategy:** briefly note, with dates of databases searches, without including MeSH terms.

**Selection strategy:** include randomised and quasi-randomised controlled trials relevant to the subject.

**Data collection and analysis:** describe how data were extracted (independent reviewers, number of reviewers). Note whether or not authors were contacted regarding missing data. Include the types of data points (short-term, long-term and, in certain cases, specific discussion of the primary data points and secondary data points). Meta-analysis was performed to calculate typical relative risk and typical risk difference, along with the 95% confidence intervals (CI).

**Main results:** note the number of trials included in the review. Report first on the primary outcome of interest and, if possible, include the typical relative risk and typical risk difference of any meta-analyses performed regarding the primary outcome. Then discuss the secondary outcomes. If a significant result was noted, these should be specifically stated in the main results.

**Reviewers conclusions:** Briefly summarise the results from the systematic overview and state the impact on clinical care and the potential for future studies.

## ABSTRACT EXAMPLE:

### Background

With improvements in neonatal intensive care, more premature infants are surviving the neonatal period. With this increase, more are presenting for surgery in early infancy. Of predominance in this period is the repair of inguinal herniae, appearing in 38% of infants whose birth weight is between 751g and 1000g. Most postoperative studies show that approximately 20% to 30% of otherwise healthy former preterm infants having inguinal herniorrhaphy under general anaesthesia have one or more apnoeas in the postoperative period. Regional anaesthesia might reduce postoperative apnoea in this population.

### Objectives

To determine if regional anaesthesia, in preterm infants undergoing inguinal herniorrhaphy, reduces post-operative apnoea, bradycardia, and the use of assisted ventilation, in comparison to those infants undergoing inguinal herniorrhaphy with general anaesthesia.

### Search Strategy

Randomised controlled trials were identified by searching MEDLINE (1966-Nov 2002), EMBASE (1982-Nov 2002), Cochrane Central Register of Controlled Trials (CENTRAL, The Cochrane Library, Issue 1, 2002), reference lists of published trials and abstracts published in *Pediatric Research*.

### Selection Criteria

Randomised and quasi-randomised controlled trials of spinal versus general anaesthesia in preterm infants undergoing inguinal herniorrhaphy in early infancy.

### Data collection and analysis

Data were extracted and the analyses performed independently by two reviewers. Authors of each eligible study were contacted for missing data. Studies were analysed for methodologic quality using the criteria of the Cochrane Neonatal Review Group. All data were analysed using RevMan 4.1. When possible meta-analysis was performed to calculate typical relative risk, typical risk difference, along with their 95% confidence intervals (CI).

### Main Results

Four small trials comparing spinal with general anaesthesia in the repair of inguinal hernia were identified. One trial was excluded due to inadequate information. There was no statistically significant difference in the proportions of infants having postoperative apnoea/bradycardia, typical RR 0.69 (0.40, 1.21) or postoperative oxygen desaturations, RR 0.91 (0.61, 1.37). If infants having preoperative sedatives were excluded, then the meta-analysis supported a reduction in postoperative apnoea in the spinal anaesthetic group, typical RR 0.39 (0.19, 0.81). There was a reduction of borderline statistical significance in the use of postoperative assisted ventilation with spinal anaesthesia. There was an increase of borderline statistical significance in anaesthetic placement failure when spinal anaesthesia was attempted.

### Reviewers' conclusions

There is no reliable evidence from the trials reviewed concerning the effect of spinal as compared to

general anaesthesia on the incidence of post-operative apnoea, bradycardia, or oxygen desaturation in ex-preterm infants undergoing herniorrhaphy. The estimates of effect in this review are based on a total population of only 108 patients or fewer.

A large well designed randomised controlled trial is needed to determine if spinal anaesthesia reduces post-operative apnoea in ex-preterm infants not pretreated with sedatives. Adequate blinding, follow up and intention to treat analysis are required.

## Background

State the importance of the topic of the review in terms of both biological rationale and health care. If relevant, identify competing biological rationales. Justify the choice of clinical outcomes, both beneficial and harmful. If relevant, develop the rationale for any planned subgroup analyses. The background section is usually no more than 1.5 pages in length.

### Additional references section

The full reference for each report cited in the text of the review (usually in the Background) should be placed in the additional references section (unless it is a citation for a study which belongs in the included, excluded, waiting assessment or ongoing studies reference section).

## Objectives

Specify a priori the main objective of the review in terms of the population, intervention and (adverse) outcome(s): i.e. In \_\_\_\_\_ does \_\_\_\_\_ reduce \_\_\_\_\_. Include all outcomes which are clinically or biologically important, both primary and secondary.

