



## The Cochrane Renal Group

This booklet has been produced to make the whole process of preparing a protocol as painless as possible. The editorial base has developed guidelines that detail each section of the protocol and what should be included. These guidelines are a distillation of the Reviewers handbook, other review group policies and recommendations from the Renal Group Editorial Team.

There are several sections of this booklet.

- Getting started
- Creating a protocol
- Renal Group guidelines
- Editorial process
- Checklist for protocol submission

### Cochrane Renal Group Editorial Team



**Endorsements:** Asia Pacific Society of Nephrology, International Pediatric Nephrology Association, International Society of Nephrology, National Kidney Foundation  
**Industry sponsors:** AMGEN Australia, Janssen-Cilag, Novartis Pharmaceuticals, Wyeth Australia

## Getting started

Now that your title has been registered there are several files you will need. All are available at [www.cochrane.de](http://www.cochrane.de). If you have problems downloading these files please contact the Coordinator.

### 1) RevMan 4.2

This is the program which you must use to write your protocol and later your review.

- [www.cc-ims.net/RevMan/download.htm](http://www.cc-ims.net/RevMan/download.htm)
- RevMan 4.2 installation program (for installation from a hard drive or network) 8.1 Mb : [revman42.exe](#)

### 2) Reviewers' Handbook

This explains the Review process (and has been summarised in this document). The handbook is also incorporated in the RevMan software.

- [www.cochrane.de/cochrane/hbook.htm](http://www.cochrane.de/cochrane/hbook.htm)
- The Handbook is several hundred pages long so it is not normally distributed in print. You can either browse the handbook on-line or download the handbook in pdf format.

### 3) RevMan user guide

This guide explains how to use RevMan. It is available from within the RevMan 4.2, under the help menu, or it can be downloaded from;

- [www.cochrane-net.org/download/revman/Documentation/User%20guide.pdf](http://www.cochrane-net.org/download/revman/Documentation/User%20guide.pdf)

### 4) RevMan style guide

This guide explains the style conventions for a Cochrane review.

- [www.liv.ac.uk/lstm/ehcap/CSR/CSG.pdf](http://www.liv.ac.uk/lstm/ehcap/CSR/CSG.pdf)

### 5) RevMan training exercise

This is a good training guide for those who haven't as yet attended a workshop (or those who would like a quick how-to guide). The PDF version can be accessed from the RevMan 4.2 help menu. It is currently not available to download.

### 6) Installation of RevMan

Once you have installed RevMan, and have opened the program for the first time, it will ask you for your contact ID and name. You should have received a letter on registration of your title with both your contact ID and the review ID (if not contact the Coordinator). Enter the contact ID, your first name and last name and then click OK.

# Creating a Cochrane Protocol

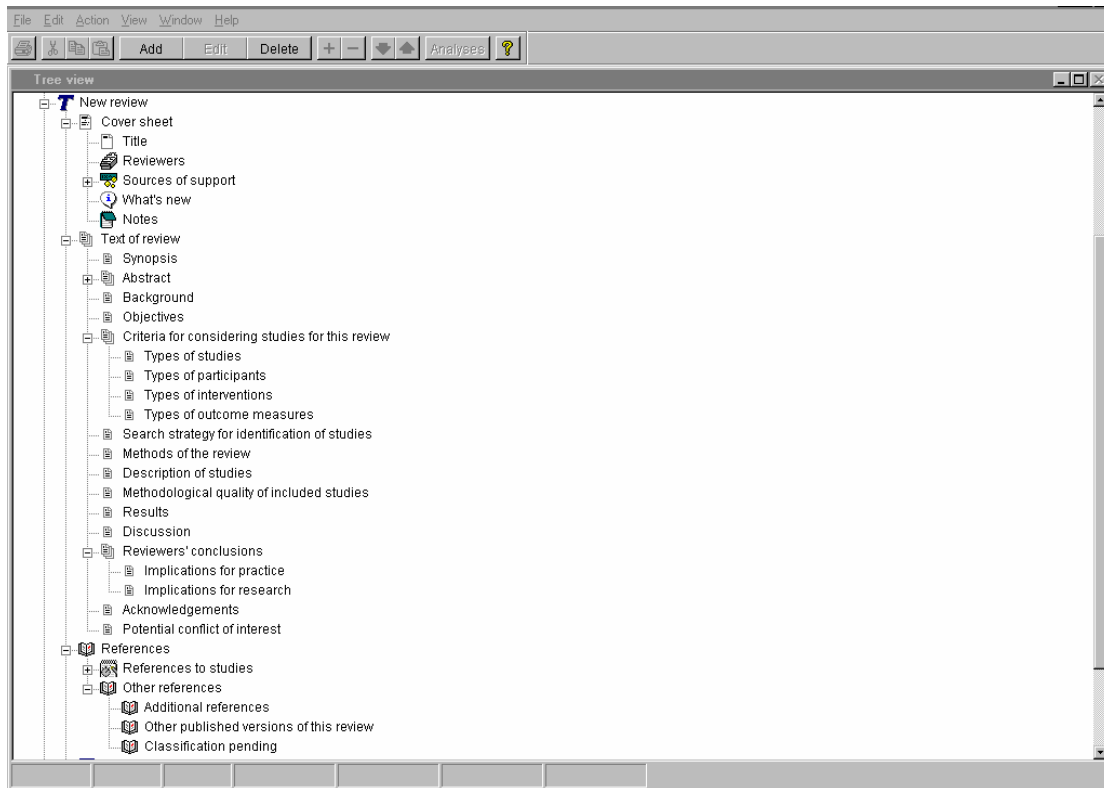


Fig 1. A view of the RevMan window. To access any of these sections, simply double click

## Please note:

Only the sections required for a protocol are listed here.

