



# protocol\_template\_for\_intervention\_review

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<sup>1</sup>Systematic Review Work Shop-Peer Support Group

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?? is the guarantor. ?? drafted the manuscript.

All authors contributed to the development of the selection criteria, the risk of bias assessment strategy and data extraction criteria.

?? developed the search strategy. ?? provided statistical expertise. ?? provided expertise on ?. All authors read, provided feedback and approved the final manuscript.

Support: [REDACTED]

## 1. Introduction

## 2. Research question

P:

I:

C:

O:

## 3. Method

### 3.1 Protocol

We used a systematic review protocol template. [REDACTED] [REDACTED] We followed the Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 for preparing this protocol. <sup>1</sup> [REDACTED] We will publish this protocol in protocols.io

(<https://www.protocols.io/>).

### 3.2 Inclusion criteria of the articles for the review

#### 3.2.1 Type of studies

We will include randomized controlled trials that assess ??????. We will not apply language or country restrictions. We will include all papers including published, unpublished articles, abstract of conference and letter.

We will exclude ??????. We will not exclude studies based on the observation period or publication year.

#### 3.2.2 Study participants

??????

Inclusion criteria:

??????

Exclusion criteria:

??????

#### 3.2.3 Intervention

#### 3.2.4 Control

### 3.3 Type of outcomes

#### 3.3.1 Primary outcomes

1.

Definition:

Period:

2.

Definition:

Period:

3.

Definition:

Period:

#### 3.3.2 Secondary outcomes

1.

Definition:

Period:

2.

Definition:

Period:

#### 3. All adverse events

Definition: definition of adverse events are set by original authors.

Incidence proportion of all adverse events

Period: during follow up period

### 3.4 Search method

#### 3.4.1 Electronic search

We will search the following databases:

1. the Cochrane Central Register of Controlled Trials (CENTRAL);
2. MEDLINE via PubMed;
3. EMBASE via ProQuest Dialog;

See Appendix 1, 2, and 3 for the search strategies.

#### 3.4.2 Other resources

We will also search the following databases for ongoing or unpublished trials:

1. the World Health Organization International Clinical Trials Platform Search Portal (ICTRP);
2. ClinicalTrials.gov;

See Appendix 4, 5 for the search strategies.

We will check the reference lists of studies, including international guidelines ?? as well as the reference lists of eligible studies and articles citing eligible studies. We will ask the authors of original studies for unpublished or additional data.

### 3.5 Data collection and analysis

#### 3.5.1 Selection of the studies

Two independent reviewers (??) will screen titles and abstracts, followed by the assessment of the eligibility based on the full texts.[\[6\]](#) We will contact original authors if relevant data is missing. Disagreements between the two reviewers will be resolved by discussion, and if this fails, a third reviewer will act as an arbiter (??).

#### 3.5.2 Data extraction and management

Two reviewers (??) will perform independent data extraction of the included studies using standardized data collection form. We will use a pre-checked form using 10 randomly selected studies.

The form will include the information on [study design, study population, interventions and outcomes](#)[\[7\]](#). Any disagreements will be resolved by discussion, and if this fails, a third reviewer will act as an arbiter (??).

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

Two reviewers (??) will evaluate the risk of bias independently using the Risk of Bias 2.<sup>2</sup> Disagreements between the two reviewers will be discussed, and if this fails, a third reviewer (??) will be acting as an arbiter, if necessary.

#### 3.7 Measures of treatment effects

We will pool the relative risk ratios and the 95% confidence intervals (CIs) for the following binary variables:

We will pool the mean differences and the 95% CIs for the following continuous variables:

If several different scales have been used in the included studies, we will pool the effect estimates using standard mean differences (SMDs)

We will summarize adverse events based on the definition by the original article, but we will not perform meta-analysis..

