<https://www.sciencedirect.com/topics/neuroscience/meta-analysis>

for medical needs

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## Why perform a meta-analysis?

#### What is a meta-analysis?

Meta-analysis is the statistical procedure for combining data from multiple studies. When the [treatment effect](https://www.meta-analysis.com/pages/effects.php) (or effect size) is consistent from one study to the next, meta-analysis can be used to identify this common effect. When the effect varies from one study to the next, meta-analysis may be used to identify the reason for the variation.

#### Why perform a meta-analysis?

Decisions about the utility of an intervention or the validity of a hypothesis cannot be based on the results of a single study, because results typically vary from one study to the next. Rather, a mechanism is needed to synthesize data across studies. Narrative reviews had been used for this purpose, but the narrative review is largely subjective (different experts can come to different conclusions) and becomes impossibly difficult when there are more than a few studies involved. Meta-analysis, by contrast, applies objective formulas (much as one would apply statistics to data within a single study), and can be used with any number of studies.

#### Meta-analysis in applied and basic research

Pharmaceutical companies use meta-analysis to gain approval for new drugs, with regulatory agencies sometimes requiring a meta-analysis as part of the approval process. Clinicians and applied researchers in medicine, education, psychology, criminal justice, and a host of other fields use meta-analysis to determine which interventions work, and which ones work best. Meta analysis is also widely used in basic research to evaluate the evidence in areas as diverse as sociology, social psychology, sex differences, finance and economics, political science, marketing, ecology and genetics, among others.

### Where does meta-analysis fit in the research process?

#### Publications

Many journals encourage researchers to submit systematic reviews and meta-analyses that summarize the body of evidence on a specific question, and this approach is replacing the traditional narrative review. Meta-analyses also play supporting roles in other papers.  For example, a paper that reports results for a new primary study might include a meta-analysis in the introduction to synthesize prior data and help to place the new study in context.

#### Planning new studies

Meta-analyses can play a key role in planning new studies. The meta-analysis can help identify which questions have already been answered and which remain to be answered, which outcome measures or populations are most likely to yield significant results, and which variants of the planned intervention are likely to be most powerful.

#### Grant applications

Meta-analyses are used in grant applications to justify the need for a new study.  The meta-analysis serves to put the available data in context and to show the potential utility of the planned study. The graphical elements of the meta-analysis, such as the forest plot, provide a mechanism for presenting the data clearly, and for capturing the attention of the reviewers. Some funding agencies now require a meta-analysis of existing research as part of the grant application to fund new research.

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Comprehensive Meta-Analysis is a powerful computer program for meta-analysis. The program combines ease of use with a wide array of computational options and sophisticated graphics.

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# Meta-Analysis

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#### Definition

A subset of systematic reviews; a method for systematically combining pertinent qualitative and quantitative study data from several selected studies to develop a single conclusion that has greater statistical power. This conclusion is statistically stronger than the analysis of any single study, due to increased numbers of subjects, greater diversity among subjects, or accumulated effects and results.

Meta-analysis would be used for the following purposes:

* To establish statistical significance with studies that have conflicting results
* To develop a more correct estimate of effect magnitude
* To provide a more complex analysis of harms, safety data, and benefits
* To examine subgroups with individual numbers that are not statistically significant

If the individual studies utilized randomized controlled trials (RCT), combining several selected RCT results would be the highest-level of evidence on the evidence hierarchy, followed by systematic reviews, which analyze all available studies on a topic.

#### Advantages

* Greater statistical power
* Confirmatory data analysis
* Greater ability to extrapolate to general population affected
* Considered an evidence-based resource

#### Disadvantages

* Difficult and time consuming to identify appropriate studies
* Not all studies provide adequate data for inclusion and analysis
* Requires advanced statistical techniques
* Heterogeneity of study populations

#### Design pitfalls to look out for

The studies pooled for review should be similar in type (i.e. all randomized controlled trials).

Are the studies being reviewed all the same type of study or are they a mixture of different types?

The analysis should include published and unpublished results to avoid publication bias.

Does the meta-analysis include any appropriate relevant studies that may have had negative outcomes?