## Cover sheet

The cover sheet includes the following information:

### Title

**Title:** Title as agreed upon by the Renal Group

**Version:** One version of each review must be marked as the primary version and this is the one that should be submitted for publication in the *Cochrane Database of Systematic Reviews (CDSR)*.

**Status:** This specifies what stage the review is at: title, protocol or full review. Click protocol.

**Unique ID:** The unique ID is created automatically by RevMan 4.2.

**Date edited:** This date is entered automatically any time the review is amended.

Date of last substantive update: The date of most significant change.

Date next stage expected: The date the review is expected.

### Reviewers

Contact reviewer: Main contact person for this review.

Co-reviewers: Contact details for any co-reviewers on the review.

Contributions: Describes the contribution of each reviewer.

The following potential contributions have been adapted from (Yank 1999).

This is a suggested scheme (please put into own words)

- Conceiving the review

- Designing the review

- Coordinating the review

- Data collection for the review

  - Developing search strategy

  - Undertaking searches

  - Screening search results

  - Organising retrieval of papers

  - Screening retrieved papers against inclusion criteria

  - Appraising quality of papers

  - Abstracting data from papers

  - Writing to authors of papers for additional information

  - Providing additional data about papers

  - Obtaining and screening data on unpublished studies

- Data management for the review

  - Entering data into RevMan

- Analysis of data

- Interpretation of data

  - Providing a methodological perspective

  - Providing a clinical perspective

  - Providing a policy perspective

  - Providing a consumer perspective

- Writing the review

- Providing general advice on the review

- Securing funding for the review

- Performing previous work that was the foundation of current study

List of reviewers for citation: This can be considered the 'byline' for Cochrane. The list of reviewers for citations can be the name of an individual, several individuals or a collaborative. Ideally, the order of authors should

relate to their relative contributions to the review. The person who contributed most should be listed first.

### Sources of support

Intramural: Support from within your organisation

Extramural: Outside financial support (other institutions or funding agencies).

### What's new

Protocol first published: Issue \_\_\_ Year \_\_\_ \_\_\_ \_\_\_ (Coordinator shall enter these values on submission to the Cochrane Library).

Date of last minor update: Automatically entered

### Notes

Unpublished CRG notes: These notes will not be published in the *CDSR*.

Published notes: These notes will be published in the *CDSR*.

Amended sections: These boxes can be checked to make it easier for co-reviewers or the CRG's editorial team to locate changes in the review. This information is not published in the *CDSR*.

## Text of review

### Background

See next section - Renal Group guidelines

### Objectives

See next section - Renal Group guidelines

### Criteria for considering studies for this review:

#### Types of studies

See next section - Renal Group guidelines

#### Types of participants

See next section - Renal Group guidelines

#### Types of interventions

See next section - Renal Group guidelines

#### Types of outcome measures

See next section - Renal Group guidelines

### Search strategy for identification of studies:

See next section - Renal Group guidelines

### Methods of the review:

See next section - Renal Group guidelines

### Acknowledgements

This section should be used to acknowledge any individuals or organisations who the reviewers wish to acknowledge but who have not made a sufficient contribution to the review to be included in the Contributions section.

**Conflict of interest:** Any conflict of interest capable of influencing the judgements of any of the reviewers should be reported, including financial, personal, political or academic conflicts (see section 2.2). If there are no conflicts of interest, this should be stated explicitly, e.g. by reporting 'None'.

## References

### Other references

**Additional references** References cited in the text should be listed here. The style is First author surname year of publication (eg Smith 2001)

**Other published versions of the review;** e.g. if the review has been published in a journal or textbook it should be listed here.

## References

Dickersin 1986. Dickersin K, Hewitt P. Look before you quote. *BMJ* 1986; 293:1000-2.

Eichorn 1987. Eichorn P, Yankauer A. Do authors check their references? A survey of accuracy of references in three public health journals. *Am J Public Health* 1987; 77:1011-2.

Flanagin 1998. Flanagin A, Carey LA, Fontarosa PB, Philips SG, Pace BP, Lundberg GD, Rennie D. Prevalence of articles with honorary articles and ghost authors in peer-reviewed medical journals. *JAMA* 1998; 280: 222-4.

ICMJE 1997. International Committee of Medical Journal Editors. Uniform requirements for manuscripts submitted to biomedical journals. *Canadian Medical Association Journal* 1997; 156: 270-85.

