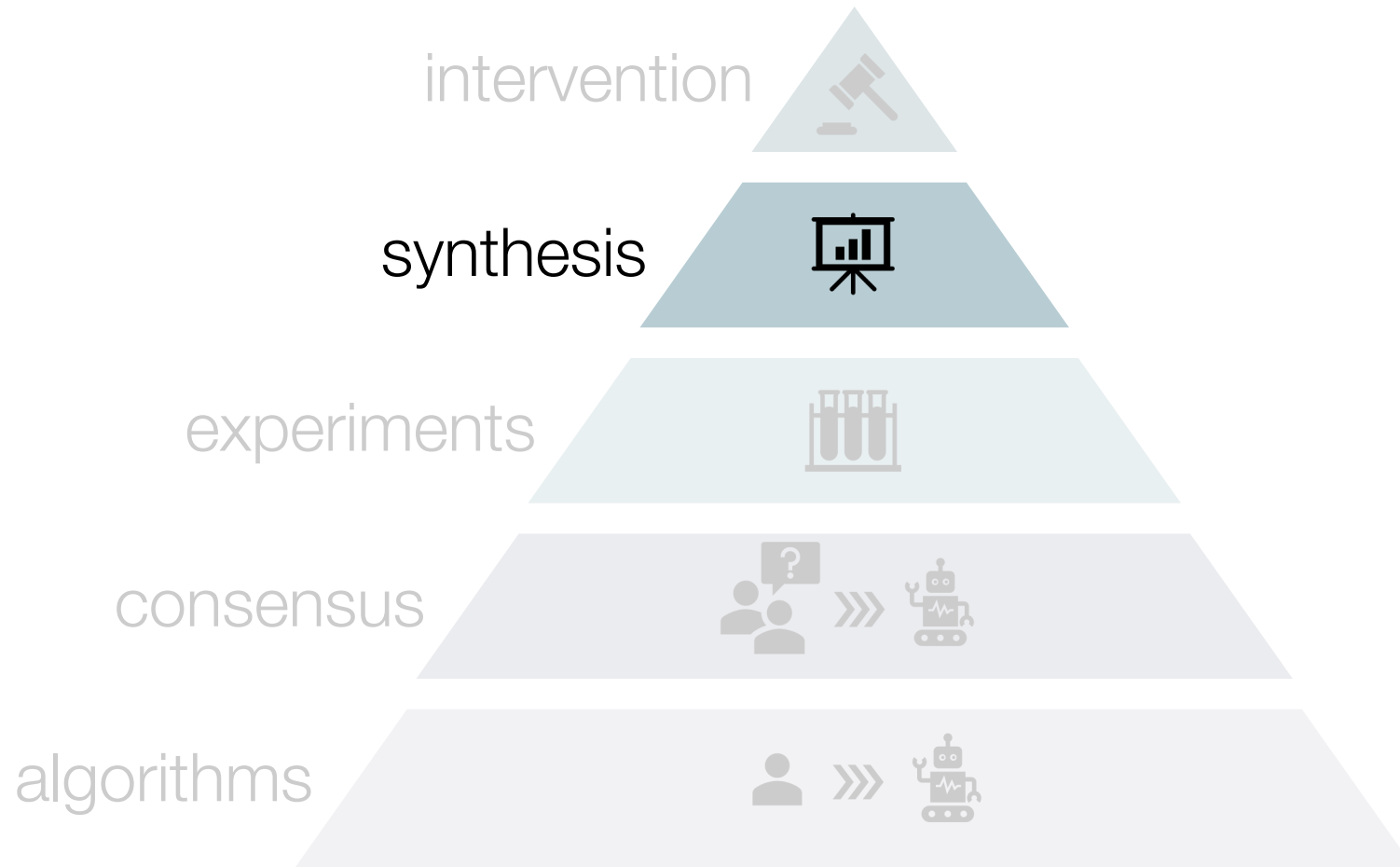


Evidence-based Decision Making Synthesis: Overview

Rui Mata, FS 2024

Version: February 23, 2024

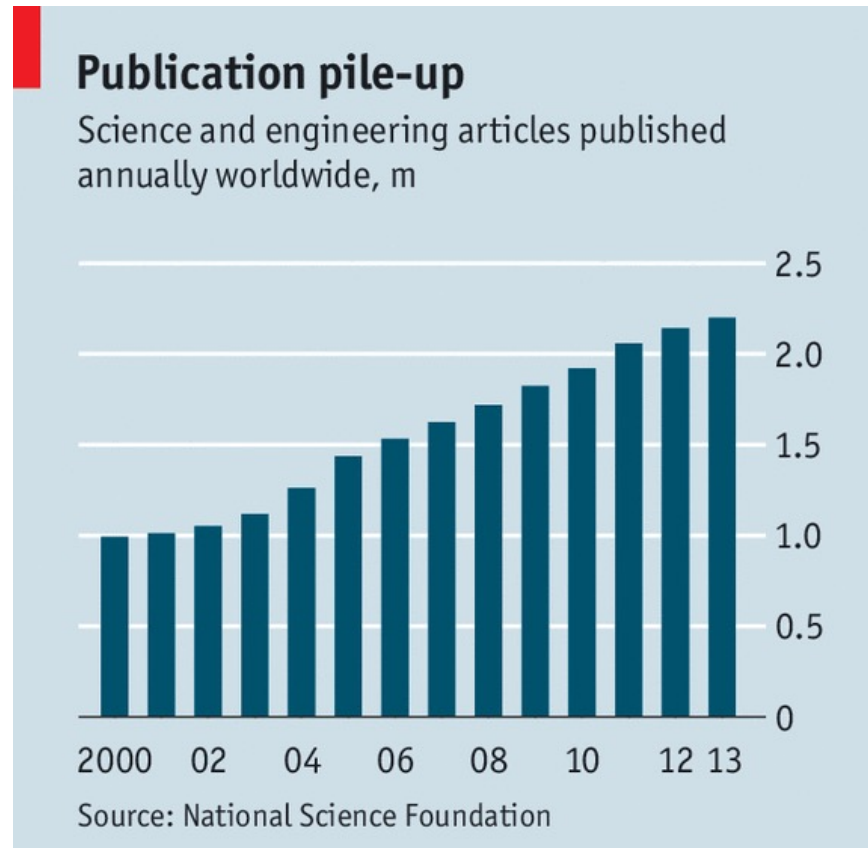


Goals for today

- understand the relevance of research synthesis
- be able to sketch a brief history of research synthesis
- define key terms associated with research synthesis (e.g., systematic review, meta-analysis, protocol)
- recognize different types of research synthesis

Why research synthesis matters...

