

# TEMPLATE PROTOCOL FOR PAPAS

This guidance document contains information regarding the Cochrane Collaboration's mandatory MECIR Conduct and Reporting Standards and editorial suggestions specific to PaPaS, to support the development of your protocol.  
See comments below.

## Protocol information

**Review type:** Intervention

### Authors

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Citation example: Hobson A. TEMPLATE PROTOCOL FOR PAPAS. Cochrane Database of Systematic Reviews , Issue . Art. No.: . DOI: .

- Check that authors are listed in the correct order, with the correct affiliations, and have agreed to the order in which they are listed.
- Do not add any authors or amend contact details in RevMan: new authors and new contact details must be added centrally by the CRG. Email [anna.hobson@ndcn.ox.ac](mailto:anna.hobson@ndcn.ox.ac) for assistance.

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### Dates

**Assessed as Up-to-date:** Not provided  
**Date of Search:** Not provided  
**Next Stage Expected:** Not provided  
**Protocol First Published:** Not specified  
**Review First Published:** Not specified  
**Last Citation Issue:** Not specified

- Complete the 'Date next stage expected' field, estimating when the Cochrane Review will be completed (no later than 2 years from anticipated publication of the protocol).
- Do not insert any other dates.

### What's new

Date	Event	Description
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- No need to add anything here.

### History

Date	Event	Description
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## Abstract

Background

Objectives

Search methods

Selection criteria

Data collection and analysis

## Main results

## Authors' conclusions

## Plain language summary

[Plain language title]

[Summary text]

## Background

**This guidance document contains information regarding the Cochrane Collaboration's mandatory MECIR Conduct and Reporting Standards (also visible in the right-hand viewing pane in RevMan 5.3), and editorial suggestions specific to PaPaS**

Information has been added in individual sections under headings/sub-headings, or as yellow notes, for your attention. Comments can be deleted once your first draft is ready for submission.

Please ensure you refer to the [MECIR Standards](#), the [Cochrane Style Guide](#) and the [Cochrane Handbook](#) during the development of your protocol. If these minimum required standards are not met, you will be asked to submit a revised version which will prolong the editorial process.

First draft protocols are expected to be submitted for editorial approval **within 6 months** of registering the title. Protocols are expected to be published within 12 months of registration. PaPaS reserves the right to withdraw titles that greatly exceed the submission deadlines.

The PaPaS website contains more useful links and guidance in our Resource Hub [here](#), as well as screenshots ([here](#)) to help with some common queries you may have as you get started. Our '[Author and Referee Guide](#)' may also help.

For further training and support:

- Find your local Cochrane Centre [here](#).
- Visit the Cochrane Training website [here](#).
- Online learning is available on the Cochrane website [here](#) and videos are available on YouTube [here](#).
- For technical hitches, please see the Help section in RevMan, or visit the [IKMD website](#) here.

### ***A few important points to remember:***

- Always check your protocol in and out using RevMan. You can create as many versions as necessary. We strongly recommend not saving files locally, as files can get lost and version control can be disrupted. 'Checking in' via RevMan ensures your latest draft is always available to everyone.
- Style: use the future tense and active voice.
- All the authors listed must see and approve this version and take full responsibility for the accuracy of the contents. Ensure all affiliation details are correct (see yellow note above).
- Activate the relevant headings in RevMan and complete each section.
- Complete a validation check in RevMan (File menu > Reports > Validation report), and make corrections where possible.
- Complete a spell check in RevMan (Tools menu > Check spelling).
- Proofread the Cochrane Protocol carefully in accordance with the [Cochrane Style Guide Basics](#).
- If additional subheadings have been added, select the appropriate Heading Style using the drop down box on the RevMan toolbar.
- Use either UK or US English consistently throughout the review (e.g. either 'randomised' or 'randomized').
- Explain all acronyms and abbreviations in full on first use (e.g. World Health Organization (WHO)).
- Spell in full all numbers at the beginning of a sentence, and those up to and including nine. For numbers 10 and higher, and all numbers in tables, please use numerals.
- Include a space before and after each unit of measurement or mathematical symbol (e.g. 5 mL, P = 0.03).
- Back up all key supporting statements with references and avoid the use of plagiarized text. The editorial team will use plagiarism detection software upon receipt of your first draft, in accordance with Cochrane's [Plagiarism Policy](#). You can check references are correctly linked using the 'Find and Mark Links' tool in RevMan.
- Before accepting our standard suggested wording, please check that you agree with the statements.