In setting objectives, consider what is the main clinical question. If you were designing a trial to answer this, what would your objectives and outcomes be? What question would a clinician (or public health professional) search for in the Cochrane library? Don't base your objectives on what published trials have done - use what is important.

Specify a priori any planned sub-group analyses by sub-categories of population, intervention or outcome. Remember, subgroups will depend on your objectives, and the rationale for these subgroups will be stated in the background. Include as much detail as possible.

### EXAMPLE:

To evaluate the effects of the use of mechanical ventilation compared with no mechanical ventilation on mortality and morbidity in newborn infants with severe respiratory failure due to pulmonary disease.

Pre-specified sub-group analyses were to be carried out according to:

1. RDS as cause of respiratory failure vs all other causes
2. Early vs late (rescue) treatment with MV
3. Type of MV - either IPPV or INPV
4. Gestation (cut-offs at about 28 and 32 weeks)
5. Birth weight (cut-offs at about 1000 and 1500 grams)

## Criteria for considering studies for this review

### Types of studies

Specify a priori the criteria concerning study design used to select trials (for example, randomised controlled trials, quasi-randomised trials, cross-over or cluster trials). Specify any exclusion criteria used to reject studies.

EXAMPLE: Randomised and quasi-randomised controlled trials were included. (Throughout Criteria for considering studies, use future tense for the protocol, and past tense in the completed review.)

### **Types of participants**

Specify a priori the criteria concerning characteristics of the population used to select trials.

EXAMPLE: Preterm infants (<37 weeks gestation)

### **Types of interventions**

Specify a priori the criteria concerning characteristics of the intervention used to select trials. Also specify the types of control interventions, eg. placebo or no therapy.

EXAMPLE: prophylactic administration of drug A vs drug B

### **Types of outcome measures**

Specify a priori the criteria concerning eligible outcome measures used to select trials. For each outcome include when the outcome should be assessed, relevant Units, and a definition.

EXAMPLE 1:

Mortality

- first week
- 28 days
- hospital discharge

Morbidity

- pneumothorax
- intraventricular haemorrhage (all grades and severe grades 3 or 4)
- chronic lung disease (ventilatory support or oxygen at 28 days or at 36 weeks)
- proven systemic infection (positive culture blood, urine, cerebrospinal fluid or other normally sterile body fluid)
- necrotising enterocolitis
- retinopathy of prematurity
- neurodevelopmental abnormalities in childhood (developmental delay, cerebral palsy)

EXAMPLE 2:

Primary

Failed extubation (unable to wean from intermittent positive pressure ventilation (IPPV) and extubate, or re-intubation for IPPV) within about one week

Secondary

1. Death before discharge
2. Duration of IPPV
3. Side effects leading to cessation of therapy (tachycardia, agitation, seizures, hypertension or feed intolerance)
3. Chronic lung disease (oxygen requirement at about 28 days and at about 36 weeks post menstrual age)
4. Reduced somatic growth (weight, length and head circumference) and delayed neurodevelopment (more than 2 SDs below the mean on a standard developmental assessment, or abnormal neurological signs) during infancy and childhood

## **Search strategy for identification of studies**

Report the search strategy used for detecting relevant trials. Cite the standard search method of the Cochrane Neonatal Group which is described in the Cochrane Library.

Name the electronic databases searched [e.g. MEDLINE, CINAHL, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL)]. Specify the inclusive dates (month, year) for searches of these databases. State the issue and year for the search of CENTRAL in the Cochrane Library. State if any language restrictions were used (e.g. English only). We recommend applying no restriction by language. Report any additional effort to detect relevant trials, including the use of sources such as other trial registries, computerised bibliographic databases, review articles, abstracts, conference and symposia proceedings, dissertations, books, expert informants, granting agencies, industry, and personal files.

State the names of societies whose proceedings were searched, and the inclusive years searched. State if unpublished trials were sought and, if so, how.

State the Medical Subject Headings (MeSH) and text words which were used in the searches of electronic databases.

EXAMPLE: (This should be written in future tense for a protocol and past tense in the review)

See: Cochrane Neonatal Group search strategy. (This can be found in the Cochrane Library - Neonatal Review Group, and also in the Neonatal Review Group checklist:

<http://hiru.mcmaster.ca/cochrane/centres/canadian/neonatal/checklist.pdf>)

Randomised controlled trials comparing drug A with drug B in preterm neonates were identified from MEDLINE (1996 to September 2004) using MeSH headings: (list headings here . . .)