Rennie 1997. Rennie D, Emanuel L, Yank V. When authorship fails: a proposal to make contributors accountable. *JAMA* 1997;278:579-85.

Rennie 1998. Rennie D, Yank V. If authors become contributors, everyone would gain, especially the reader. *Amer J Public Health* 1998;88:828-30.

Yank 1999. Yank V, Rennie D. Disclosure of researcher contributions: a study of original research articles in the *Lancet*. *Annals of Internal Medicine* 1999; 130: 661-70.

# Renal Group protocol guidelines

## Background

The background should support the need for the systematic review by providing sufficient information on the frequency and severity of the clinical problem and the uncertainties in its management.

## Objective

- A well formulated objective should be specified in terms of the interventions, the population with the clinical problem and the outcomes.
- In the renal group we have broad inclusion criteria but we separate trials at the analysis stage.
- The objective should be sufficiently broad to allow for variations in the interventions (different drugs, different doses of the same drug, different durations of the same drug) and populations (different age groups, different sexes) unless there are good reasons not to do so. Defining how broad or how narrow a review should be can be difficult. A narrow review is easier for the reviewer but is less useful for the reader. Generally there should be only one clinical problem but in the renal group we try to be as broad as we can for populations, interventions and outcomes. This is mainly because we want to provide as much assistance to the decision making of health care providers and consumers as we can. Limiting a review to one intervention when there are many, possible means that many different places have to be searched to obtain all of the information, and trial data becomes duplicated in many reviews. In renal medicine, there are usually only a small number of trials on any one intervention and so a “lumping” approach is usually feasible. Having a range of populations and interventions means that variations in treatment effects can also be explored which makes application of the review results to clinical practice easier.
- All clinically relevant outcomes both beneficial and harmful should be included.

## Types of studies

- In the renal group (as in most groups) we only include randomised and quasi-randomised trials, because they provide unconfounded comparisons of the effects of intervention.
- A randomised controlled trial (RCT) uses a truly random sequence generation such as computer-generated or a random number table.
- In quasi- (or pseudo) randomised trials (q-RCT), the allocation process is known to all so that the physician or subject could influence the treatment group to which the subject is allocated. Examples of q-RCTs are where patients are allocated to groups according to odd and even medical record numbers or month of birth.

## Interventions/comparisons

- In general a systematic review is of more value to a user if all interventions for the clinical problem are included. In general all possible interventions available for the clinical problem should be included unless this is not feasible.
- Just because all interventions are included in a review does not mean that they will be pooled to achieve a (potentially) meaningless summary effect measure.

## Types of outcomes

- The outcomes to be considered should be those that are of clinical relevance and of relevance to the patient. Surrogate outcomes, which measure a change in a laboratory measurement (eg protein excretion), are less valuable than a clinical outcome (eg requiring dialysis for end stage renal failure) even if the surrogate is believed to be a marker for the clinical outcome. Clinical outcomes such as survival tend to be those considered most important by investigators. They may however not capture all the outcomes considered important by the patient. For example interventions that improve patient survival, may result in adverse reactions that the patient may consider so detrimental to their quality of life that they may prefer not to have the intervention. One way to construct this list of benefits and harms is to consider yourself as the patient and think of all of the outcomes that would matter to you. You can then add the biochemical markers if you like. Remember that timing of outcomes also needs to be considered. Long term outcomes are generally going to be more

important for patients even though they are more difficult for triallists to obtain.

- The outcomes included should include all effects of the intervention - both the benefits and harms.

## Search strategy

- We are in the process of developing a clean and comprehensive register of all nephrology trials. This will mean that once you provide us with your title, we can provide you with a list of all relevant trials. Until then our Trials Search Coordinators ([ruthm4@chw.edu.au](mailto:ruthm4@chw.edu.au) or [lindah3@chw.edu.au](mailto:lindah3@chw.edu.au)) will work with you as you develop your search strategy.
- The aim of the search strategy is to locate all relevant trials. The strategy used by the Cochrane Renal Group for searching MEDLINE and EMBASE is shown in Appendix 1. However neither database provides a complete list of published trials and, of course, they do not include trials that were never published.
- The biases that result from an incomplete literature search are publication bias, duplication bias, location bias and language bias.
- Publication bias: A trial in which the experimental intervention proves to be no more effective than the control intervention is less likely to be published. Failure to locate such studies and include them in a systematic review could result in the summary estimate of effect overestimating the true effect of an intervention due to publication bias. Hand-searching conference proceedings and reference lists of textbooks and previous trials and contacting experts in the field may help to identify unpublished studies. A graphical test that can be used to detect publication bias if large numbers of studies are available is described later in the "Methods of the Review" section.
- Duplication bias: Many trials are published more than once under the same or different authors and may include different amounts of data, especially if initial reports do not cover the entire period of follow-up. Where there are multiple reports of the same trial, with different data sets included in each publication, you may need to extract data from several different publications to obtain all the outcomes. It is important to specify in the protocol how duplicate publication will be dealt with.
- Location bias: New or exciting results with large treatment effects are more likely to be published in major journals. Results deemed to be less interesting may be published in second line or local journals that may not be indexed in the major databases.