## Background

Suggested wording for this section, to acknowledge the use of PaPaS 'template' text if applicable: This protocol is partly based on suggested wording from the Pain, Palliative and Supportive Care Review Group (PaPaS CRG).

- Use the sub-headings below to complete the 'Background' section of your protocol

### Description of the condition

- Provide a concise description of the condition or problem addressed by the review question, including how it occurs, where it occurs, who is affected (including high risk groups, vulnerable/disadvantaged groups), diagnosis, symptoms and consequences.

### Description of the intervention

- Describe the intervention, including for whom it is intended, its context in usual practice, comparison interventions, the

treatment regimen or intervention components, and known adverse effects.

- Describe any likely differences in the use or outcomes of the intervention for specific populations (e.g. children, vulnerable/disadvantaged groups), and define those populations where necessary.

### How the intervention might work

- Provide a concise description of the definition of the intervention and how it might work.

### Why it is important to do this review

- Provide a concise description of why it is important to do this review.

## Objectives

Suggested wording: 'To assess the effects of [intervention or comparison] for [health problem] for/in [types of people, disease or problem and setting if specified]'

## Methods

### Criteria for considering studies for this review

#### *Types of studies*

##### Mandatory MECIR Conduct Standards for protocols

- C9: Define in advance the eligibility criteria for study designs in a clear and unambiguous way, with a focus on features of a study's design rather than design labels.
- C10: State that you will include randomized trials as eligible for inclusion in the review if they are feasible for the interventions and outcomes of interest.
- C12: State that you will include studies irrespective of their publication status, or explicitly justify your decision if this will be restricted.

Suggested wording: We will include studies if they are randomised controlled trials (RCTs) with double-blind assessment of participant outcomes. We require full journal publication, with the exception of online clinical trial results; summaries of otherwise unpublished clinical trials and abstracts with sufficient data for analysis. We will exclude studies that were non-randomised, studies of experimental pain, case reports and clinical observations.

#### *Types of participants*

##### Mandatory MECIR Conduct Standard for protocols

- C5: Define in advance the eligibility criteria for participants in the studies.

Suggested wording: Studies will include [adults] aged [18 years and above].

#### *Types of interventions*

Suggested wording: '[Drug] at [any dose], by [any route], administered for [the relief of neuropathic pain] and [compared to placebo or any active comparator].'

#### *Types of outcome measures*

##### Mandatory MECIR Conduct Standards for protocols

- C8: Explain whether outcomes listed under 'Criteria for considering studies for this review' are used as criteria for including studies (rather than as a list of the outcomes of interest within whichever studies are included).
- C14: State which outcomes are primary and secondary, using the sub-headings below.
- Select a maximum of seven important outcomes, including adverse effects, to be included in the Summary of findings table(s) in the full review (see Cochrane Handbook [Section 11.5.2](#) ).
- Suggested wording: We will include a 'Summary of findings' table as set out in the PaPaS author guide ([AUREF 2012](#)) and recommended in the Cochrane Handbook, chapter 4.6.6 ([Higgins 2011](#)). The 'Summary of findings' table will include outcomes of [a, b, and c].
- Suggested wording, based on recommendation from the Cochrane Drugs and Alcohol Group:

### Grading of evidence

This section is taken from the Cochrane Drugs and Alcohol Group recommended text. The overall quality of the evidence for each outcome will be assessed using the GRADE system ([GRADEpro 2008](#)) and presented in the 'Summary of findings' tables, to present the main findings of a review in a transparent and simple tabular format. In particular, we will include key information concerning the quality of evidence, the magnitude of effect of the interventions examined, and the sum of available data on the main outcomes.