Other databases, including CINAHL (1982-CURRENT DATE), Current Contents (1998-CURRENT DATE), EMBASE (DATES), and CENTRAL (The Cochrane Library, Issue 4, 2004) were searched using a similar strategy. Bibliographies of published trials and conference proceedings were reviewed. No language restrictions were applied. Unpublished studies were sought by hand searching the conference proceedings of the Society for Pediatric Research and the European Society for Pediatric Research from 1993 to 2004.

## **Methods of the review**

Cite the standard method of the Cochrane Neonatal Review Group for conducting a systematic review which is described in the checklist:

<http://hiru.mcmaster.ca/cochrane/centres/canadian/neonatal/checklist.pdf>. (Also see the Cochrane Collaboration Handbook).

State the method used for assessing the methodologic quality of included trials (see the Appendix to the CNRG checklist for reviewers and editors).

If relevant, state that you contacted the investigators for additional information or clarification of patient characteristics, details of interventions, definitions of events, additional outcomes, losses to follow up. If relevant, describe the type of data retrieved and for what trials.

For categorical outcomes, define the outcome as the negative outcome (e.g. death, not survival).

To the extent possible, extract outcome data on all patients randomised.

If outcome data are extracted and presented for other than the number of patients randomised (e.g. only for survivors) build that distinction into the name of the outcome (e.g. cerebral palsy in survivors). Ensure that the outcome is defined consistently with respect to the denominator within each meta-analysis.

State whether a second reviewer worked independently and at what stages of the review (e.g. assessment of trials for inclusion, assessment of methodologic quality, data extraction) and, if so, state level of agreement and how differences were resolved.

State briefly the statistical methods that were used for data analyses (see Appendix 1 of the NRG checklist <http://hiru.mcmaster.ca/cochrane/centres/canadian/neonatal/checklist.pdf>).

Define abbreviations here [relative risk (RR), risk difference (RD), number needed to treat (NNT), weighted mean difference (WMD)] etc.

**EXAMPLE:** (This should be written in future tense for a protocol and past tense in the review)  
The standard methods of the Cochrane Collaboration and its Neonatal Review Group were used. Two reviewers worked independently to search for and assess trials for inclusion and methodological quality. Eligible studies were assessed using the following key criteria: allocation concealment (blinding of randomisation), blinding of intervention, completeness of follow up and blinding of outcome measurement. The reviewers extracted data independently. Differences were resolved by discussion. Study investigators were contacted for additional information or data as required (include in protocol and include in review if this happened).

At least two reviewers independently extracted data using prepared data extraction forms. Any discrepancies were resolved by discussion. We used Review Manager software (RevMan 2003) for statistical analyses. Categorical data were analysed using relative risk (RR), risk difference (RD) and number needed to treat (NNT). Continuous data were analysed using weighted mean difference (WMD), unless the data had different units, in which case standardised mean difference was used. 95% confidence intervals were reported for all estimates. We used sensitivity analyses to evaluate the effect of the trial quality. Heterogeneity was tested using an I-squared test. In the absence of heterogeneity, we used a fixed effect model to pool results.

## **Description of studies**

Identify the potentially eligible trials that were considered, those that were included, and those that were excluded (and briefly, why - put more detail in the Table of Excluded Studies). Identify any potentially relevant trials awaiting assessment, or on-going.

Summarise in the text the important clinical details (emphasising similarities and differences) of the included trials as listed in the Table, Characteristics of Included Studies, in the columns headed Participants, Interventions and Outcomes (see below).

**EXAMPLE:** No studies were found meeting the inclusion criteria for this review.

**EXAMPLE:** Five studies were identified. None was excluded. No ongoing trials were identified. Then write a summary of these trials, highlighting similarities and differences, rather than a detailed description - which goes in the table of included studies.

Before you enter details in the Tables of Included and Excluded Studies, references to these studies must be added to the appropriate references section (e.g. included studies, excluded studies).

#### References to studies included in the review

Distinguish between studies and reports. There can be more than one report published from a single study.

Each study must be assigned a unique identifier consisting of author, year (e.g. Smith 2000). If Smith was lead author on more than one study published in 2000, the unique identifiers can read Smith 2000a, Smith 2000b.

If a study has more than one report, one of them must be selected as the primary report. The primary report is identified by an asterisk\* (selected in the add/edit reference section). Other reports from the same study should be listed under this same unique identifier, i.e. these secondary reports do not get a unique identifier of their own.

