

Protocol Submission 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/m²/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 α 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.