The GRADE system uses the following criteria for assigning grade of evidence:

- High = further research is very unlikely to change our confidence in the estimate of effect
- Moderate = further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
- Low = further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to

- change the estimate
- Very low = any estimate of effect is very uncertain

We will decrease grade if:

- Serious (-1) or very serious (-2) limitation to study quality
- Important inconsistency (-1)
- Some (-1) or major (-2) uncertainty about directness
- Imprecise or sparse data (-1)
- High probability of reporting bias (-1)

We will increase grade if:

- Strong evidence of association - significant relative risk of  $>2$  ( $<0.5$ ) based on consistent evidence from two or more observational studies, with no plausible confounders (+1)
- Very strong evidence of association - significant relative risk of  $>5$  ( $<0.2$ ) based on direct evidence with no major threats to validity (+2)
- Evidence of a dose response gradient (+1)
- All plausible confounders would have reduced the effect (+1)

### Primary outcomes

- List your primary outcome(s) here, and define acceptable ways of measuring them, e.g. numerical rating scale (NRS), visual analogue scale (VAS)
- Other

### Secondary outcomes

- Adverse events
- Other

### Search methods for identification of studies

[This can be left blank]

#### Electronic searches

- Suggested wording:

We will search the following databases without language restrictions.

- The Cochrane Central Register of Controlled Trials (CENTRAL) (via the Cochrane Library)
- MEDLINE (via Ovid)
- EMBASE (via Ovid)
- [Other]

Medical subject headings (MeSH) or equivalent and text word terms will be used. There will be no language restrictions. Searches will be tailored to individual databases. The search strategy for MEDLINE is in [Appendix 1](#). [Ensure this links correctly]

Mandatory MECIR Conduct Standard for protocols

- C35 Justify the use of any restrictions in the search strategy on publication date, publication format or language.

#### Searching other resources

- Suggested wording: We will search the metaRegister of controlled trials (mRCT) ([www.controlled-trials.com/mrct](http://www.controlled-trials.com/mrct)), clinicaltrials.gov ([www.clinicaltrials.gov](http://www.clinicaltrials.gov)) and the WHO International Clinical Trials Registry Platform (ICTRP) (<http://apps.who.int/trialsearch/>) for ongoing trials. In addition, reference lists of reviews and retrieved articles will be checked for additional studies and citation searches will be performed on key articles. Experts in the field will be contacted for unpublished and ongoing trials. Authors will be contacted where necessary for additional information.

### Data collection and analysis

[This can be left blank]

#### Selection of studies

- Suggested wording: Two review authors [XX, YY] will independently determine eligibility by reading the abstract of each study identified by the search. Independent review authors will eliminate studies that clearly do not satisfy inclusion criteria, and obtain full copies of the remaining studies. Two review authors [XX, ZZ] will read these studies independently to select relevant studies, and in the event of disagreement, a third author will adjudicate [YY]. We will not anonymise the studies in any way before assessment. We will include a Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow chart in the full review which will show the status of identified studies ([Moher 2009](#)) as recommended in Part 2, Section 11.2.1 of the Cochrane Handbook ([Higgins 2011](#)). We will include studies in the review irrespective of whether measured outcome data are reported in a 'usable' way.

#### Data extraction and management

- Suggested wording: Two review authors [XX, YY] will independently extract data using a standard form and check for

agreement before entry into Review Manager ([RevMan 2012](#)). We will include information about [a, b, and c]. We will 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 collect characteristics of the included studies in sufficient detail to populate a table of 'Characteristics of included studies' in the full review.

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

- Suggested wording:

This section is taken from the PaPaS template for protocols.

Two authors [XX, ZZ] will independently assess risk of bias for each study, using the criteria outlined in the Cochrane Handbook for Systematic Reviews of Interventions ([Higgins 2011](#)) and adapted from those used by the Cochrane Pregnancy and Childbirth Group, with any disagreements resolved by discussion. We will complete a 'Risk of bias' table for each included study using the Risk of bias tool in RevMan ([RevMan 2012](#)).