- Language bias: Failure to search for and include trials published in a language other than English can result in language bias.

## Quality assessment

- Often we assume that all trials are equally valid (accurate), but this is not the case. Some trials are better than others. Assessment of the quality of a trial is necessary because quality can affect (bias) the results of a trial. Because we want our systematic reviews to limit bias we need to analyse trial quality. Low quality trials tend to overestimate the benefits of interventions<sup>1</sup>. Important quality domains are allocation concealment, blinding (of investigators, subjects and those assessing outcomes), intention-to-treat analysis and completeness of follow-up.
- Adequate allocation concealment is the most important factor in reducing bias in RCTs. Trials with inadequate allocation concealment tend to overestimate the effectiveness of the intervention by 30-40% while trials, that are not double-blinded, tend to overestimate effectiveness by 17%<sup>2</sup>. Unblinded outcome assessment has been shown to overestimate efficacy by 35%<sup>3</sup>. Intention-to-treat analysis and loss to follow-up seem to be less important in contributing to bias.

## Quality items

The quality items to be assessed are shown in the appendix 2. Trial quality is a difficult but important area, so we will spend some time on it.

- *Allocation concealment*: It is important to determine if the random allocation of a subject to an intervention group in a trial could be influenced by the investigator (or subject) resulting in biased selection of subjects to one group or the other. This is prevented if there is no way of knowing what the next subject is going to get, and is called "adequate allocation concealment". If the investigator is aware or could be aware of the intervention group to which the subject could be assigned, it is possible for that knowledge to influence the intervention the subject receives. This is obviously the situation in quasi-randomised trials. It may be less obvious in RCTs but may occur if allocation is simply using sealed but non-opaque envelopes. If the investigator preferred one intervention over another, they might decide not to enter their patient into the trial at that time but wait until an envelope containing the preferred treatment group was opened. Alternatively the investigator could change the order of

envelopes to achieve their preferred sequence. The randomisation method needs to be described in detail (e.g. central computerised randomisation system) for a reviewer to determine whether allocation was concealed or not. In many trials, the method of randomisation is not described and allocation concealment has to be considered “not stated” unless more information can be obtained from the investigators.

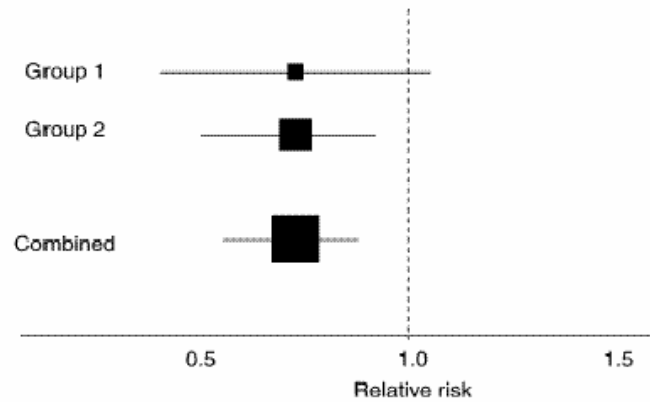
- *Blinding:* Ideally trials should be quadruple blind - the treatment assignment should be unknown to the investigators, the subjects, those evaluating outcomes and those analysing the data. Double-blinded trials mean neither the investigator nor the patient are aware of treatment assignment, but they do not refer to blinded outcome assessment, which is probably the most important. Blinding prevents performance or co-intervention bias (differences in care provided apart from the intervention being evaluated) and detection bias (differences in outcome assessment). Blinding becomes particularly important with subjective outcomes such as pain. It may not be possible to implement completely. For example it is not possible to blind the investigator and subject if a surgical intervention (ureteric reimplantation for ureteric reflux) is compared with a medical intervention (antibiotic prophylaxis). In that situation, it is essential that those evaluating the outcomes (new cortical renal scars on intravenous pyelogram) are blinded to the intervention. In some trials, the investigators and subjects may be blinded but the investigators may be able to determine the intervention group from the adverse effects experienced by the patients.
- *Intention-to-treat analysis:* Adequate allocation concealment will generally ensure that the intervention groups are similar at entry to a trial (if the trial is large enough). Publications of most trials will include a table demonstrating the similarity of treatment groups at the beginning of the trial. It is important that the groups be similar at the completion of the evaluation to avoid attrition bias. This requires that the results should be analysed with the patients in the intervention groups to which they were allocated even if they did not receive the intervention, if they deviated from protocol or if they withdrew from the study but follow-up continued. Frequently a publication report will only include data on those patients who actually received the interventions and completed the study.
- *Completeness of follow-up:* Losses of participants to follow-up will also lead to differences between treatment groups at the end of the study. In assessing a study, it is important to account for all the participants in the study.

## Reporting on quality items

- In the Cochrane Renal Group we assess each quality item separately rather than combine quality items in a scoring system. This is because only individual items of quality have been found to be associated with observed treatment effects, and scoring systems give unpredictable and unreliable results<sup>3</sup>.

