

# Meta-analysis

**Meta-analysis** is a scientific method that collectively **analyzes data from several sub-independent studies**. The goal is the identification and quantification of prevailing trends or finding out the causes of different conclusions of these works.

A simplified procedure for processing a meta-analysis can be summarized in the following steps:

1. definition of research question
2. search for all (even yet unpublished) works
3. selection of all suitable studies
4. data extraction
5. assessment of data homogeneity and efforts in increasing it
6. own meta-analysis

This article is devoted to the application of meta-analyses in medicine, where they are **part of EBM**. However, it is worth mentioning that meta-analyses are also widely used outside the medical field.

## Importance of meta-analyses

If done correctly, a meta-analysis will **provide much more accurate and objective data than individual analyzed studies**, reduce the incidence of false negative results, identify the causes of different conclusions of some studies and allow hypothesis testing. The disadvantage of meta-analyses is that they take a lot of time to prepare. [1][2]

## The process of creating a meta-analysis

Template:Detail

A part of meta-analysis is a systematic review,

### Definition of the problematics

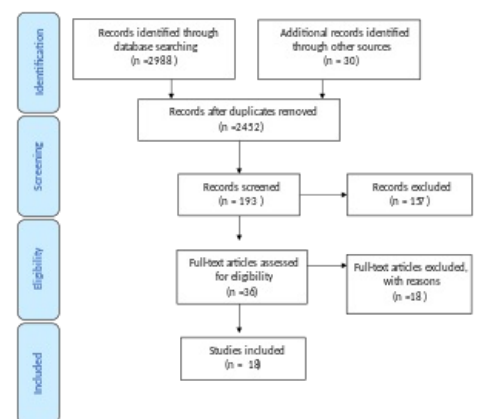
In every meta-analysis, it must be clearly described what problem is being analyzed, which study participants were selected, what the final result is, etc. To clarify these clinical questions, a methodology known as **PICO system**. [3]

### Literature search

To search for relevant studies, library databases are primarily used, which enable the identification of officially published studies. Among the most important are Pubmed (MEDLINE) (<https://pubmed.ncbi.nlm.nih.gov/>), Cochrane (<https://www.cochranelibrary.com/>) and ScienceDirect (<https://www.sciencedirect.com/>).

However, the studies available on these portals make up only a fraction of the scientific material on the given topic – many data are published, for example, within book titles, or some works are not officially published at all. Especially in cases where the proven hypothesis was not confirmed by the work. The creation of a meta-analysis presupposes the acquisition of the largest possible spectrum of relevant data, with which it is subsequently possible to work. That is why it is necessary to search carefully even in sources other than the mentioned main databases. [4]

In order to be able to trace back (and refine or review) the individual steps of identifying relevant studies, it is important to properly record the literature search. The freely available **[PRISMA diagram]**, in which the author of the meta-analysis numerically and verbally describes the details of the search. [5]



Emotional and Psychological Impact of Interpreting for Clients with Traumatic Histories on interpreters - Flow diagram

### Selection of suitable studies

After the identification of individual studies, it is necessary to establish "criteria" (e.g. the minimum number of study participants, their age or study design, etc.), according to which only the most suitable citations for the given meta-analysis are selected. The term **eligibility criteria** is widely used in the English literature.

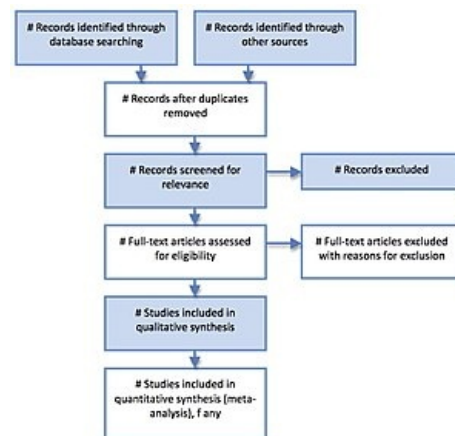
### Methodological biases

The danger that can threaten the credibility of the entire meta-analysis is the influence of systematic and methodological errors. Examples of these errors can be found in a separate article on Sources of error in scientific studies, that cover them in detail. Evaluation methodological bias of individual studies is a crucial step in creating not only meta-analyses, but also systematic reviews [6]. There are a wide range of tools that can be used to assess this bias, here are a few examples:

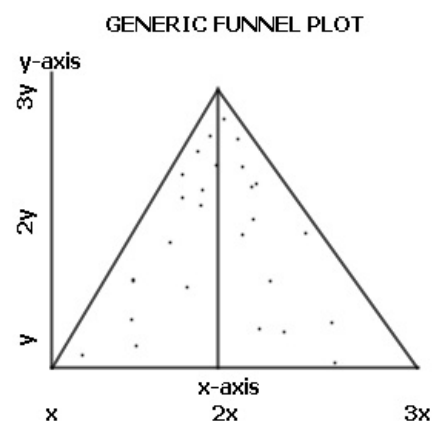
- Cochrane Risk of Bias Tool (<https://www.riskofbias.info>) – the best known and most used tool, it can be applied to different types of studies;
- Newcastle-Ottawa Scale ([http://www.ohri.ca/programs/clinical\\_epidemiology/oxford.asp](http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp)) – applicable only to cohort studies or case studies, it is necessary to set individual parameters according to the nature of the meta-analysis;
- QUADAS-2 (<https://www.bristol.ac.uk/population-health-sciences/projects/quadas/quadas-2/>) – a tool for assessing the quality of studies focusing on accuracy of diagnostic tests;
- AMSTAR ([https://amstar.ca/Amstar\\_Checklist.php](https://amstar.ca/Amstar_Checklist.php)) – very simple tool, used mainly for systematic overviews. [7]

To assess possible methodological (bias) the [https://en.wikipedia.org/wiki/Funnel\\_plot](https://en.wikipedia.org/wiki/Funnel_plot) *funnel plot* is used. The sample size of each primary study is plotted against its effect size. Funnel plots are commonly used in systematic reviews and meta-analyses. If there is no systematic publication bias, then studies with higher precision should be plotted near the mean, and studies with lower precision should be evenly distributed on either side of the mean, so that the distribution of studies in the graph is funnel-shaped. Asymmetry of the funnel plot suggests meta-analysis bias [8].

