The Cochrane Renal Group	**Referee comments (protocol)**

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 protocols on page 3

Background

Objectives

METHODS: Criteria for considering studies for this review

Types of studies:

Types of participants:

Types of interventions

Types of outcome measures:

METHODS: Search methods for identification of studies

METHODS: Data collection and analysis

METHODS: Assessment of risk of bias

METHODS: Statistical analysis

Please use this section as guide for assessing this protocol

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

- Is 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 intend to include randomised controlled trials?
- Did the authors intend to include quasi-randomised trials?

Types of participants:

- Are 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
- Has a clear case definition for establishing the presence of the clinical problem been included?
  Example The child, who becomes free of oedema and whose urine protein is $\leq$ 1+ on dipstick or < 4mg/m^2/hr for 3 consecutive days after receiving corticosteroid therapy.
- Have 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
- Have the appropriate population groups been excluded?

Types of interventions

- Have the study interventions been described?
- Have the control interventions been described?
- Have 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*
- Have the interventions to be excluded been described?
- Are the interventions to be excluded appropriate?

Types of outcome measures:

- 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 (beneficial and harmful) been 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 not been included, do they conform with the question asked?

Methods - Search methods for identification of studies

Will the following data sources be searched?

- 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

- Are there any additional key words you think should be included?
- Are studies in languages other than English to be included?

Methods - Data collection and analysis

Will at least two authors of the review:-

- Screen literature search results to determine study eligibility?
- Assess the risk of bias?
- Extract data?

- Will authors work independently?
- Will consensus and/or liaison with a third author be used to resolve disagreement between the primary authors?
- Will authors of primary studies be contacted for clarification of unclear data or to obtain missing information?

Assessment of risk of bias

Does 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

- Will the results of primary studies be reported with 95% CI using risk ratio (RR) for dichotomous outcomes and mean difference (MD) for continuous outcomes?
- Will the RR and MD summary statistics be calculated using a random effects model?
- Have the authors stated how they will test for heterogeneity?
- Will plausible explanations for variations in treatment effect be explored using subgroup analysis based on study quality, population and interventions?
- Have the authors specified how they will 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.