Protocol of meta-analysis

Content

I. Introduction

The University of Pécs Centre for Translational Medicine (UP CTM) wishes to provide all its partners, clinicians and basic researchers, the opportunity to initiate meta-analyses. Workflow is supported by mentors and statisticians. Support covers the whole work of meta-analysis production including

- an education course on how to do a meta-analysis (every September)
- adaptation of clinical questions to the genre of meta-analysis
- set-up of a meta-analysis protocol
- steps search, selection, data collection, and risk of bias assessment
- statistical analysis
- technical and language proofreading of the manuscript

Note that adherence to our quality control system and the deadlines of work is required to guarantee proper methodology, high quality of work, and the transparent co-authorships.

Please, consult our meta-analysis coordinator before starting a new meta-analysis via meta@tm-centre.org

II. Personnel involved

JI	Junior investigator
SI	Senior investigator
JM	Junior mentor
SM	Senior mentor
BIOS	Biostatistician
TP	Technical proofreader
LP	Language proofreader
MC	Meta-analysis coordinator

Provided by your team:

JI: Junior investigator: ideally 2 persons in each project (at least 1 person) whose task is to manage search, selection, and data collection.

SI: Senior investigator: ideally 1 person in each project whose task is to raise questions in PICO format, supervise search, selection, and data collection, interpret results, and publish.

Provided by PTE TMC:

JM: Junior mentor: persons with expertise in search, selection, and data collection for meta-analysis who will provide methodological support and coordinate the workflow to ensure quality. Others will be responsible for the support in setting up meta-analysis protocols (PROSPERO registration) and risk of bias assessment.

SM: Senior mentor: persons with expertise in the writing of the discussion section of manuscripts, their tasks include support in interpretation and publication.

BIOS: Biostatistician: qualified statisticians who are responsible for data analysis and proper interpretation of the results.

TP: Technical proofreader: his task include revision, correction, and approval of methods sections of the manuscript.

LF: Language proofreader: language improvement of the manuscript.

MC: Meta-analysis coordinator: a person who is the link between your centrum and PTE-TMC. His tasks includes the organization of meta-analysis meetings every 4-6 weeks and the annual education course. The coordinator supervises the whole process of work from the phase of question raising to the submission of manuscripts. He is the guarantor of the quality of meta-analyses.

III. Technical support

Provided by your team:

Relevant clinical questions

Provided by PTE-TMC:

Education course on the genre of meta-analysis annually, participation is free of charge.

Consultations: every 4-6 weeks, participants should provide an up-to-date summary of the status of each project in 5 minutes. Questions and problems can be addressed at the meetings.

IV. Schedule of meta-analysis

1. Questions in a proper format, preliminary search, and meta-analysis protocol: Clinical questions should meet PICO format.
   P: population or problem
   I: intervention
   C: comparator
   O: outcome
   I and C can be merged if appropriate. An additional M (method) item can be added to PICO. It is advised to perform a preliminary search to identify the key articles giving the mainstay for the meta-analysis. Identification of previous meta-analyses and systematic reviews are of utmost importance. In the case of promising projects, the protocol of meta-analysis should be registered in PROSPERO *a priori*.
   JI+SI+JM+MC
   Aim: to raise a clinical question in PICO format

2. Search: A systematic search with a tailored query and search filters should be planned in at least 3 databases (MEDLINE, Embase, and Cochrane Trials).
   JI+SI+JM
   Aim: to assemble a pool containing relevant reports

3. Selection: It is recommended using a software to facilitate selection (e.g., EndNote). The first step is the removal of duplicates. Then, a three-phase selection model includes the screening of records against your eligibility criteria by titles, abstracts, and full-texts. Articles meeting the inclusion criteria will be assigned for data extraction. Each step of selection should be performed by two review authors in duplicate.
   JI+SI+JM
   Aim: to gather articles eligible for meta-analysis

4. Data collection: Data should be collected onto pre-defined tables but the use of programs, such as RevMan, is supported, as well. A consultation with a statistician is recommended before executing data collection to ensure that data will be in an appropriate format for analysis.
   JI+SI+JM+BIOS
   Aim: to gather raw data from articles eligible for meta-analysis

5. Risk of bias assessment: Bias of individual studies should be assessed with standard tools (Cochrane Tool for RCTs and Newcastle-Ottawa Scale for cohort, case-control, and cross-sectional studies). Bias assessment involves the screening for potential confounding factors and the enrollment of studies in low-, high-, and uncertain-risk groups. High risk of bias might result in the exclusion of study from analysis or can be a limiting factor of conclusions drawn from results.
   JI+SI+JM
   Aim: to assess risk of bias within studies included

6. Statistical analysis: Results of studies included will be pooled and compared with proper statistics.
   JI+JM+BIOS
   Aim: to obtain results and construct figures

7. Interpretation of results, preparation of the manuscript: It is of utmost importance to identify, assess, and cope with limitations of results which might bias conclusions. If present, statistical heterogeneity should be explored in details. Selection of the target journal belongs to this phase, as well.
   JI+SI+JM+SM+BIOS+TP+LF+MC
   Aim: to draw reliable conclusions and choose a journal for publication

8. Publication: Conditions for publication in Q1 journal:
   a. **relevant clinical question,**
   b. **transparent and reproducible methodology,**
   c. **valid interpretation.**

   JI+SI
   Aim: to publish the results

V. Authors' obligations

Authors are obliged to

- participate in meta-analysis education programs
- participate in regular consultations designed to advance the projects and address problems emerged every 4-6 weeks (at least 1 person per project)
- ensure the consecutive flow of work and reach the milestones
- cooperate with the personnel of PTE TMC assigned for methodological help, regular consultations according to schedule (either in person or via the internet)
- adhere to the co-authorship system and fulfil the obligations of co-authors

VI. Publication rules

- Complete transparency.
- Review authors should nominate the first and last authors of the project, PTE TMC can nominate the co-authors who contributed significantly to the execution of the project. Co-authorship tables will be public and completely transparent.

VII. Collection of useful links

Cochrane Handbook: detailed instruction on how to carry a meta-analysis
http://handbook-5-1.cochrane.org/

PRISMA 2009 Statement: detailed methodology on how to set up a protocol for meta-analysis
http://www.prisma-statement.org/documents/PRISMA%20EandE%202009.pdf

PRISMA 2009 Checklist: list of mandatory items in protocols
http://prisma-statement.org/documents/PRISMA%202009%20checklist.pdf

PRISMA 2009 Flowchart: characteristic figure of workflow (mandatory in meta-analysis)
http://prisma-statement.org/documents/PRISMA%202009%20flow%20diagram.pdf

PROSPERO: a site for registration of protocols
https://www.crd.york.ac.uk/prospero/

Cochrane Risk of Bias Tool for the assessment of RCTs
https://www.ncbi.nlm.nih.gov/books/NBK132494/bin/appf-fm1.pdf

Newcastle-Ottawa Scale for the assessment of bias in non-randomized studies
https://www.ncbi.nlm.nih.gov/books/NBK115843/bin/appe-fm3.pdf

Download of a 30-day trial version of EndNote
http://endnote.com/downloads/30-day-trial

Download of RevMan 5
http://community.cochrane.org/tools/review-production-tools/revman-5/revman-5-download

GRADE approach: to grade the evidence of results in meta-analysis
http://training.cochrane.org/path/grade-approach-evaluating-quality-evidence-pathway

Ranking of scientific journals
http://www.scimagojr.com/