CAG standard protocol text – MECIR compliant

**Background**

*[Please refer to the Cochrane Handbook for Systematic Reviews of Interventions (www.cochrane-handbook.org; in RevMan 5: Help > Handbook) for guidelines on the development and completion of your protocol. See Guide to the contents of a Cochrane protocol or review in Section 4.5 of the Handbook.*

*The Methodological Expectations of Cochrane Intervention Reviews (MECIR) project has specified conduct and reporting expectations for Cochrane protocols and reviews, and is designed to support authors and editorial bases to produce Cochrane reviews of the highest possible standard (www.editorial-unit.cochrane.org/mecir). The Cochrane Airways Group has devised this standard protocol text to capture the main standards for most intervention reviews. However, you may need to modify the text to fit your specific review questions, but do follow guidance in the Handbook.*

*Before checking your draft in for editorial approval, please check there are no 'Errors' and review the 'Warnings' on the Validation Report (File > Reports > Validation Report). When you are ready to submit your protocol for editorial approval, check it back in to Archie - see Quick Start Guide for Authors for details (http://ims.cochrane.org/archie/documentation).*

*If the text is in regular font, you should not change it. However, you can modify it if you have good reason. If the text is italicised and in square brackets it is for guidance only and you should delete it before you submit your first protocol draft.*

*If you have any questions about the development of your protocol, please email Emma at ewelsh@sgul.ac.uk].*

**Description of the condition**

[See reporting standard R19 to R22; www.editorial-unit.cochrane.org/mecir].

**Description of the intervention**

**How the intervention might work**

[It is highly desirable for you to include any details of equity and how the intervention relates to specific populations, if this is relevant].

**Why it is important to do this review**

**Objectives**

**Methods**

**Criteria for considering studies for this review**

**Types of studies**

We will include randomised controlled trials (RCTs). We will include studies reported as full-text, those published as abstract only, and unpublished data.

[You must include RCTs in your review, but if you want to include any additional study designs, you must justify the choice of eligible study deigns].

**Types of participants**

We will include [adults or children or both] with a diagnosis of [asthma/COPD/other]. We will exclude participants with the following co-morbidities/characteristics:

[Predefine unambiguous criteria for participants. Define in advance how you will handle studies that include only a subset of relevant participants. Restrictions to study populations must be based on sound rationale and described here. Define age cut-off for adults/children/infants].

**Types of interventions**

We will include trials comparing [insert intervention] with [placebo/usual care/other]. We will include the following cointerventions provided they are not part of the randomised treatment:

[Define in advance the eligible interventions and the interventions against which these can be compared in the included studies. Pay attention to active comparator interventions (e.g. a different variant of the same intervention, a different drug, or a different kind of therapy). If you plan more than one comparison, define each one (e.g. steroids versus placebo; steroid versus steroid plus LABA)].

**Types of outcome measures**

**Primary outcomes**

[Define in advance which primary and secondary outcomes are of interest. Keep the total number of outcomes as small as possible. Choose outcomes that are relevant to stakeholders such as consumers, health professionals and policy makers. Avoid trivial outcomes and biochemical, interim and process outcomes, but consider the importance of resource-use outcomes. The Cochrane Airways Group suggest including around seven outcomes in total. Define in advance details of what are acceptable outcome measures (e.g. diagnostic criteria, scales, or composite outcomes). Define in advance how you will select outcome measures when there are several possible measures (e.g. multiple definitions, assessors, or scales) and time points of interest. Include a rationale to explain why you have chosen the primary and secondary outcomes listed].

* Serious adverse events.

**Secondary outcomes**

* Adverse events/side effects.

Reporting one of more of the outcomes listed here in the trial is not an inclusion criterion for the review.

[You may not use reporting of outcomes in trials as an inclusion criterion unless you have a very good reason and provide a rationale within the protocol].

**Search methods for identification of studies**

**Electronic searches**

We will identify trials from the Cochrane Airways Group's Specialised Register (CAGR), which is maintained by the Trials Search Co-ordinator for the Group. The Register contains trial reports identified through systematic searches of bibliographic databases including the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, CINAHL, AMED, and PsycINFO, and handsearching of respiratory journals and meeting abstracts (please see Appendix 1 for further details). We will search all records in the CAGR using the search strategy in Appendix 2.