Synthesis as a way to deal with information explosion



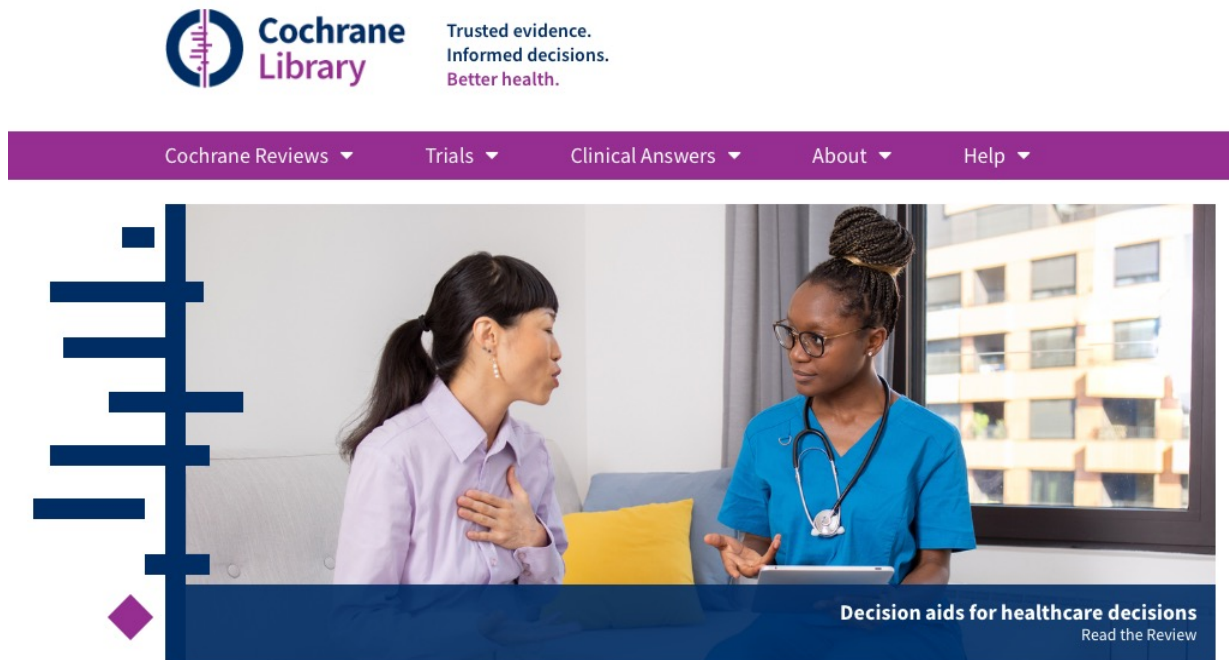
Economist.com

- rough estimates:
 - # of articles double every ~10 years
 - # of journals double every ~15 years

Why research synthesis matters...

Synthesis as a way to deal with conflicting or bad evidence

“In addition to providing a summary of what is known about a given topic, reviews evaluate individual studies, identifying the most reliable ones and flagging those that are less robust.”



Salandra, R., Criscuolo, P., & Salter, A. (2022). The power of weak signals: How systematic reviews direct researchers away from potentially biased primary studies. *Cochrane Database of Systematic Reviews*, 2022(11). <https://doi.org/10.1002/14651858.ED000160>

A brief history of research synthesis

Pre-1970s

- narrative literature reviews
- vote counting methods
- some early forms of quantitative synthesis (medicine/vaccination: Pearson (1904); agriculture: Cochran (1937); physics: Birge (1932))

Post-1970s


- Origin of term “meta-analysis” (Glass, 1976)
- Textbooks: Light & Pillemer (1984), Hedges & Olkin (1985)
- Evidence-based libraries: Cochrane, Campbell
- Guidelines, guidelines, guidelines (CONSORT, PRISMA)...


O'Rourke, K. (2007). An historical perspective on meta-analysis: dealing quantitatively with varying study results. *Journal of the Royal Society of Medicine*, 100(12), 579–582.
<http://doi.org/10.1258/jrsm.100.12.579>

Chalmers, I., Hedges, L. V., & Cooper, H. (2002). A brief history of research synthesis. *Evaluation & the Health Professions*, 25(1), 12–37.

A brief history of research synthesis



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1993

 **THE CAMPBELL COLLABORATION**

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What helps?

What harms?

Based on what **evidence?**

www.campbellcollaboration.org

1999



Definitions

Term	Definition
Systematic review	A systematic review attempts to collate all relevant evidences that fits pre-specified eligibility criteria to answer a specific research question. It uses explicit, systematic methods to minimize bias in the identification, selection, synthesis, and summary of studies. When done well, this provides reliable findings from which conclusions can be drawn and decisions made [25,26]. The key characteristics of a systematic review are (a) a clearly stated set of objectives with an explicit, reproducible methodology; (b) a systematic search that attempts to identify all studies that would meet the eligibility criteria; (c) an assessment of the validity of the findings of the included studies (e.g., assessment of risk of bias and confidence in cumulative estimates); and (d) systematic presentation, and synthesis, of the characteristics and findings of the included studies
Meta-analysis	Meta-analysis is the use of statistical techniques to combine and summarize the results of multiple studies; they may or may be contained within a systematic review. By combining data from several studies, meta-analyses can provide more precise estimates of the effects of health care than those derived from the individual studies
Protocol	In the context of systematic reviews and meta-analyses, a protocol is a document that presents an explicit plan for a systematic review. The protocol details the rationale and <i>a priori</i> methodological and analytical approach of the review