#### Fictitious Example

Do individuals who wear sunscreen have fewer cases of melanoma than those who do not wear sunscreen? A MEDLINE search was conducted using the terms melanoma, sunscreening agents, and zinc oxide, resulting in 8 randomized controlled studies, each with between 100 and 120 subjects. All of the studies showed a positive effect between wearing sunscreen and reducing the likelihood of melanoma. The subjects from all eight studies (total: 860 subjects) were pooled and statistically analyzed to determine the effect of the relationship between wearing sunscreen and melanoma. This meta-analysis showed a 50% reduction in melanoma diagnosis among sunscreen-wearers.

#### Real-life Examples

Goyal, A., Elminawy, M., Kerezoudis, P., Lu, V., Yolcu, Y., Alvi, M., & Bydon, M. (2019). [Impact of obesity on outcomes following lumbar spine surgery: A systematic review and meta-analysis.](https://pmid.us/30583093) Clinical Neurology and Neurosurgery, 177, 27-36. https://doi.org/10.1016/j.clineuro.2018.12.012

This meta-analysis was interested in determining whether obesity affects the outcome of spinal surgery. Some previous studies have shown higher perioperative morbidity in patients with obesity while other studies have not shown this effect. This study looked at surgical outcomes including "blood loss, operative time, length of stay, complication and reoperation rates and functional outcomes" between patients with and without obesity. A meta-analysis of 32 studies (23,415 patients) was conducted. There were no significant differences for patients undergoing minimally invasive surgery, but patients with obesity who had open surgery had experienced higher blood loss and longer operative times (not clinically meaningful) as well as higher complication and reoperation rates. Further research is needed to explore this issue in patients with morbid obesity.

Nakamura, A., van Der Waerden, J., Melchior, M., Bolze, C., El-Khoury, F., & Pryor, L. (2019). [Physical activity during pregnancy and postpartum depression: Systematic review and meta-analysis.](https://pmid.us/30576955) Journal of Affective Disorders, 246, 29-41. https://doi.org/10.1016/j.jad.2018.12.009

This meta-analysis explored whether physical activity during pregnancy prevents postpartum depression. Seventeen studies were included (93,676 women) and analysis showed a "significant reduction in postpartum depression scores in women who were physically active during their pregnancies when compared with inactive women." Possible limitations or moderators of this effect include intensity and frequency of physical activity, type of physical activity, and timepoint in pregnancy (e.g. trimester).

#### Related Terms

Systematic Review

Publication Bias

#### Now test yourself!

Top of Form

1. A Meta-Analysis pools together the populations from different studies, such as Randomized Controlled Trials, into one statistical analysis and treats them as one large study population with one conclusion.

a) True
b) False

2. One potential design pitfall of Meta-Analyses that is important to pay attention to is:

a) Whether it is evidence-based.
b) If the authors combined studies with conflicting results.
c) If the authors appropriately combined studies so they did not compare apples and oranges.
d) If the authors used only quantitative data.

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<https://www.ccace.ed.ac.uk/research/software-resources/systematic-reviews-and-meta-analyses> Nota Bene!!

## Systematic reviews and meta-analyses: a step-by-step guide

If you are considering doing a systematic review or meta-analysis, this step-by-step guide aims to support you along the way. It explains the background to these methodologies, what is involved, and how to get started, keep going, and finish!

It will direct you to useful resources provided by CCACE researchers and external bodies. There is a ‘wiki’ section for you, and others who have been through the process, to add useful hints and tips, and up-to-date resources particularly relevant to researchers and students in CCACE.

**What is a systematic review or meta-analysis?**

A **systematic review** answers a defined research question by collecting and summarising all empirical evidence that fits pre-specified eligibility criteria.

A **meta-analysis** is the use of statistical methods to summarise the results of these studies.

Systematic reviews, just like other research articles, can be of varying quality. They are a significant piece of work (the Centre for Reviews and Dissemination at York estimates that a team will take 9-24 months), and to be useful to other researchers and practitioners they should have:

* clearly stated objectives with pre-defined eligibility criteria for studies
* explicit, reproducible methodology
* a systematic search that attempts to identify all studies
* assessment of the validity of the findings of the included studies (e.g. risk of bias)
* systematic presentation, and synthesis, of the characteristics and findings of the included studies

It is essential that each review is approached rigorously and with careful attention to detail. Plan carefully, and document everything. The consensus reporting guidelines for different study designs proposed by EQUATOR (<http://www.equator-network.org/>) are a useful starting point. PRISMA provides guidance on what you should include when reporting a systematic review.