We will assess the following for each study:

- Random sequence generation (checking for possible selection bias). We will assess the method used to generate the allocation sequence as: low risk of bias (any truly random process, e.g. random number table; computer random number generator); unclear risk of bias (method used to generate sequence not clearly stated). Studies using a non-random process (e.g. odd or even date of birth; hospital or clinic record number) will be excluded.
- Allocation concealment (checking for possible selection bias). The method used to conceal allocation to interventions prior to assignment determines whether intervention allocation could have been foreseen in advance of, or during recruitment, or changed after assignment. We will assess the methods as: low risk of bias (e.g. telephone or central randomisation; consecutively numbered sealed opaque envelopes); unclear risk of bias (method not clearly stated). Studies that do not conceal allocation (e.g. open list) will be excluded.
- Blinding of outcome assessment (checking for possible detection bias). We will assess the methods used to blind study participants and outcome assessors from knowledge of which intervention a participant received. We will assess the methods as: low risk of bias (study states that it was blinded and describes the method used to achieve blinding, e.g. identical tablets; matched in appearance and smell); unclear risk of bias (study states that it was blinded but does not provide an adequate description of how it was achieved). Studies that were not double-blind will be excluded.
- Incomplete outcome data (checking for possible attrition bias due to the amount, nature and handling of incomplete outcome data). We will assess the methods used to deal with incomplete data as: low risk (< 10% of participants did not complete the study and/or used 'baseline observation carried forward' analysis); unclear risk of bias (used 'last observation carried forward' analysis); high risk of bias (used 'completer' analysis).
- Size of study (checking for possible biases confounded by small size). We will assess studies as being at low risk of bias ( $\geq 200$  participants per treatment arm); unclear risk of bias (50 to 199 participants per treatment arm); high risk of bias ( $< 50$  participants per treatment arm).

### **Measures of treatment effect**

- Describe a strategy for measuring treatment effect in the full review, eg. We will/We plan to...

### **Unit of analysis issues**

- Describe a strategy for addressing unit of analysis issues in the full review, eg. We will/We plan to...

### **Dealing with missing data**

- Describe a strategy for dealing with missing data and following intention-to-treat principles in the full review, if appropriate, eg. We will/We plan to...

### **Assessment of heterogeneity**

- Describe a strategy for assessing heterogeneity, eg. We will/We plan to...

### **Assessment of reporting biases**

- Describe a strategy for assessing reporting biases, eg. We will/We plan to...

### **Data synthesis**

Mandatory MECIR Conduct Standards for protocols

- C21 State the methods you plan to use to synthesize the results of the included studies, including whether a quantitative synthesis is planned, how heterogeneity will be assessed, choice of effect measure (e.g. odds ratio, risk ratio, risk difference or other for dichotomous outcomes), and methods for meta-analysis (e.g. inverse variance or Mantel Haenszel, fixed-effect or random-effects model), eg. We will/We plan to...
- C63: State that you will undertake (or display) a meta-analysis only if participants, interventions, comparisons and outcomes can be judged to be sufficiently similar to ensure an answer that is clinically meaningful, eg. We will/We plan to...
- Include a reference to the software you plan to use for analyses, eg. [RevMan 2012](#)

### **Subgroup analysis and investigation of heterogeneity**

Mandatory MECIR Conduct Standards for protocols

- C22: Explicitly pre-define potential effect modifiers (e.g. for subgroup analyses); restrict these in number; and provide rationale for each.
- C68: State which formal statistical test will be used to compare subgroup analyses.

## Results

### Description of studies

#### *Results of the search*

#### *Included studies*

#### *Excluded studies*

### Risk of bias in included studies

#### *Allocation (selection bias)*

#### *Blinding (performance bias and detection bias)*

#### *Incomplete outcome data (attrition bias)*

#### *Selective reporting (reporting bias)*

#### *Other potential sources of bias*

### Effects of interventions

## Discussion

### Summary of main results

### Overall completeness and applicability of evidence

### Quality of the evidence

### Potential biases in the review process

### Agreements and disagreements with other studies or reviews

## Authors' conclusions

### Implications for practice

### Implications for research

## Acknowledgements

- Acknowledge those people who contributed to the protocol but are not named as authors, and include the reasons for acknowledging each person. Ensure permission has been granted from all the people named to include them in this section.
- All PaPaS reviews must contain the following wording:

Cochrane Review Group funding acknowledgement: The National Institute for Health Research (NIHR) is the largest single funder of the Cochrane PaPaS Group. Disclaimer: The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the NIHR, National Health Service (NHS) or the Department of Health.

## Contributions of authors

- Describe each author's contribution to the design and development of the Cochrane Protocol, e.g. XX developed the search strategy, YY wrote the Background section, ZZ will be responsible for data extraction in the full review. All authors will be responsible for completing the protocol, full review, and updating the review in future.