PRISMA-P Group, Moher, D., Shamseer, L., Clarke, M., Gherzi, D., Liberati, A., et al. (2015). Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Systematic Reviews*, 4(1), e1000326–9. <http://doi.org/10.1186/2046-4053-4-1>

Types of research synthesis: Meta-analysis

Meta-analysis summarize effect sizes of several studies. Effect sizes can mean different things (and be calculated in different ways), it can refer to either a treatment effect (e.g., the effect of drug vs. no drug on some outcome), or a single group summary (e.g., average correlation between two variables in a population), or a generic statistic (e.g., the average value of one variable in the population). The actual calculations to compute an effect size differ by type of data and study design. Manuals tend to provide a roadmap of formulas and examples for conducting different types of meta-analyses.

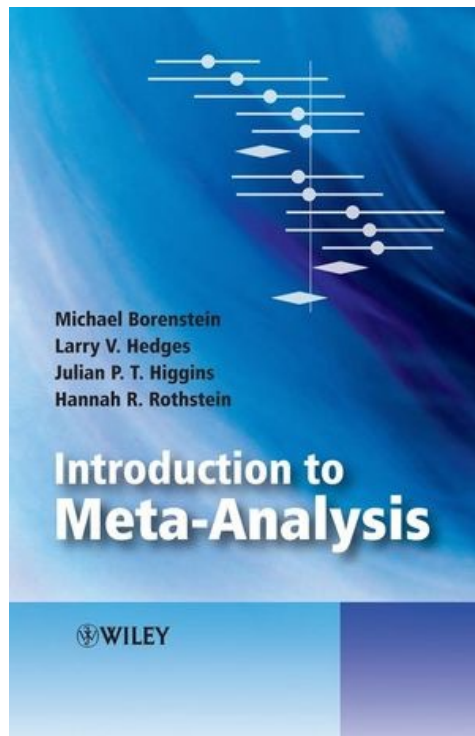


Table 3.1 Roadmap of formulas in subsequent chapters.

Effect sizes based on means (Chapter 4)

Raw (unstandardized) mean difference (D)

Based on studies with independent groups

Based on studies with matched groups or pre-post designs

Standardized mean difference (d or g)

Based on studies with independent groups

Based on studies with matched groups or pre-post designs

Response ratios (R)

Based on studies with independent groups

Effect sizes based on binary data (Chapter 5)

Risk ratio (RR)

Based on studies with independent groups

Odds ratio (OR)

Based on studies with independent groups

Risk difference (RD)

Based on studies with independent groups

Effect sizes based on correlational data (Chapter 6)

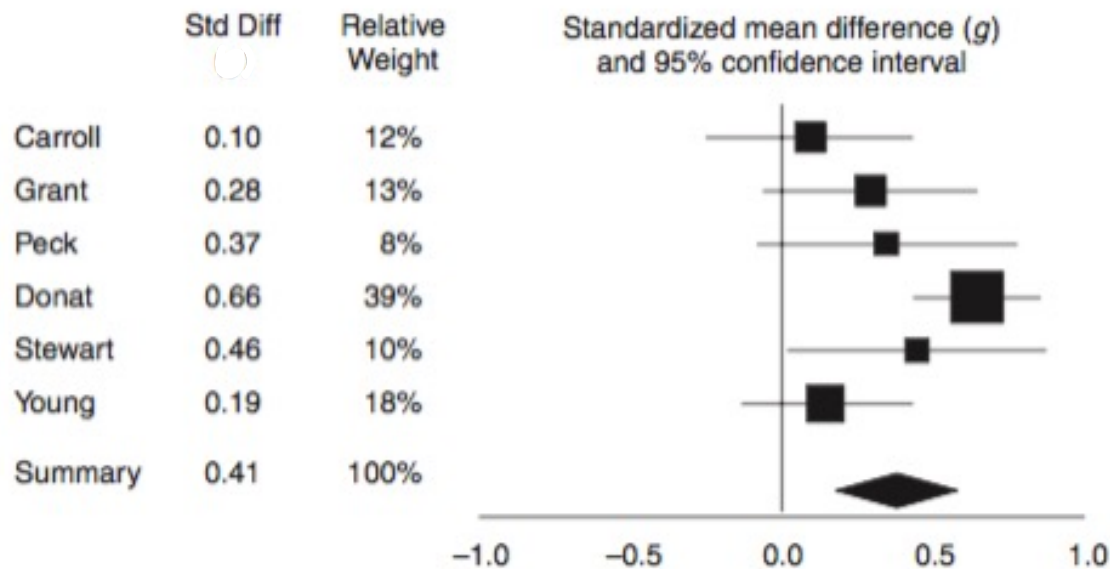
Correlation (r)