**Step 1:** Why do a systematic review?  [*Click here*](https://www.ccace.ed.ac.uk/research/software-resources/systematic-reviews-and-meta-analyses/step1?phpMyAdmin=UlK8xfSbayFQJAV7hgjO-sdYkp3)

**Step 2:** Who will be involved? [Click here](https://www.ccace.ed.ac.uk/research/software-resources/systematic-reviews-and-meta-analyses/step2?phpMyAdmin=UlK8xfSbayFQJAV7hgjO-sdYkp3)

**Step 3:** Formulate the problem. Has it been done before? Registering your review. [Click here](https://www.ccace.ed.ac.uk/research/software-resources/systematic-reviews-and-meta-analyses/step3?phpMyAdmin=UlK8xfSbayFQJAV7hgjO-sdYkp3)

**Step 4**: Perform your search. [Click here](https://www.ccace.ed.ac.uk/research/software-resources/systematic-reviews-and-meta-analyses/step4?phpMyAdmin=UlK8xfSbayFQJAV7hgjO-sdYkp3)

**Step 5:** Data extraction. [Click here](https://www.ccace.ed.ac.uk/research/software-resources/systematic-reviews-and-meta-analyses/step5?phpMyAdmin=UlK8xfSbayFQJAV7hgjO-sdYkp3)

**Step 6:** Critical appraisal of studies (quality assessment). [Click here](https://www.ccace.ed.ac.uk/research/software-resources/systematic-reviews-and-meta-analyses/step6?phpMyAdmin=UlK8xfSbayFQJAV7hgjO-sdYkp3)

**Step 7**Data synthesis. [Click here](https://www.ccace.ed.ac.uk/research/software-resources/systematic-reviews-and-meta-analyses/step7?phpMyAdmin=UlK8xfSbayFQJAV7hgjO-sdYkp3)

**Step 8:** Presenting results (writing the report). [Click here](https://www.ccace.ed.ac.uk/research/software-resources/systematic-reviews-and-meta-analyses/step8?phpMyAdmin=UlK8xfSbayFQJAV7hgjO-sdYkp3)

**Step 9:** Archiving and updating. [Click here](https://www.ccace.ed.ac.uk/research/software-resources/systematic-reviews-and-meta-analyses/step9?phpMyAdmin=UlK8xfSbayFQJAV7hgjO-sdYkp3)

**Useful Resources:** [*Click here*](https://www.ccace.ed.ac.uk/research/software-resources/systematic-reviews-and-meta-analyses/useful-resources?phpMyAdmin=UlK8xfSbayFQJAV7hgjO-sdYkp3)

Note: If you have any useful resources that would be beneficial for this guide, please let us know (contact Kate McAllister, ke.ccace@ed.ac.uk) and she'll add them here.

**Acknowledgements and References**

Much of this advice is based on the excellent (and extensive) guidance from the Cochrane Collaboration (<http://www.cochrane-handbook.org/> ) and the Centre for Reviews and Dissemination at York ([http://www.york.ac.uk/inst/crd/SysRev/!SSL!/WebHelp/SysRev3.htm](http://www.york.ac.uk/inst/crd/SysRev/%21SSL%21/WebHelp/SysRev3.htm)). If you are proposing to perform a systematic review these provide invaluable detailed advice, and useful examples.

<https://www.ccace.ed.ac.uk/research/software-resources/systematic-reviews-and-meta-analyses>

<https://ebn.bmj.com/content/16/1/3>

When clinicians begin their search for the best available evidence to inform decision-making, they are usually directed to the top of the ‘evidence pyramid’ to find out whether a systematic review and meta-analysis have been conducted. The Cochrane Library[1](https://ebn.bmj.com/content/16/1/3#ref-1) is fast filling with systematic reviews and meta-analyses that aim to answer important clinical questions and provide the most reliable evidence to inform practice and research. So what is meta-analysis and how can it contribute to practice?