## Methods of the Review

- To reduce errors, two reviewers should carry out each step of the review. Simple differences should be resolved in discussion between the two reviewers but more substantial differences and unresolved differences should be resolved in discussion with a third reviewer.
- Each reviewer should extract data on to a standard data collection form. A specimen data extraction form is shown in Appendix 3.
- If a large number of studies are available for review, it is useful to investigate for publication bias using a funnel plot<sup>4</sup>. In a funnel plot, individual study weights are plotted on the y-axis against the study relative risks on the x-axis. Smaller studies have less precision than large studies so are more likely to have a result further from the "true" result than a large study. If no publication bias is present, the graph should have an inverted funnel shape with the largest study at the apex of the funnel and smaller studies distributed equally on either side of the large study. If publication bias is present, the bottom right of the funnel (assuming that relative risks less than one indicate positive results) will be missing reflecting that small studies with a negative result are not included. Bias is also suggested if the summary effect estimate is situated to the left of the relative risk for the largest study.
- Reviewers have the opportunity to explore whether there is a constant intervention effect or whether it varies across studies based upon plausible factors like quality (see above), population (age, gender), clinical problem (severity of disease), intervention (dose, duration), and outcome (particularly timing). Reviewers need to decide which of these factors they would like to explain based upon biological plausibility, before they look at the trial results. Sub-group analysis is used to see whether these potential factors actually do influence treatment effect, by comparing the treatment effect of studies with the factor of interest with those studies without the factor of interest. This is formally tested as for effect modification, but you will get a reasonable idea by seeing whether the 95% confidence intervals of the two groups of studies cross.



**› Hypothetical study showing combined and subgroup analysis: subgroups 1, 2 and the combined effect are all equivalent, but only group 2 and the combined groups are statistically significant**

The general approach to subgroup analysis should be to assume similarity unless a difference can be demonstrated. Thus individual subgroups should not be tested for significance of their main effects, but should be tested to see whether the subgroups differ significantly. In the figure, we have a hypothetical study which is clearly significant (the 95%CI do not cross 1). Now if subdivided into 2 groups, group 1 is no longer significant even though the intervention effect is clearly no different from group 2.

## Statistical analysis

- By convention the outcome we chose is a bad one, which we aim to reduce with an intervention. This will mean, that if beneficial, an intervention will reduce the number of adverse events and the point estimate will be to the left of the line of no effect.
- Relative risk and random effects models:  
You don't have to be a statistician to do a systematic review, as RevMan does much of the work for you. You simply need to decide which option to choose. Our default position is to use the relative risk measure for individual study and summary results, with the random effects model used for the summary effect measure. The random effects model incorporates possible between study differences as well as within study differences and so is more conservative. The fixed effects model assumes that no between study differences exist. As expected both models give very similar results unless there is significant between study differences (heterogeneity). We have chosen relative risk (rather than odds ratios or risk difference) because we believe it provides the best trade-off in ease of understanding, consistency across studies, and mathematical properties<sup>5,6</sup>.

- Heterogeneity

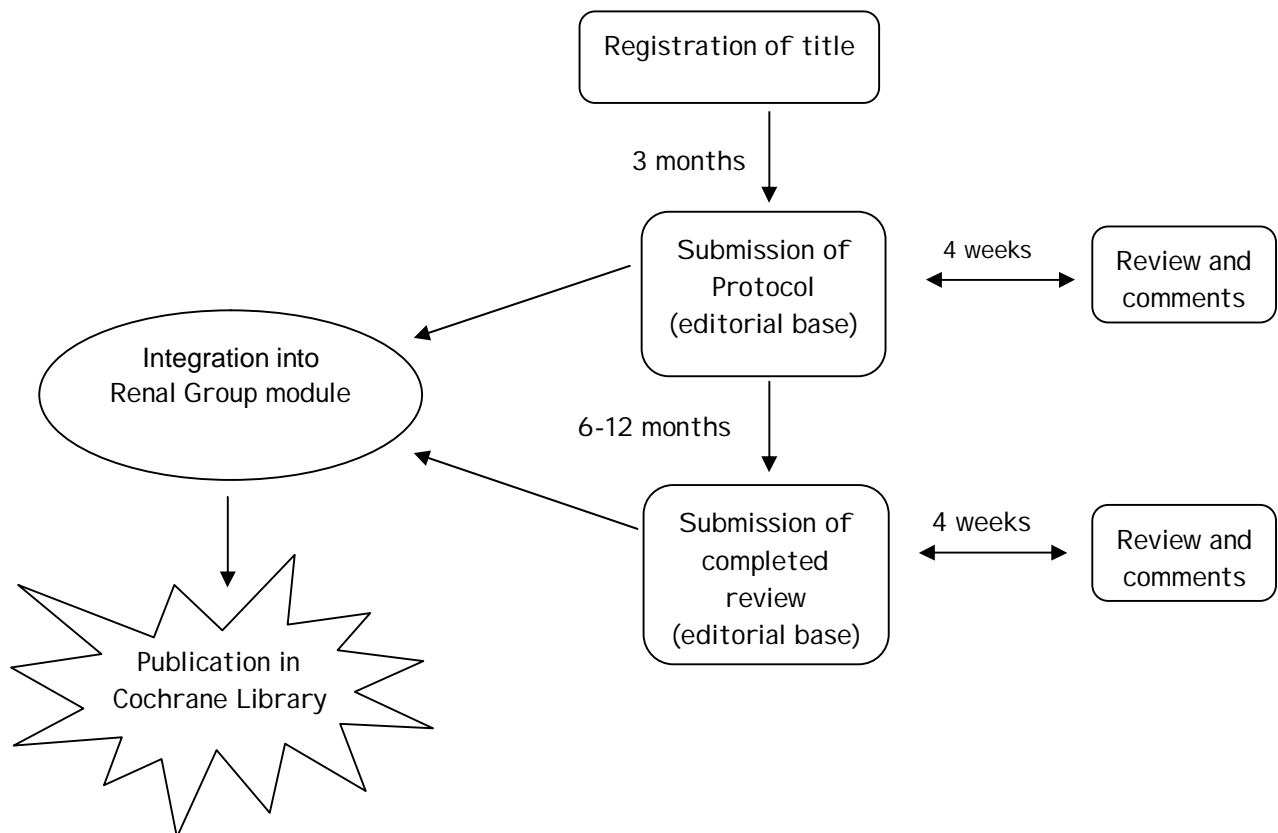
RevMan automatically tests for significant between study differences (heterogeneity). Heterogeneity will also be evident by looking at the forest plot (the plot of the individual trial results). It is important to distinguish between qualitative and quantitative differences. If all study results show benefit but there is heterogeneity in terms of how much benefit then the clinical implication is not likely to be as large as if some studies showed benefit and others showed harm. Heterogeneity should be welcomed and explored using subgroup analysis of the factors already stipulated in the protocol. If heterogeneity cannot be explained then it is probably better to disregard the pooled result and discuss the results of the study qualitatively. Cochran's  $Q$  is the test statistic for heterogeneity. In RevMan this is provided with its degrees of freedom. The corresponding  $p$ -value can be found in any statistical table. As a rough guide, heterogeneity is not significant if the degrees of freedom is greater than or equal to the Cochran  $Q$  statistic.