Give the full reference (authors, title of article, journal, year, volume, pages) for each report included. We do not require the issue number. Reference should be in the following style: (Smith JA, Jones BA. Title of article. *New England Journal of Medicine* 2000;155:75-80). Check accuracy and formatting of your references using Citation Matcher <http://www.ncbi.nlm.nih.gov/PubMed/wgetcit.html>

#### Table: Characteristics of Included Studies

For each included trial, list in this table the important features of study design and the results of your quality assessments (Methods column), and the clinically important details concerning participants, interventions and outcomes. Use the Notes column to record other features about the trial which are relevant to the review.

In the Intervention column give a brief description of the experimental and control exposures. State (N= ) to show the number of subjects randomised to each group; for cross-over trials, state the total number of patients randomised in the trial.

The column Allocation Concealment is meant for rating the quality specifically of allocation concealment in the trial - Adequate = A, Unclear = B, Inadequate = C. This is not meant to put a rating of the quality of the trial as a whole.

#### References to studies excluded from the review

Give the full reference for each possibly relevant trial which was assessed and then excluded. The editors suggest that if you can decide from the title and abstract that a report which you have retrieved on your search obviously does not describe an eligible trial, you don't have to list it as an excluded trial. On the other hand, if you need to consult the full report before making the decision that it is not eligible, then it should be listed as excluded and the reason given. In any case you should retain in your files all the references you retrieve from your search, for your own records and also to answer any queries from users.

#### Characteristics of Excluded Studies (Table)

List such studies by study identifier, stating the reason/s for exclusion.

#### References to studies awaiting appraisal

Give the reference for each possibly relevant trial which is awaiting appraisal.

#### Ongoing studies -

Give the reference for each possibly relevant trial which is ongoing.

### Characteristics of Ongoing Studies (Table)

Provide all available information regarding name, participants, intervention, outcomes, start date, contact details for principal investigator.

Classification pending

Give the full reference for reports awaiting clarification from authors.

## **Methodological quality of included studies**

Summarize in the text the results of the quality assessments of the included trials (as listed in the Methods column of the Table: Characteristics of Included Studies).

### EXAMPLE:

All included trials used either quasi-random or random patient allocation, had at least one clinically meaningful outcome, and so were included in the analyses. The overall methodological quality of the included trials was fair.

Two trials had adequate allocation concealment: (REFERENCE IDs) used central telephone randomisation, and (REFERENCE ID) used a method of sealed envelopes. Allocation concealment was unclear in the other three trials. The other three trials were truly randomised. No trials blinded the intervention. Four of the included studies had adequate short term outcome measure ascertainment. The (REFERENCE ID) study did not report mortality, but it is assumed that outcome data were reported only on survivors.

## **Results**

Preamble:

It is essential to set up the Table of Comparisons before extracting and analysing data from eligible studies. Notes on setting up the Table of Comparisons are provided under "Notes" at the end of this review.

In describing the results of the review in the text, organize by Comparisons, and under each Comparison, by Outcome. Use headings and subheadings for comparisons and outcomes. To help the reader, follow the same order of comparisons and outcomes, and use the same data table numbers (for example, 01.01.01) as in your Table of Comparisons, so that the text matches the order of the outcome data tables. For any pre-specified comparisons or outcomes which could not be analysed, or for any planned sub-group analyses which could not be undertaken (in each case because of lack of data from eligible studies) that is a result which should be described as such.

The following plan generally works well:

Within each comparison, describe the results for each major outcome in sequence.

For each outcome, consider presenting

- the number of trials that assessed that outcome, and the total number of subjects included
- the overall proportion of treated and control patients that experienced the event
- whether any individual trials found a significant effect and, if so, which trials
- a quantitative description of the typical effect (meta-analysis result)

For each outcome, consider the result of the meta-analysis in terms of its statistical significance (is the effect real?) and its clinical importance (is the effect large enough to be important?).

Note any important heterogeneity of effect among trials and, if important, consider not citing a typical effect but simply summarise the treatment effect found in each trial.

Distinguish (and describe as such) any data-driven (a posteriori) analyses and results.

**EXAMPLE:**

Five trials (LIST REFERENCE IDs), which included a total of 197 infants, met eligibility criteria.

**Outcome 1. Mortality**

All five trials reported effect on mortality. In two trials (REFERENCE IDs), mortality was significantly reduced in the group treated with drug A compared with control. The meta-analysis of all five trials also shows a significant reduction in mortality [RR 0.70 (0.55, 0.88), RD -0.22 (-0.35, -0.09), NNT 5 (3, 11)].