## What is meta-analysis?

Meta-analysis is a research process used to systematically synthesise or merge the findings of single, independent studies, using statistical methods to calculate an overall or ‘absolute’ effect.[2](https://ebn.bmj.com/content/16/1/3#ref-2) Meta-analysis does not simply pool data from smaller studies to achieve a larger sample size. Analysts use well recognised, systematic methods to account for differences in sample size, variability (heterogeneity) in study approach and findings (treatment effects) and test how sensitive their results are to their own systematic review protocol (study selection and statistical analysis).[2](https://ebn.bmj.com/content/16/1/3#ref-2) ,[3](https://ebn.bmj.com/content/16/1/3#ref-3)

## The Five-step process

There is debate about the best practice for meta-analysis, however there are five common steps.

### Step 1: the research question

A clinical research question is identified and a hypothesis proposed. The likely clinical significance is explained and the study design and analytical plan are justified.

### Step 2: systematic review

A systematic review (SR) is specifically designed to address the research question and conducted to identify all studies considered to be both relevant and of sufficiently good quality to warrant inclusion. Often, only studies published in established journals are identified, but identification of ‘unpublished’ data is important to avoid ‘publication bias’ or exclusion of studies with negative findings.[4](https://ebn.bmj.com/content/16/1/3#ref-4) Some meta-analyses only consider randomised control trials (RCTs) in the quest for highest quality evidence. Other types of ‘experimental’ and ‘quasi-experimental’ studies may be included if they satisfy the defined inclusion/exclusion criteria.

### Step 3: data extraction

Once studies are selected for inclusion in the meta-analysis, summary data or outcomes are extracted from each study. In addition, sample sizes and measures of data variability for both intervention and control groups are required. Depending on the study and the research question, outcome measures could include numerical measures or categorical measures. For example, differences in scores on a questionnaire or differences in a measurement level such as blood pressure would be reported as a numerical mean. However, differences in the likelihood of being in one category versus another (eg, vaginal birth versus cesarean birth) are usually reported in terms of risk measures such as OR or relative risk (RR).

### Step 4: standardisation and weighting studies

Having assembled all the necessary data, the fourth step is to calculate appropriate summary measures from each study for further analysis. These measures are usually called Effect Sizes and represent the difference in average scores between intervention and control groups. For example, the difference in change in blood pressure between study participants who used drug X compared with participants who used a placebo. Since units of measurement typically vary across included studies, they usually need to be ‘standardised’ in order to produce comparable estimates of this effect. When different outcome measures are used, such as when researchers use different tests, standardisation is imperative. Standardisation is achieved by taking, for each study, the mean score for the intervention group, subtracting the mean for the control group and dividing this result by the appropriate measure of variability in that data set.

The results of some studies need to carry more weight than others. Larger studies (as measured by sample sizes) are thought to produce more precise effect size estimates than smaller studies. Second, studies with less data variability, for example, smaller SD or narrower CIs are often regarded as ‘better quality’ in study design. A weighting statistic that seeks to incorporate both these factors, known as inverse variance, is commonly used.

### Step 5: final estimates of effect

The final stage is to select and apply an appropriate model to compare Effect Sizes across different studies. The most common models used are Fixed Effects and Random Effects models. Fixed Effects models are based on the ‘assumption that every study is evaluating a common treatment effect’.[5](https://ebn.bmj.com/content/16/1/3#ref-5) This means that the assumption is that all studies would estimate the same Effect Size were it not for different levels of sample variability across different studies. In contrast, the Random Effects model ‘assumes that the true treatment effects in the individual studies may be different from each other’.[5](https://ebn.bmj.com/content/16/1/3#ref-5) and attempts to allow for this additional source of interstudy variation in Effect Sizes. Whether this latter source of variability is likely to be important is often assessed within the meta-analysis by testing for ‘heterogeneity’.

### Forest plot

The final estimates from a meta-analysis are often graphically reported in the form of a ‘Forest Plot’.

In the hypothetical Forest Plot shown in [figure 1](https://ebn.bmj.com/content/16/1/3#F1), for each study, a horizontal line indicates the standardised Effect Size estimate (the rectangular box in the centre of each line) and 95% CI for the risk ratio used. For each of the studies, drug X reduced the risk of death (the risk ratio is less than 1.0). However, the first study was larger than the other two (the size of the boxes represents the relative weights calculated by the meta-analysis). Perhaps, because of this, the estimates for the two smaller studies were not statistically significant (the lines emanating from their boxes include the value of 1). When all the three studies were combined in the meta-analysis, as represented by the diamond, we get a more precise estimate of the effect of the drug, where the diamond represents both the combined risk ratio estimate and the limits of the 95% CI.