#### 3.8 Unit of analysis issues

Clustering at the level of the enrolled units in clusterrandomised studies

In dealing with cluster-RCTs, for dichotomous data, we will apply the design effect and calculate effective sample size and number of events using the intracluster correlation coefficient (ICC) among each unit and the average cluster size, as described in Chapter 16.3.5 of the Cochrane Handbook.<sup>3</sup> If the ICC has not been reported, we will use the ICC of a similar study as a substitute. For continuous data, only the sample size will be reduced; means and standard deviation will remain unchanged.<sup>3</sup>

#### Randomised cross-over studies

We will consider only data from the first period.

#### Multiple comparisons

All intervention groups that are relevant to this review will be included.

#### 3.9 Handling of missing data

We will ask not-presented data to the original authors.

##### 3.9.1 Missing outcomes

We will perform the intention-to-treat (ITT) analysis for all dichotomous data as much as possible.

For continuous data, we will not impute missing data based on the recommendation by Cochrane handbook.<sup>3</sup> We will perform meta-

analysis about the available data in the original study.

### 3.9.2 Missing statistics

When original studies only report standard error or p-value, we will calculate the standard deviation based on the method by Altman.<sup>4</sup> If we don't know these values when we contact the authors, standard deviation will be calculated by confidence interval and t-value based on the method by Cochrane handbook<sup>3</sup>, or validated method.<sup>4</sup> Validity of these methods will be analyzed by sensitivity analysis.

### 3.10 Assessment of heterogeneity

We will evaluate the statistical heterogeneity by visual inspection of the forest plots and calculating the I<sup>2</sup> statistic (I<sup>2</sup> values of 0% to 40%: might not be important; 30% to 60%: may represent moderate heterogeneity; 50% to 90%: may represent substantial heterogeneity; 75% to 100%: considerable heterogeneity). When there is substantial heterogeneity (I<sup>2</sup> > 50%), we will assess the reason of the heterogeneity. Cochrane Chi<sup>2</sup> test (Q-test) will be performed for I<sup>2</sup> statistic, and P value less than 0.10 will be defined as statistically significant.

### 3.11 Assessment of reporting bias

We will search the clinical trial registry system (ClinicalTrials.gov and ICTRP) and will perform extensive literature search for unpublished trials. We will assess the potential publication bias by visual inspection of the funnel plot. Egger test will be performed as well. We will not conduct the test when we find less than 10 trials or trials which have similar sample size. We will assess the potential publication bias by visual inspection of the funnel plot

### 3.12 Meta-analysis

Meta-analysis will be performed using Review Manager software (RevMan 5.4). We will use a random-effects model.

### 3.13 Subgroup analysis

To elucidate the influence of effect modifiers on results, we will evaluate the subgroup analyses of the primary outcomes on the following factors when sufficient data are available.

1. (For participants) ??[8]
2. (For intervention) ??

### 3.14 Sensitivity analysis

We will undertake the following sensitivity analyses for the primary outcomes to assess whether the results of the review are robust to the decisions made during the review process.

1. Exclusion of studies using imputed statistics.
2. Missing participants: verify the robustness of the results by seeking informative missingness odds ratios.<sup>5</sup>
3. Only the participants who complete the study with complete data

## 4. Summary of findings table

Summary of findings table will be made for the following outcome based on the Cochrane handbook.<sup>3</sup>

We will include grading to evaluate the quality of evidence based on the GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach for each Summary of findings table.<sup>6</sup>

1. ??

## 5. Conflict of Interest

The authors declare no conflicts of interests.

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Appendix 1: CENTRAL search strategy

Appendix 2: MEDLINE (via PubMed) search strategy

Appendix 3: EMBASE (via ProQuest Dialog) search strategy

Appendix 4: ICTRP search strategy

Appendix 5: ClinicalTrials.gov search strategy  
 Condition or disease:  
 Intervention:

[1]RCT"efficacy"  
  
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC351867/>

[2]  
 self funding

[3]protocols.io

[TY4]

[5]citationMendeley

[6]3two of three independent

[7][7]

[8]A vs. B