## References

1. Moher D, Pham B, Jones A, Cook DJ, Jadad AR, Moher M, Tugwell P, Klassen TP. Does quality of reports of randomised trials affect estimates of intervention efficacy reported in meta-analyses? *Lancet* 1998;352:609-613.
2. Schulz KF, Chalmers I, Hayes RJ, Altman DG. Empirical evidence of bias. Dimensions of methodological quality associated with estimates of treatment effects in controlled trials. *JAMA* 1995;273:408-412.
3. Jüni P, Witschi A, Bloch, R, Egger M. The hazards of scoring the quality of clinical trials for Meta-analysis. *JAMA* 1999: 282: 1054-1060.
4. Egger M, Davey-Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple graphical test. *BMJ* 1997;315:629-634.
5. Sackett DL, Deeks JJ, Altman DG. Down with odds ratios! *Evidence-Based Medicine* 1996: 1: 164.
6. Berlin JA, Laird NM, Sacks HS, Chalmers TC. A comparison of statistical methods of combining event rates from clinical trials. *Statistics in Medicine* 1989: 8(2): 141-151.

## Renal Group editorial process

The overall process can be seen below



On completion of the draft protocol it should be submitted to the Coordinator who then organises four referees. They include; a Renal Group Editor, two content experts and a consumer. Once these referees have agreed to referee the protocol the relevant documents are sent and there is an understanding that the comments should be returned to the Coordinator within two weeks. In addition to the four referees, the Coordinating Editor also referees all protocols.

The Coordinator compiles all the comments and emails them to the reviewer. Prompt reply and amendment will ensure quick inclusion into Cochrane Library. On resubmission, the Coordinating Editor and the Coordinator will then review the changes. Once the changes have been approved, the Coordinator will copy edit the protocol (checking with the authors) and then submit the protocol to the Cochrane Library.

# Appendix 1

## Medline Search Strategy for RCTs

1. *RANDOMIZED CONTROLLED TRIAL.pt.*
2. *CONTROLLED CLINICAL TRIAL.pt.*
3. *RANDOMIZED CONTROLLED TRIALS/*
4. *RANDOM ALLOCATION/*
5. *DOUBLE BLIND METHOD/*
6. *SINGLE BLIND METHOD/*
7. *1 or 2 or 3 or 4 or 5 or 6*
8. *(ANIMAL not HUMAN)/*
9. *7 not 8*
10. *CLINICAL TRIAL.pt.*
11. *exp CLINICAL TRIALS/*
12. *(clin\$ adj25 trial\$.tw.*
13. *CROSS-OVER STUDIES/*
14. *(crossover or cross-over or cross over).tw.*
15. *((singl\$ or doubl\$ or trebl\$ or tripl\$) adj25 (blind\$ or mask\$)).tw.*
16. *PLACEBOS/*
17. *placebo\$.tw.*
18. *random\$.tw.*
19. *RESEARCH DESIGN/*
20. *10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19*
21. *20 not 8*
22. *9 or 21*