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Figure 1

Hypothetical Forest Plot

### Relevance to practice and research

Many Evidence Based Nursing commentaries feature recently published systematic review and meta-analysis because they not only bring new insight or strength to recommendations about the most effective healthcare practices but they also identify where future research should be directed to bridge the gaps or limitations in current evidence. The strength of conclusions from meta-analysis largely depends on the quality of the data available for synthesis. This reflects the quality of individual studies and the systematic review. Meta-analysis does not magically resolve the problem of underpowered or poorly designed studies and clinicians can be frustrated to find that even when a meta-analysis has been conducted, all that the researchers can conclude is that the evidence is weak, there is uncertainty about the effects of treatment and that higher quality research is needed to better inform practice. This is still an important finding and can inform our practice and challenge us to fill the evidence gaps with better quality research in the future.

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## Footnotes

* Competing interests None.

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Molika Ashford, 360Dx

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# Meta-Analysis

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**Original** [**research**](https://explorable.com/what-is-research) **experiments can be time consuming and expensive, and may yield data that contains large margins of error. An alternative is to conduct a meta-analysis, which is a statistical technique developed to analyze the total data from a large, already-existing collection of experiments.**

Social scientists can have difficulty designing and implementing [true experiments](https://explorable.com/true-experimental-design), so meta-analysis provides them a [quantitative](https://explorable.com/quantitative-research-design) tool to statistically analyze data drawn from a number of past studies. The fields of medicine and psychology increasingly use this method as a way of avoiding time-consuming and intricate studies.



## What is Meta-Analysis?

Studies in the social sciences often use small sample sizes, so any statistics used generally give results containing large margins of [error](https://explorable.com/type-I-error). Small sample size can be a problem when interpreting and [drawing conclusions](https://explorable.com/drawing-conclusions), because it can mask any underlying trends or [correlations](https://explorable.com/correlation-and-causation). Conclusions from small studies are tenuous at best, and leave the [research](https://explorable.com/what-is-research) open for criticism.

[Meta-analysis](http://en.wikipedia.org/wiki/Meta-analysis), on the other hand, is the process of drawing from a larger body of research, and using powerful statistical analysis to come to conclusions. It can be thought of as a “study of studies.” This gives researchers a much larger sample population and is more likely to generate meaningful and usable outcomes.



## The Advantages of Meta-Analysis

Meta-analysis is an excellent way of simplifying the complexity of research. A single research team can reasonably only output so much data in a given time. But meta-analysis gives access to possibly more data than that team could produce in a lifetime, and allows them to condense it in useful ways. As we make technological developments in computational power, new database programs have made the process even easier.

For rare medical conditions, meta-analysis allows researchers to collect data from further afield than would be possible for one research group. This allows them to conduct meaningful statistical analyses when a small local sample would have told them nothing about the disease.

When professionals working in parallel can upload their results and access all known data on a topic, there is a built-in quality control. The effects of error or bias in studies are kept in check. Meta-analysis also ensures there is no unnecessary repeat research and allows researchers to pool resources and compare methods. As papers can often take many months to be physically published, instant computer records ensure that other researchers are always aware of the latest work and [results](https://explorable.com/statistically-significant-results) in the field.

A meta-study allows a much wider net to be cast than a traditional [literature review](https://explorable.com/what-is-a-literature-review), and is excellent for highlighting [correlations](https://explorable.com/statistical-correlation) and links between studies that may not be readily apparent as well as ensuring that the compiler does not subconsciously infer correlations that do not exist. Perhaps best of all, meta-studies are economical and allow research funds to be diverted elsewhere.

## The Disadvantages of Meta-Analysis

There are nevertheless disadvantages to meta-analysis, of which a researcher must be aware before relying on the data and [statistics](https://explorable.com/statistics-tutorial) it generates. The main problem is the potential for [publication bias](https://explorable.com/publication-bias) and skewed data.

Research generating results that don’t reject null [hypotheses](https://explorable.com/research-hypothesis) may tend to remain unpublished, or risk not being entered into a database. If the meta-study is restricted to research with positive results, then the [validity](https://explorable.com/types-of-validity) of the entire endeavor is compromised.

The researcher compiling the data must also make sure that all research is

<http://www.bandolier.org.uk/painres/download/whatis/Meta-An.pdf>