An example of an asymmetrical and symmetrical funnel chart can be found here: [1] ([https://www.researchgate.net/publication/318995857\\_Met](https://www.researchgate.net/publication/318995857_Met) hodological\_Standards\_for\_Meta-Analyses\_and\_Qualitative\_Systematic\_Re



PRISMA\_flow\_diagram



An example of a funnel plot showing no meta-analysis bias. Each dot represents a study (eg measuring the effect of a particular drug); the "y" axis represents the precision of the study (e.g., the number of patients in the study) and the "x" axis shows the outcome of the study (e.g., the measured average drug effect).

views\_of\_Cardiac\_Prevention\_and\_Treatment\_Studies\_A\_Scientific\_Statement\_From\_the\_American\_Heart\_Association/figures?lo=1)

## Work with the data

Once we have the final studies (properly evaluated and meeting the set criteria), the actual work with the information contained in them follows. First, it is necessary to determine which data are important for our meta-analysis and then extract them. The processing of this data can be done using static programs, e.g. using publicly available and open source ones at OpenMeta(Analyst) (<http://www.cebm.brown.edu/openmeta/>).

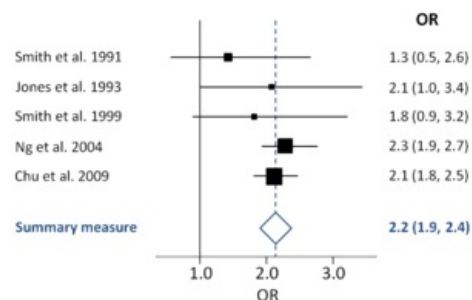
The final interpretation of the results is most often converted into a **graphic representation** in the form of a so-called forest plot.



Visualization of extracting and combining data in meta-analysis

## Discussion

In addition, the discussion serves to **clarify and compare** possible differences between meta-analyses that deal with the same or similar topic. If these differences are present, it is necessary to explain the reasons for this state of affairs.



The conclusions of a meta-analysis may be invalid if the results in the primary studies are statistically incompatible with each other (*statistical heterogeneity*) or if the subjects of the research differ significantly (*clinical heterogeneity*). If the studies show *statistical* or *clinical heterogeneity* among themselves, the results of the primary studies cannot be mathematically aggregated.

Incomplete or biased selection of primary studies can lead meta-analysis to misleading results. This occurs mainly because compared to studies with negative results, studies with positive results are more likely to be published, published in English, and listed in citation databases.

Iron

- ws:Metaanalýza

- Evidence based medicine
- Systemic preview
- Sources of error in scientific studies
- Odds ratio
- Confidence interval
- Epidemiology

- Přednáška pojednávající o systematických přehledech a metaanalýzách (<https://www.youtube.com/watch?v=aG7jvwDNXtk>)
- Návod pro tvorbu metaanalýzy (<https://journals.sagepub.com/doi/full/10.3102/0034654319877153>)
- Veřejně dostupný software pro výpočty a ucelení informací o tvorbě metaanalýz (<https://www.erim.eur.nl/research-support/meta-essentials/>)
- Sekundární analýza dat a metaanalýza (WikiSofia) ([https://wikisofia.cz/wiki/21.\\_Sekund%C3%A1rn%C3%AD\\_anal%C3%BDza\\_dat\\_a\\_metaanal%C3%BDza](https://wikisofia.cz/wiki/21._Sekund%C3%A1rn%C3%AD_anal%C3%BDza_dat_a_metaanal%C3%BDza))
- Aktualizovaný PRISMA diagram ke stažení (<http://prisma-statement.org/prismastatement/flowdiagram.aspx>)
- Příklady otázek s výběrem odpovědí v medicíně založené na důkazech (<https://pmj.bmj.com/content/76/899/594>)
- Práce s metodickým zkreslením studií, praktická aplikace ([https://handbook-5-1.cochrane.org/chapter\\_8/8\\_assessing\\_risk\\_of\\_bias\\_in\\_included\\_studies.htm](https://handbook-5-1.cochrane.org/chapter_8/8_assessing_risk_of_bias_in_included_studies.htm))
- Bias v metaanalýze zjištěný jednoduchým grafickým testem (<https://www.bmj.com/content/315/7109/629>)
  - <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2127453/>
- Cochrane Risk of Bias Tool (<https://www.riskofbias.info>)
- Newcastle-Ottawa Scale ([http://www.ohri.ca/programs/clinical\\_epidemiology/oxford.asp](http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp))
- QUADAS-2 (<https://www.bristol.ac.uk/population-health-sciences/projects/quadas/quadas-2/>)
- AMSTAR ([https://amstar.ca/Amstar\\_Checklist.php](https://amstar.ca/Amstar_Checklist.php))
- OpenMeta(Analyst) (<http://www.cebim.brown.edu/openmeta/>)

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8. Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. BMJ. 1997;315(7109):629-634. doi:10.1136/bmj.315.7109.629, dostupné také z <https://www.bmj.com/content/315/7109/629>