## EMBASE Search Strategy for RCTs

- 1 *exp controlled study/ or controlled study.ti,ab,hw,tn,mf.*
- 2 *exp statistical analysis/ or clincial study.ti,ab,hw,tn,mf.*
- 3 *exp major clinical study/ or major clinical study.ti,ab,hw,tn,mf.*
- 4 *exp randomized controlled trial/ or randomised controlled study.ti,ab,hw,tn,mf.*
- 5 *random\$.ti,ab,hw,tn,mf.*
- 6 *exp double blind procedure/ or double blind procedure.ti,ab,hw,tn,mf.*
- 7 *exp single blind procedure/ or single blind procedure.ti,ab,hw,tn,mf.*
- 8 *exp multicenter study/ or multicenter study.ti,ab,hw,tn,mf.*
- 9 *exp placebo/ or placebo.ti,ab,hw,tn,mf.*
- 10 *or/1-9*
- 11 *(human not animal).sh,de,hw.*
- 12 *10 and 11*

## Appendix 2

### Quality Checklist

#### 1. Allocation Concealment

- Adequate (randomisation method described that would not allow investigator/participant to know or influence intervention group before eligible participant entered in the study)
- Unclear (randomisation stated but no information on method used is available)
- Inadequate (method of randomisation used such as alternate medical record numbers or unsealed envelopes; any information in the study that indicated that investigators or participants could influence intervention group)

#### 2. Blinding

- Investigators: Yes/No/not stated
- Participants: Yes/No/not stated
- Outcome assessor/s: Yes/No/not stated
- Data analysis: Yes/No/not stated

#### 3. Intention to treat analysis

- Yes - Specifically reported by authors that intention-to-treat analysis was undertaken and this was confirmed on study assessment.
- Yes - Not specifically reported but confirmed on study assessment.
- No - Not reported and lack of intention-to-treat analysis confirmed on study assessment. (Patients who were randomised were not included in the analysis because they did not receive the study intervention, they withdrew from the study or were not included because of protocol violation).
- No - Stated but not confirmed on study assessment.
- Unclear - unable to determine or confirm with authors.

#### 4. Completeness of follow-up:

- Number of participants with outcome data/total number of participants randomised, expressed as a percentage

## Appendix 3 Renal Group data extraction form

Date..... Reviewer: .....

Review Title .....

Study details .....

First author	
Year of publication	
Country of publication	
Publication type	Journal / Abstract / other (specify)

### Study Eligibility/Characteristics

	Inclusion Criteria	Study
Type of study		Yes no unclear
Participants	<ul style="list-style-type: none"> <li>•</li> <li>•</li> <li>•</li> </ul>	Other:
Types of intervention	<ul style="list-style-type: none"> <li>•</li> <li>•</li> <li>•</li> </ul>	Other:
Types of outcome measures	<ul style="list-style-type: none"> <li>•</li> <li>•</li> <li>•</li> </ul>	Other:

Include \*\* Exclude \*\*

Reason for exclusion:

---

	Study
Trial inclusion criteria	
Trial exclusion criteria	
Participants	<ul style="list-style-type: none"> <li>• age:            median..... Mean..... range.....</li> <li>• ethnicity</li> <li>• Other</li> </ul>
Setting	source eg multicentre, university teaching hospitals:
Trial Intervention (incl duration)	
Trial control (incl. Duration)	
Duration of follow-up	

## Methods: Trial Quality

Method of randomisation	
Allocation concealment score	A/B/C (see appendix 2)
Study design	Parallel/crossover
Blinding	<ul style="list-style-type: none"> <li>• Participants</li> <li>• Investigators</li> <li>• Outcomes assessors</li> </ul>
Outcome assessment and measurement	<ul style="list-style-type: none"> <li>• Outcome methods</li> <li>• Outcome definitions</li> </ul>
Intention-to-treat analysis	
Compliance	
Matching of interventions	eg taste, smell, appearance, colour
Similarity between groups	
Funding source	
Notes	

## Results

Comparison: \_\_\_\_\_

Outcome: \_\_\_\_\_

Subcategory: \_\_\_\_\_

Experimental:		Control:	
Observed (n)	total (N)	observed (n)	total (N)

	Experiment:	Control:
Total randomised		
excluded*		
Observed		
lost to follow up*		

\*Reasons for loss/exclusion:

\_\_\_\_\_

\_\_\_\_\_

Subcategory: \_\_\_\_\_

Experimental:		Control:	
Observed (n)	total (N)	observed (n)	total (N)

	Experiment:	Control:
Total randomised		
excluded*		
Observed		
lost to follow up*		

\*Reasons for loss/exclusion

\_\_\_\_\_

\_\_\_\_\_

## Other

Contact with primary investigators	<ul style="list-style-type: none"><li>• Clarify methods</li><li>• Clarify results</li></ul>
Notes	

# Cochrane Renal Group Protocol Checklist

This checklist is sent with your protocol to the referees. Please ensure all sections have been addressed by your protocol. This will speed up the process and ensure your protocol is quickly included on the Cochrane Library. Please remove this section and use to check your protocol before submitting to the Coordinator.

