



The Cochrane  
Renal Group

## Referee comments (review)

### General comments

### Major issues

### Minor issues

**Name:**

**Date:**

***If there are specific sections you would like to comment on, please use the next sections of this form. There is also a guide for assessing Cochrane reviews on page 3***

## **Abstract**

## **Background**

## **Objectives**

## **Methods of review**

*Selection criteria*

*Search strategy*

*Risk of bias assessment*

*Statistical analysis*

## **Results**

*Description of studies*

*Risk of bias in included studies*

*Effects of interventions*

## **Discussion**

*Summary of main results*

*Overall completeness and applicability of evidence*

*Quality of the evidence*

*Potential biases of the review process*

*Agreements and disagreements with other studies or reviews*

## **Authors conclusion**

*Implications for practice*

*Implications for research*

**Please use this section as guide for assessing this review**

## **Abstract**

Does each section of the abstract accurately reflect the equivalent section in the review

- Background
- Objectives
- Search strategy
- Selection criteria
- Data collection and analysis
- Main results
- Authors conclusions

## **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?
- Does the background address the important issues for consumers?

## **Objective/s**

- Was the main objective of the review specified in terms of intervention(s), clinical problem, population and outcomes (both beneficial and harmful)?  
*Example: To evaluate the benefits (reduction in number of children who relapse) and harms (serious infections, cystitis) of different agents, other than corticosteroids, that are used in children who pursue a relapsing course of steroid responsive nephrotic syndrome*

## **Methods - Criteria for considering studies for this review**

### ***Types of studies:***

- Did the authors include randomised controlled trials?
- Did the authors include quasi-randomised trials?

### ***Types of participants:***

- Were the characteristics of the clinical problem and the population with the clinical problem described?  
*Example: Children aged 3 months to 18 years with steroid responsive nephrotic syndrome who have suffered one or more relapses*
- Was a clear case definition for establishing the presence of the clinical problem included?  
*Example: The child, who becomes free of oedema and whose urine protein is  $\leq 1+$  on dipstick or  $< 4\text{mg/m}^2/\text{hr}$  for 3 consecutive days after receiving corticosteroid therapy.*
- Were the population groups to be excluded specified?  
*Example: 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*
- Were the appropriate population groups excluded?

### ***Types of interventions***

- Were the study interventions described?
- Were the control interventions described?
- Were all relevant interventions for the clinical problem and question asked identified?

#### *Example*

- 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

- Were the interventions excluded described and if yes were they appropriate?

### ***Types of outcome measures***

- Were the outcome measures for benefits and harms of the intervention(s) clearly defined in nature and in timing?
- Were the outcome measures used important to the population with the clinical problem?
- Were all relevant outcomes (beneficial and harmful) included?

#### *Example*

- 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
- Serious adverse effects of therapy

- If specific outcomes have been included, did they conform with the question asked?

### **Methods - Search methods for identification of studies**

Were the following data sources searched and dates listed?

- Cochrane Renal Group's specialised register
- Cochrane Central Register of Controlled Trials (most recent)
- MEDLINE (from 1950 – most recent)
- EMBASE (from 1980 – most recent)
- Reference lists of textbooks, reviews (including previous systematic reviews), and previous studies
- Did the authors contact experts in the field?
- Were studies in languages other than English included?
- Did the authors identify and deal with duplicate publications of the same study in the way that they said they would in the protocol?
  - If not, did they deal with duplicate publications in a way that would reduce bias?

### **Methods - Data collection and analysis**

- **Did at least two authors of the review:-**
  - Screen the literature search results to determine study eligibility?
  - Assess study quality?
  - Extract data?
- Did the authors work independently?
- Was there consensus and/or liaison with a third author to resolve disagreement between the primary authors?

- Were authors of primary studies contacted for clarification of unclear data or to obtain missing information?
  - If so, was this information provided to the authors?
- Did the authors attempt to analyse for possible publication bias using funnel plots or other methods?
  - If not, did the authors state why this could not be done?

### **Assessment of risk of bias**

Did the criteria to be used to assess the risk of bias of studies include:-

- Sequence generation
- Sequence allocation
- Blinding of key people involved in the study (e.g. participants, investigators, outcome assessor, data analysts)
- Incomplete reporting of outcomes (e.g. drop outs, loss to follow-up)
- Outcome reporting bias (selective outcome reporting)
- Other potential biases

### **Statistical analysis**

- Were the results of primary studies reported with 95% CI using risk ratio (RR) for dichotomous outcomes and mean difference (MD) for continuous outcomes?
- Were the RR and MD summary statistics calculated using a random effects model?

Did the authors test for heterogeneity as pre-specified in the protocol?

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

*Example: Sub-group analysis was planned based on study quality, patient type (age, presence of abnormal radiological findings) and intervention (type of antibiotic used) as we postulated that the relative treatment effect could vary these factors.*

- Did the authors attempt to determine the applicability of the results to individual patients?

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

### **Results - Description of studies**

- Were the important details of the included studies summarised in the text of the review?
- Were the important details of study design, participants, interventions and definitions of outcomes included in the table "Characteristics of included studies"?
- Were the reasons for excluding any studies clearly reported in the text and in the table "Characteristics of excluded studies"?
- If studies were excluded, are the reasons for exclusion consistent with the inclusion/exclusion criteria in the section on "Criteria for considering studies for the review"?
- Are you aware of any other studies that should have been included?

### **Results – Risk of bias in included studies**

- Was a short summary of the potential sources of bias of the included studies included in the text?

## **Results – Effects of interventions**

### ***Key results***

- Are the key results of the review provided in the text?
- Did the key results address the objectives of the review?

### ***Meta analysis***

- If results were pooled, was this appropriate?
- Did between study heterogeneity exist?
  - If yes, was it appropriately explained?

### ***Outcomes***

- Were all outcomes described in the protocol included in the results?

### ***Subgroup analysis***

- Were planned subgroup analyses included?  
*Example: Sub-group analysis showed that there was no difference in relative treatment effects (recurrence of urinary tract infections) between sulphonamide containing antibiotics (RR 1.20; 95% CI 0.47,3.10) and non sulphonamide based antibiotics (RR 1.77; 95% CI 0.96,3.29).*
- If planned subgroup analyses were not included, did the authors explain the reasons for this?
- Were subgroup analyses that were not specified in the protocol performed (post hoc analysis)?
  - If so, were these analyses described as being post hoc?

## **Discussion**

### ***Summary of main results***

- Were the principal results (both benefits and harms) summarised?
- Was the potential clinical importance of these results discussed?
- Are the conclusions of the study consistent with the results?

### ***Overall completeness and applicability of evidence***

- Was the consistency/inconsistency of study results discussed?

### ***Quality of the evidence***

Were the implications of the following methodological problems discussed:

- Publication bias
- Impression of results (sample size, CI)
- Uncertainty of harms

### ***Potential biases of the review process***

- Did the authors discuss the bias they had identified and their implications for the interpretation of results?

### ***Agreements and disagreements with other studies or reviews***

- Were the review findings discussed in relation to relevant evidence from other studies or reviews?

### **Authors' conclusions**

#### ***Implications for practice***

- Did the authors attempt to demonstrate the applicability of the results of benefits and risks to patients of low medium and high risk of adverse outcomes?

#### ***Implications for research***

- Did the authors determine which questions had been answered by the review?
  - If so, do you agree?
- Did the authors determine which questions require further studies?
  - If so, do you agree?
- Did the authors suggest new studies based on the reviewed research?
  - If so, do you believe that these studies are appropriate?
- Can you suggest further studies that should be done?