**Outcome 2. Systemic infection**

Not reported in any of the five trials.

**Outcome 3. etc**

## **Discussion**

Use the structural conventions to guide the discussion section ([Docherty 1999](#); [Moher 1999](#)):

1. Statement of main findings
2. Consider the strengths of this review, i.e. both the strengths of the primary studies and of the review methodology. State any important methodologic limitations, both of the primary studies and of this systematic review. If present, consider whether they are sufficient to pose a serious threat to validity. Consider publication bias.
3. If relevant, consider additional issues such as consistency of treatment effect, dose-response relationship, limits of applicability of results.
4. Implications for clinicians or policy makers. Consider the potential clinical importance of the results. Relevant here is the size of treatment effect in reducing adverse outcomes compared to side effects caused and, if relevant, increased economic costs.
5. Unanswered questions and future research - develop the rationale for future research.

## **Reviewers' conclusions**

### **Implications for practice**

State the major result/s of the review and the implication/s for practice. If there is no statistically significant effect, say 'there is no evidence of effect' (not 'there is no effect', or the intervention is 'no different' from the control intervention); it is safer to conclude that the data, with a confidence interval, are compatible with either a reduction or an increase in the outcome. Clinical significance as well as statistical significance should be considered. There may be outcomes where the P-value is in the range 0.06-0.08, or the confidence interval just excludes 1 (RR) or 0 (OR). While not statistically significant, these results may be clinically important. These borderline results may also reflect low numbers in the meta-analysis.

The conclusions of the systematic review should simply summarise the likely benefits and risks of the intervention. It is not necessary, and often not justified, to go beyond this and make a recommendation for practice. Consider the strength of inference regarding the clinical implications of the results, which varies directly with the comprehensiveness of search for all relevant trials, the methodological quality of the primary trials on which the review was based, and the degree of consistency of results among the trials. For results which have the potential to influence clinical practice, state their potential clinical importance in terms of

- the beneficial effects vs any unwanted side effects or increased economic costs
- limits of applicability, i.e. in whom the treatment should be considered (e.g. baseline risk for primary outcome above which benefits are likely to outweigh harms)

### **Implications for research**

Consider which questions have been well answered (further trials not warranted), which questions remain important because they have not been answered clearly (further trials warranted), and which questions remain important in only certain populations (further trials in selected populations warranted).

Consider hypotheses generated by data-driven (a posteriori) analyses which now require testing in future trials.

Consider new questions that arise from the reviewed research (e.g. new interventions, modification of dose, combination of therapies).

Statements like "more research is needed" are not very informative; reviewers should state more precisely what research is needed and why.

## Characteristics of included studies

Study ID	Methods	Participants	Interventions	Outcomes	Notes	Allocation concealment
<b>Fictitious 2001</b>	<p>Include notes on methodological quality</p> <p>EXAMPLE: Randomised trial. Blinding of randomisation: can't tell</p> <p>Blinding of intervention: no</p> <p>Blinding of outcome assessment: no</p> <p>Complete follow up: yes</p>	<p>Where study conducted, time, numbers enrolled, describe those enrolled - inclusion criteria, exclusion criteria</p> <p>EXAMPLE: Single centre, trial of 25 preterm infants on IPPV, birth weight &lt;1250 gms, FiO2 &lt; 0.31, PIP &lt; 21, rate &lt;11.</p> <p>Ineligible: major CNS cong. abnormalities, previous multiple extubation failures.</p>	<p>Describe numbers assigned to each group; interventions in all groups.</p> <p>EXAMPLE: Theophylline 6 mg/kg load and 2 mg/kg 12 hrly (all but 1 IV) (n=14) vs Placebo (N saline) (n=11)</p>	<p>List outcomes assessed in the study</p> <p>EXAMPLE: Unable to extubate or need for reintubation for IPPV within 5 days (reason: hypercarbia, acidosis, hypoxemia)</p>	<p>EXAMPLE: This was a cross-over designed trial, with cross-over after 2 days intervention.</p> <p>EXAMPLE: This is the only trial in which all infants received surfactant.</p>	B

## **Characteristics of excluded studies**

### **Study ID**

### **Reason for exclusion**

#### **Excludio 2003**

State reasons for exclusion. EXAMPLE 1: This randomised trial addressed a different question from that under review. It compared the use of atmospheric air versus 80% oxygen for preterm infants during initial stabilization in the delivery room, and was thus excluded from the review.