## Title

Does the title follow the preferred format, i.e. *intervention for clinical problem in population?*

*Corticosteroids for steroid responsive nephrotic syndrome in children*

## Background

Does the background support the need for a systematic review by providing sufficient information on the frequency and severity of the clinical problem and the uncertainties in its management?

## Objective/s

Is the main objective of the review specified in terms of intervention(s), clinical problem, population and outcomes (both beneficial and harmful)?

*To evaluate the benefits and harms of different agents, other than corticosteroids, that are used in children who pursue a relapsing course of steroid responsive nephrotic syndrome*

## Selection criteria

### Types of participants:

Are the characteristics of the clinical problem and the population with the clinical problem described?

*Children aged 3 months to 18 years with steroid responsive nephrotic syndrome who have suffered one or more relapses.*

Has a clear case definition for establishing the presence of the clinical problem been included?

*The child, who becomes free of oedema and whose urine protein is < 1+ on dipstick or < 4mg/m<sup>2</sup>/hr for 3 consecutive days after receiving corticosteroid therapy.*

Have the population groups to be excluded been specified?

*Children in their first episode of nephrotic syndrome, children with steroid resistant nephrotic syndrome, children with congenital nephrotic syndrome and children with other renal or systemic forms of nephrotic syndrome defined on renal biopsy, clinical features or serology*

Have the appropriate population groups been excluded?

### Types of studies:

Do you intend to include only randomised controlled trials?

Do you intend to include quasi-randomised trials?

### Types of interventions and comparisons

Have the study interventions been described?

Have the control interventions been described?

Have all relevant interventions for the clinical problem and question asked been identified?

*Non corticosteroid agent versus placebo*

*Non-corticosteroid agent versus prednisone used alone.*

*Two different non-corticosteroid agents*

*Different doses and durations of the same non-corticosteroid agent*

Have the interventions to be excluded been described?

Are the interventions to be excluded appropriate?

### Types of outcomes:

Are the outcome measures for benefits and harms of the intervention(s) clearly defined in nature and in timing?

Are the outcome measures used important to the population with the clinical problem?

Have all relevant outcomes (both beneficial and harmful) been included?

*The prevention of relapse in steroid responsive nephrotic syndrome as measured by: The numbers of children with and without relapse at 6 months, 12 months and 2 years*

*Mean relapse rates per patient per year*

*Mean length of time to next relapse*

*Serious adverse effects of therapy*

If specific outcomes have not been included, does this conform with the question asked?

## Search strategy

Has the search strategy been included?

Are the dates that each source will be searched been indicated?

Will the following data sources be searched?

Cochrane Controlled Trials Register (most recent)

MEDLINE (from 1966 - )

EMBASE (from 1980 - )

Reference lists of textbooks, reviews (including previous systematic reviews), and previous trials

Conference proceedings

Does the search strategy include contacting experts in the field?

Have the appropriate subject headings, key words and text words for the clinical problem and population been used?

Has the Cochrane Collaboration search strategy to identify RCTs been used?

Has the Trials Search Coordinator been contacted?

Are studies in languages other than English to be included?

How will duplicate publications of the same trial be identified and dealt with?

## Assessment of quality

Have the criteria to be used to assess study quality been reported?

Does the criteria to be used to assess study quality include: -

Allocation concealment

Blinding of participants

Blinding of investigators

Blinding of outcome assessment

Intention-to-treat analysis

Completeness of follow-up

Are these items to be assessed separately rather than 'combined' in a scoring system?

## Methods of the Review

Will at least two authors of the review:-

Perform the literature search?

Determine study eligibility?

Assess study quality?

Extract data?

Enter data in RevMan?

Will reviewers work independently?

Will consensus and/or liaison with a third reviewer be used to resolve disagreement between the primary reviewers?

Will authors of primary studies be contacted for clarification of unclear data or to obtain missing information?

Will you attempt to analyse for possible publication bias using funnel plots or other methods?

Will plausible explanations for variations in treatment effect be explored using subgroup analysis based on study quality, population and interventions?

## Statistical analysis

Will the results of primary studies be reported with 95% confidence intervals using relative risk (RR) for dichotomous outcomes and weighted mean difference (WMD) for continuous outcomes?

Have the methods used to pool the results of the primary studies been reported?

Are these methods pertinent?

Will RR and WMD summary statistics be calculated using a random effects model?

*Statistical analysis will be performed using RevMan. For dichotomous outcomes (relapse or no relapse) results will be expressed as relative risks with 95% confidence intervals. Data will be pooled using the random effects model. Where continuous scales of measurement are used to assess the effects of treatment (e.g. time to relapse), the weighted mean difference will be used, or the standardised mean difference if different scales have been used*

Have you stated how you will test for heterogeneity?

*Heterogeneity will be analysed using the Cochran Q test on N-1 degrees of freedom, with an  $\alpha$  of 0.1 used for statistical significance.*

Have you specified how you will determine the applicability of the results to individual patients?

*Calculation of absolute risk reductions with therapy in relation to different baseline risk of the event with no treatment or a different therapy.*