Based on studies with one group

Types of research synthesis: Meta-analysis

A typical meta-analysis will often include the following two steps:

- 1 Calculate an effect size and its precision for each study
- 2 Calculate a weighted average of the effect sizes across studies



Types of research synthesis: Meta-analysis

1 Calculate an effect size and its precision (variance) for each study

We can estimate the standardized mean difference (d) from studies that used two independent groups as

$$d = \frac{\bar{X}_1 - \bar{X}_2}{S_{within}} \quad (4.18)$$

In the numerator, \bar{X}_1 and \bar{X}_2 are the sample means in the two groups. In the denominator S_{within} is the within-groups standard deviation, pooled across groups,

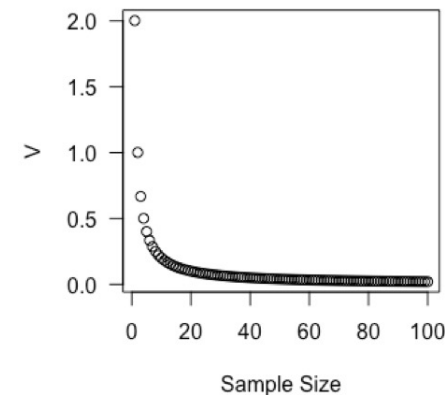
$$S_{within} = \sqrt{\frac{(n_1 - 1)S_1^2 + (n_2 - 1)S_2^2}{n_1 + n_2 - 2}} \quad (4.19)$$

where n_1 and n_2 are the sample sizes in the two groups, and S_1 and S_2 are the standard deviations in the two groups. The reason that we pool the two sample estimates of the standard deviation is that even if we assume that the underlying population standard deviations are the same (that is $\sigma_1 = \sigma_2 = \sigma$), it is unlikely that the sample estimates S_1 and S_2 will be identical. By pooling the two estimates of the standard deviation, we obtain a more accurate estimate of their common value.

The variance of d is given (to a very good approximation) by

$$V_d = \frac{n_1 + n_2}{n_1 n_2} + \frac{d^2}{2(n_1 + n_2)} \quad (4.20)$$

In this equation the first term on the right of the equals sign reflects uncertainty in the estimate of the mean difference (the numerator in (4.18)), and the second reflects uncertainty in the estimate of S_{within} (the denominator in (4.18)).



The effect size will often be a standardised value that represents the magnitude of the effect; the variance of the effect size captures the precision of the estimate and will be largely a function of the sample size (see figure)

Types of research synthesis: Meta-analysis

2 Calculate a weighted average of the effect sizes across studies

In its simplest form, the weight is a function of the precision (variance) associated with each study

$$W_i = \frac{1}{V_{Y_i}},$$

The overall effect size across studies is obtained by averaging the studies in a weighted form

$$M = \frac{\sum_{i=1}^k W_i Y_i}{\sum_{i=1}^k W_i}, \quad (11.3)$$

that is, the sum of the products $W_i Y_i$ (effect size multiplied by weight) divided by the sum of the weights.