[Contact Liz Stovold (estovold@sgul.ac.uk), the Cochrane Airways Group's Trials Search Co-ordinator, to discuss your search terms before submitting your protocol for editorial approval].

We will also conduct a search of ClinicalTrials.gov (www.ClinicalTrials.gov) and the WHO trials portal (www.who.int/ictrp/en/). We will search all databases from their inception to the present, and we will impose no restriction on language of publication.

**Searching other resources**

We will check reference lists of all primary studies and review articles for additional references. We will search relevant manufacturers' websites for trial information.

We will search for errata or retractions from included studies published in full-text on PubMed (www.ncbi.nlm.nih.gov/pubmed) and report the date this was done within the review.

**Data collection and analysis**

**Selection of studies**

Two review authors [or more; initials here] will independently screen titles and abstracts for inclusion of all the potential studies we identify as a result of the search and code them as 'retrieve' (eligible or potentially eligible/unclear) or 'do not retrieve'. We will retrieve the full-text study reports/publication and two review authors [or more; initials here] will independently screen the full-text and identify studies for inclusion, and identify and record reasons for exclusion of the ineligible studies. We will resolve any disagreement through discussion or, if required, we will consult a third person [initials here]. We will identify and exclude duplicates and collate multiple reports of the same study so that each study rather than each report is the unit of interest in the review. We will record the selection process in sufficient detail to complete a PRISMA flow diagram and 'Characteristics of excluded studies' table.

Data extraction and management

We will use a data collection form for study characteristics and outcome data which has been piloted on at least one study in the review. One review author [or more; initials here] will extract study characteristics from included studies [it is highly desirable, but not mandatory, for this process to be done in duplicate]. We will extract the following study characteristics.

* Methods: study design, total duration of study, details of any 'run in' period, number of study centres and location, study setting, withdrawals, and date of study.
* Participants: N, mean age, age range, gender, severity of condition, diagnostic criteria, baseline lung function, smoking history, inclusion criteria, and exclusion criteria.
* Interventions: intervention, comparison, concomitant medications, and excluded medications.
* Outcomes: primary and secondary outcomes specified and collected, and time points reported.
* Notes: funding for trial, and notable conflicts of interest of trial authors.

Two review authors [or more; initials here] will independently extract outcome data from included studies. We will note in the 'Characteristics of included studies' table if outcome data was not reported in a usable way. We will resolve disagreements by consensus or by involving a third person [initials here]. One review author [initials here] will transfer data into the Review Manager (RevMan 2014) file. We will double-check that data is entered correctly by comparing the data presented in the systematic review with the study reports. A second review author [initials here] will spot-check study characteristics for accuracy against the trial report.

[The contact person will have received a standard data collection form in the original email from the Managing Editor which you may adapt for use in your specific review].

**Assessment of risk of bias in included studies**

[Note: the following sections refer to individually randomised trials. If cluster-randomised or crossover trials are included, you should use appropriate methods for assessing bias in these designs. See Handbook sections 16.3.2 and 16.4.3].

Two [or more] review authors (insert initials here) will independently assess risk of bias for each study using the criteria outlined in the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2011). We will resolve any disagreements by discussion or by involving another author (insert initials here). We will assess the risk of bias according to the following domains.

* Random sequence generation.
* Allocation concealment.
* Blinding of participants and personnel.
* Blinding of outcome assessment.
* Incomplete outcome data.
* Selective outcome reporting.
* Other bias.

We will grade each potential source of bias as high, low or unclear and provide a quote from the study report together with a justification for our judgment in the 'Risk of bias' table. We will summarise the risk of bias judgements across different studies for each of the domains listed. We will consider blinding separately for different key outcomes where necessary (e.g. for unblinded outcome assessment, risk of bias for all-cause mortality may be very different than for a patient reported pain scale). Where information on risk of bias relates to unpublished data or correspondence with a trialist, we will note this in the 'Risk of bias' table.

When considering treatment effects, we will take into account the risk of bias for the studies that contribute to that outcome.

**Assesment of bias in conducting the systematic review**

We will conduct the review according to this published protocol and report any deviations form it in the 'Differences between protocol and review' section of the systematic review.

**Measures of treatment effect**

We will analyse dichotomous data as odds ratios [if you wish to use risk ratio/risk difference you must provide a reason/justification] and continuous data as mean difference or standardised mean difference. We will enter data presented as a scale with a consistent direction of effect.