EXAMPLE 2: Study published in letter form. This was a prospective randomised controlled study of 17 patients comparing post operative cardio-respiratory events in preterm infants undergoing spinal anaesthesia compared with general anaesthesia. Required outcomes not reported. Personal communication unsuccessful.

## References to studies

### Included studies

#### **Fictitious 2001**

{published data only}

\* Fictitious A, Pretend BG. Randomised trial of drug A versus placebo in preterm infants. Journal of Local Paediatrics 2001;3:265-9.

Fictitious A, Pretend BG. Randomised trial of drug A versus placebo in preterm infants. Journal of Local Paediatrics 2000;2:379 (abstract).

### Excluded studies

#### **Excludio 2003**

{published data only}

Excludio WM. Drug A versus Drug B in babies hospitalised with awful disease. Journal of Local Paediatrics 2003;2:16-21.

\* *indicates the primary reference for the study*

## **Other references**

### **Additional references**

#### **Clarke 2003**

Clarke M, Oxman AD, editors. Cochrane Reviewers' Handbook 4.2.0.  
<http://www.cochrane.dk/cochrane/handbook/handbook.htm> updated March 2003.

#### **CNRG 2003**

Organization of a Systematic Review for the Cochrane Neonatal Review Group. Guidelines for Reviewers and Editors. <http://hiru.mcmaster.ca/cochrane/centres/canadian/neonatal/checklist.pdf>.

#### **Docherty 1999**

Docherty M, Smith R. The case for structuring the discussion of scientific papers. *British Medical Journal* 1999;318:1224-5.

#### **Moher 1999**

Moher D, Cook DJ, Eastwood S, Olkin I, Rennie D, Stroup DF for the QUORUM Group. Improving the quality of reports of meta-analyses of randomised controlled trials: the QUORUM statement. *The Lancet* 1999;354:1896-900.

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## Notes

### Unpublished CRG notes

Exported from Review Manager 4.2.3

This Notes section is part of the Cover Sheet.

Exported from Review Manager 4.2.3:

Text in this field is for the reviewer and/or Review Group information only and will NOT appear in the published review. You may use it to record notes to yourself or co-reviewer. Your CRG may use it to record dates of publication for tracking purposes.

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The information below is NOT part of "Unpublished Notes".

This space is used to describe "The Table of Comparisons" in this example review so that this information would be included within the review itself and thus avoid having a separate appendix.

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The Table of Comparisons sets out:

- 1) the comparisons to be made
- 2) the outcomes under each comparison
- 3) any sub-group analyses (by sub-categories of population, intervention, or outcome)

### COMPARISONS

Comparisons can be:

- Between 2 interventions, e.g.

Treatment vs Control

Treatment A vs Treatment B

- Between 2 interventions restricted by population or by intervention, e.g.

Treatment vs Control in Babies <1500g

Oral treatment vs Control

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Intravenous treatment vs Control

## OUTCOMES

- Under each comparison, list the different outcomes
- Outcomes should ideally be assessed and reported among all randomized (intention-to-treat)
- If an outcome is reported among a sub-set of all randomized, build that distinction into the name of the outcome, e.g.
  - Cerebral palsy among survivors at 1-3 years
- Competing risks: mutually exclusive outcomes which compete with each other can be listed separately, and then aggregated, e.g.
  - Bronchopulmonary dysplasia at 28 days
  - Death up to 28 days
  - Bronchopulmonary dysplasia or death at 28 days
- Any outcome can be divided into 2 or more sub-categories (although this is usually not required)
- If sub-categories for an outcome are mutually exclusive, the meta-analysis results of the different sub-categories can be combined to give an overall result, e.g.
  - Early neonatal deaths (0-7 days)
  - Late neonatal deaths (8-28 days)
  - Total neonatal deaths (0-28 days)
- If sub-categories for an outcome are not mutually exclusive, or where it does not make sense to compute an overall result, the meta-analysis results of the different sub-categories must not be combined to give an overall result,  
e.g. "sub-totals only" would be chosen for the following sub-categories of the outcome, Death
  - Death before hospital discharge
  - Neonatal death (< 28 days)

## **Published notes**

### **Amended sections**

Cover sheet

Synopsis

Abstract

Background

Objectives

Criteria for considering studies for this review

Search strategy for identification of studies

Methods of the review

Description of studies

Methodological quality of included studies

Results

Discussion

Reviewers' conclusions

Acknowledgements

Potential conflict of interest

References to studies

Other references

Characteristics of included studies

Characteristics of excluded studies

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