The variance of the summary effect is estimated as the reciprocal of the sum of the weights, or

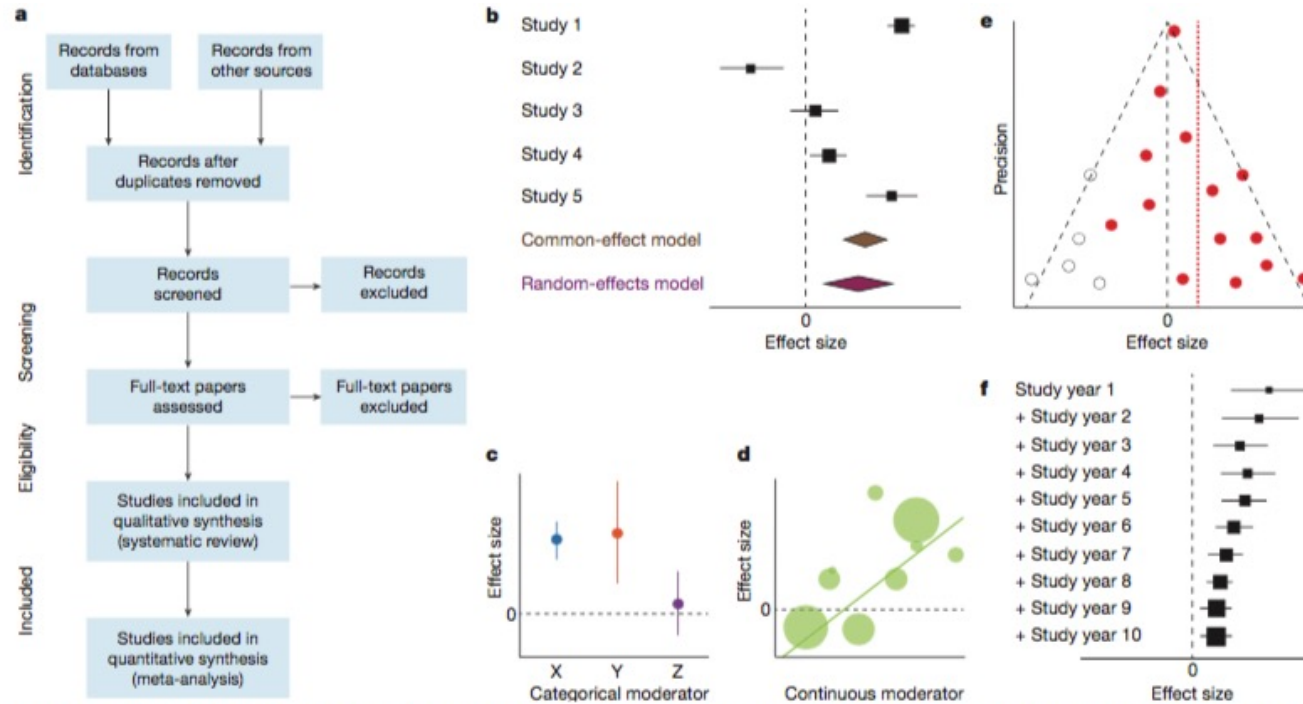
$$V_M = \frac{1}{\sum_{i=1}^k W_i}, \quad (11.4)$$

and the estimated standard error of the summary effect is then the square root of the variance,

$$SE_M = \sqrt{V_M}. \quad (11.5)$$

There are (slightly) more complex ways of aggregating studies that consider not only each study's precision but also between-study variance but the logic of weighted aggregation is the same.

Types of research synthesis: Meta-analysis



Gurevitch, J., Koricheva, J., Nakagawa, S., & Stewart, G. (2018). Meta-analysis and the science of research synthesis. *Nature*, 555, 175. <http://doi.org/10.1038/nature25753>

Types of research synthesis: Meta-analysis

The metafor Package A Meta-Analysis Package for R

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- [The R Project](#)
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The metafor Package: A Meta-Analysis Package for R

The metafor package is a free and open-source add-on for conducting meta-analyses with the statistical software environment R. The package consists of a collection of functions that allow the user to calculate various effect size or outcome measures, fit fixed-, random-, and mixed-effects models to such data, carry out moderator and meta-regression analyses, and create various types of meta-analytical plots.