We will undertake meta-analyses only where this is meaningful i.e. if the treatments, participants and the underlying clinical question are similar enough for pooling to make sense.

We will narratively describe skewed data reported as medians and interquartile ranges.

Where multiple trial arms are reported in a single trial, we will include only the relevant arms. If two comparisons (e.g. drug A versus placebo and drug B versus placebo) are combined in the same meta-analysis, we will halve the control group to avoid double-counting.

**Unit of analysis issues**

[You should describe special issues in the analysis of studies with non-standard designs here (e.g. crossover or cluster-randomised trials or where adjusted results are reported)].

**Dealing with missing data**

We will contact investigators or study sponsors in order to verify key study characteristics and obtain missing numerical outcome data where possible (e.g. when a study is identified as abstract only). Where this is not possible, and the missing data are thought to introduce serious bias, we will explore the impact of including such studies in the overall assessment of results by a sensitivity analysis.

**Assessment of heterogeneity**

We will use the I² statistic to measure heterogeneity among the trials in each analysis. If we identify substantial heterogeneity we will report it and explore possible causes by prespecified subgroup analysis.

**Assessment of reporting biases**

If we are able to pool more than 10 trials, we will create and examine a funnel plot to explore possible small study and publication biases.

[You may need to consult a statistician and the Handbook section 10.4 if you intend to explore possible publication bias].

**Data synthesis**

We will use a random-effect model and perform a sensitivity analysis with a fixed model.

[if you plan to deviate from this, justify your choice of model].

**Summary of findings table**

We will create a 'Summary of findings' table using the following outcomes [List up to seven outcomes, including your primary outcomes, adverse events and all patient important outcomes or those that are most important to guideline setters and people making decisions about healthcare]. We will use the five GRADE considerations (study limitations, consistency of effect, imprecision, indirectness and publication bias) to assess the quality of a body of evidence as it relates to the studies which contribute data to the meta-analyses for the prespecified outcomes. We will use methods and recommendations described in Section 8.5 and Chapter 12 of the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2011) using GRADEpro software. We will justify all decisions to down- or up-grade the quality of studies using footnotes and we will make comments to aid reader's understanding of the review where necessary.

[The Cochrane Airways Group recommends that you create your 'Summary of findings' table AFTER you have entered data into RevMan (RevMan 2014), written up your results and conducted the risk of bias assessment, but BEFORE you write up your discussion, abstract and conclusions. This will give you the opportunity to think about how the risk of bias in the studies contributing to each outcome affect the mean treatment effect and your confidence in it].

**Subgroup analysis and investigation of heterogeneity**

Please note that all subgroup/sensitivity analyses will need to be dichotomised and the splits specified (e.g. age [18 years and younger vs older than 18 years]) unless you have a reason not to in which case please state reason.

We plan to carry out the following subgroup analyses.

We will use the following outcomes in subgroup analyses.

We will use the formal test for subgroup interactions in Review Manager (RevMan 2014).

[You would usually restrict subgroup analysis to the review’s primary outcomes].

**Sensitivity analysis**

We plan to carry out the following sensitivity analyses.

**Acknowledgements**

[Acknowledge here people who helped you in writing the protocol. You should acknowledge financial sources of support (funding, host institution) in the section 'sources of support' below].

The background and methods section of this protocol is based on a standard template used by Cochrane Airways Group

**Contributions of authors**

J. Bloggs: describe conflict...

C. Darwin: none known.

[Describe here the contribution of each author in the protocol]. See http://www.cochrane.org/organisational-policy-manual/appendix-5-commerical-sponsorship-policy

**Declarations of interest**

[The contact person should check that any relevant conflicts of interest reported in the electronic conflict of interest (COI) forms signed by your author team are consistent with what is reported here].

*You must add something to Sources of Support (below) to acknowledge who funded you, or your employer. If no funding or support was received, you may write "The authors declare that no funding was received for this systematic review".*

**Additional references**

GRADEpro

* GRADEpro [Computer program]. Brozek J, Oxman A, Schünemann H. Version 3.2 for Windows. 2008.

Higgins 2011

* Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1 [updated March 2011]. The Cochrane Collaboration, 2011.

RevMan 2014

* Review Manager (RevMan) [Computer program]. Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014.