## Declarations of interest

- Must be completed separately for each author, noting present or past affiliations or other involvement in any organization or entity with an interest in the review's findings that might lead to a real or perceived conflict of interest, including whether authors are investigators on studies likely to be included in the review. If no potential conflicts are identified for a particular author, please state e.g. 'XY has no known conflicts of interest to declare that are relevant to the development of this protocol'.
- The DoI statements must be identical to the declarations in each electronic 'Conflicts of Interest' form, which will be circulated by the editorial team upon receipt of the first draft.
- The Cochrane Collaboration has recently updated its Commercial Sponsorship Policy (2014). Please ensure this section is fully compliant. See the [policy in full online](#) or contact PaPaS for further information.

## Commercial funding of reviews or authors

[Taken from <http://www.cochrane.org/organisational-policy-manual/appendix-5-commercial-sponsorship-policy>, accessed 10/10/2014.]

*The intent of clauses 1-5 is to ensure the independence of Cochrane reviews by making sure there is no bias associated with commercial conflicts of interest in the conduct of Cochrane reviews.*

- 1. Cochrane reviews cannot be funded or conducted by commercial sponsors or commercial sources with a real or potential vested interest in the findings of a specific review.*
- 2. Individuals who are employed by a company that has a real or potential financial interest in the outcome of the review (including but not limited to drug companies or medical device manufacturers), or who hold or have applied for a patent related to the review are prohibited from being Cochrane review authors. In most cases, employment would be characterised by the affiliation statement made by the author at the title registration, protocol or review stage of the review. Any questions about what constitutes "employment by a company with a financial interest" should be referred to the funding arbiter.*
- 3. Authors who in the last 3 years have received financial support from commercial sponsors or sources who have a real or potential financial interest in the findings of the review, but who are not covered by the restriction above should declare these interests at the earliest possible stage in the editorial process. Such financial support may include remuneration from a consultancy, grants, fees, fellowships, support for sabbaticals, royalties, stocks from pharmaceutical companies, advisory board membership or otherwise. In such cases, at the funding arbiter's discretion, and only where a majority of the review authors and lead author have no relevant COIs, it may be possible for an author who has a declared interest as listed in the previous sentence to be a Cochrane review author.*
- 4. Editors with conflicts of interest with a given product/drug/non-drug intervention should not undertake peer review or be a contact editor, or provide sign-off on a review that involves that product, drug, non-drug intervention or a competing intervention. Co-ordinating Editors with conflicts of interest should assign the relevant review to another editor within their group. Editors are prohibited from being employees of a pharmaceutical company or medical device manufacturer.*
- 5. Peer reviewers should be asked to declare COI using the ICMJE framework.*

## Differences between protocol and review

### Published notes

### Characteristics of studies

#### Characteristics of included studies

*Footnotes*

#### Characteristics of excluded studies

*Footnotes*

#### Characteristics of studies awaiting classification

*Footnotes*

#### Characteristics of ongoing studies

*Footnotes*

## Summary of findings tables

### Additional tables

### References to studies

#### Included studies

#### Excluded studies

#### Studies awaiting classification

#### Ongoing studies

### Other references

#### Additional references

##### **AUREF 2012**

Cochrane Pain, Palliative and Supportive Care Group. PaPaS Author and Referee Guidance. <http://papas.cochrane.org/papas-documents> (accessed ADD DATE).

##### **GRADEpro 2008**

GRADEpro [Computer program]. Jan Brozek, Andrew Oxman, Holger Schünemann. Version 3.2 for Windows, 2008.

##### **Higgins 2011**

Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions. Available from [www.cochrane-handbook.org](http://www.cochrane-handbook.org) edition. Vol. 5.1.0. The Cochrane Collaboration, 2009 [Updated 2011].

##### **Moher 2009**

Moher D, Liberati A, Tetzlaff J, Altman DG, the PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Medicine 2009;6(7):e1000097.

### ***RevMan 2012***

Review Manager [Computer program]. Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2012.

**Other published versions of this review**

**Classification pending references**

**Data and analyses**

**Figures**

**Sources of support**

**Internal sources**

- No sources of support provided

**External sources**

- No sources of support provided

**Feedback**

**Appendices**

**1 Add your search strategy here**

Check link to Appendix 1 in [Electronic searches](#).