On this website, you can find:

- some [news](#) concerning the package and/or its development,
- a more detailed description of the [package features](#),
- a log of the [package updates](#) that have been made over the years,
- a [to-do list](#) and a description of planned features to be implemented in the future,
- information on how to [download and install](#) the package,
- information on how to obtain [documentation and help](#) with using the package,
- some [analysis examples](#) that illustrate various models, methods, and techniques,
- a little showcase of [plots and figures](#) that can be created with the package,
- some [tips and notes](#) that may be useful when working with the package,
- a list of people that have in some shape or form [contributed](#) to the development of the package,
- a [frequently asked questions](#) section, and
- some [links](#) to other websites related to software for meta-analysis.

The metafor package was written by [Wolfgang Viechtbauer](#). It is licensed under the [GNU General Public License Version 2](#). For citation info, type `citation(package='metafor')` in R. To report any issues or bugs, please go [here](#).

metafor.txt · Last modified: 2021/02/08 21:48 by Wolfgang Viechtbauer

<http://www.metafor-project.org/>

Types of research synthesis: Scoping reviews

Scoping reviews can be conducted to meet various objectives. They may examine the extent (that is, size), range (variety), and nature (characteristics) of the evidence on a topic or question; determine the value of undertaking a systematic review; summarize findings from a body of knowledge that is heterogeneous in methods or discipline; or identify gaps in the literature to aid the planning and commissioning of future research. (...) Systematic reviews are useful for answering clearly defined questions (for example, “Does this intervention improve specified outcomes when compared with a given comparator in this population?”), whereas scoping reviews are useful for answering much broader questions (such as “What is the nature of the evidence for this intervention?” or “What is known about this concept?”).

Section	Item	PRISMA-ScR Checklist Item
Title	1	Identify the report as a scoping review.
Abstract		
Structured summary	2	Provide a structured summary that includes (as applicable) background, objectives, eligibility criteria, sources of evidence, charting methods, results, and conclusions that relate to the review questions and objectives.
Introduction		
Rationale	3	Describe the rationale for the review in the context of what is already known. Explain why the review questions/objectives lend themselves to a scoping review approach.
Objectives	4	Provide an explicit statement of the questions and objectives being addressed with reference to their key elements (e.g., population or participants, concepts, and context) or other relevant key elements used to conceptualize the review questions and/or objectives.
Methods		
Protocol and registration	5	Indicate whether a review protocol exists; state if and where it can be accessed (e.g., a Web address); and if available, provide registration information, including the registration number.
Eligibility criteria	6	Specify characteristics of the sources of evidence used as eligibility criteria (e.g., years considered, language, and publication status), and provide a rationale.
Information sources*	7	Describe all information sources in the search (e.g., databases with dates of coverage and contact with authors to identify additional sources), as well as the date the most recent search was executed.
Search	8	Present the full electronic search strategy for at least 1 database, including any limits used, such that it could be repeated.
Selection of sources of evidence†	9	State the process for selecting sources of evidence (i.e., screening and eligibility) included in the scoping review.
Data charting process‡	10	Describe the methods of charting data from the included sources of evidence (e.g., calibrated forms or forms that have been tested by the team before their use, and whether data charting was done independently or in duplicate) and any processes for obtaining and confirming data from investigators.
Data items	11	List and define all variables for which data were sought and any assumptions and simplifications made.
Critical appraisal of individual sources of evidence§	12	If done, provide a rationale for conducting a critical appraisal of included sources of evidence; describe the methods used and how this information was used in any data synthesis (if appropriate).
Summary measures	13	Not applicable for scoping reviews.
Synthesis of results	14	Describe the methods of handling and summarizing the data that were charted.
Risk of bias across studies	15	Not applicable for scoping reviews.
Additional analyses	16	Not applicable for scoping reviews.
Results		
Selection of sources of evidence	17	Give numbers of sources of evidence screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally using a flow diagram.
Characteristics of sources of evidence	18	For each source of evidence, present characteristics for which data were charted and provide the citations.
Critical appraisal within sources of evidence	19	If done, present data on critical appraisal of included sources of evidence (see item 12).
Results of individual sources of evidence	20	For each included source of evidence, present the relevant data that were charted that relate to the review questions and objectives.
Synthesis of results	21	Summarize and/or present the charting results as they relate to the review questions and objectives.
Risk of bias across studies	22	Not applicable for scoping reviews.
Additional analyses	23	Not applicable for scoping reviews.
Discussion		
Summary of evidence	24	Summarize the main results (including an overview of concepts, themes, and types of evidence available), link to the review questions and objectives, and consider the relevance to key groups.
Limitations	25	Discuss the limitations of the scoping review process.
Conclusions	26	Provide a general interpretation of the results with respect to the review questions and objectives, as well as potential implications and/or next steps.
Funding	27	Describe sources of funding for the included sources of evidence, as well as sources of funding for the scoping review. Describe the role of the funders of the scoping review.

Tricco, A. C., Lillie, E., Zarin, W., O'Brien, K. K., Colquhoun, H., Levac, D., et al. (2018). PRISMA extension for scoping reviews (PRISMA-ScR): Checklist and explanation. *Annals of Internal Medicine*, 169(7), 467–473. <http://doi.org/10.7326/M18-0850>

Types of research synthesis: Rapid reviews

“Rapid reviews are a form of knowledge synthesis in which components of the systematic review process are simplified or omitted to produce information in a timely manner.”

Table 5 Summary of rapid review streamlined approaches (n = 82 application studies)

Rapid review methods	Count (%)
General	
Duration of review	
>6 months	3 (4 %)
≤6 months	19 (23 %)
Not reported	60 (73 %)
Published protocol	
Mentioned	2 (2 %)
Not mentioned	80 (98 %)
Review question	
Clearly reported	81 (99 %)
Unclear/inferred	1 (1 %)
Identifying relevant studies	
Databases searched	
Searched more than one database	67 (82 %)
Searched one database only	2 (2 %)
Used a previous review(s) as starting point	8 (10 %)
Not reported	5 (6 %)
Grey literature	
Searched grey literature	57 (70 %)
No grey literature search	20 (24 %)
Not reported	5 (6 %)
Search strategy	
Clearly reported	64 (78 %)
Unclear	7 (9 %)
Not reported	11 (13 %)
Scanned references	
Yes	41 (50 %)
No	8 (10 %)
Not reported	33 (40 %)
Contacted authors	
Yes	18 (22 %)
No	9 (11 %)
Not reported	55 (67 %)
Limits applied	
Date	
No limit	10 (12 %)
Limited by date	56 (68 %)
Not reported	16 (20 %)
Language	
No limit	14 (17 %)
Limited by language	40 (49 %)
Not reported	28 (34 %)

Table 5 Summary of rapid review streamlined approaches (n = 82 application studies) (Continued)

Selecting relevant studies	
Titles and abstracts	
Two or more independent reviewers	28 (34 %)
One reviewer and one verifier	4 (5 %)
One reviewer only	15 (18 %)
Done but unclear number of reviewers	20 (24 %)
Not done	1 (1 %)
Not reported	14 (17 %)
Full-texts	
Two or more independent reviewers	20 (24 %)
One reviewer and one verifier	5 (6 %)
One reviewer only	9 (11 %)
Done but unclear number of reviewers	23 (28 %)
Not done	1 (1 %)
Not reported	24 (29 %)
Data abstraction and quality appraisal	
Data abstraction	
Two or more independent reviewers	8 (10 %)
One reviewer and one verifier	19 (23 %)
One reviewer only	6 (7 %)
Done but unclear number of reviewers	30 (37 %)
Not done	1 (1 %)
Not reported	18 (22 %)
Quality appraisal	
Two or more independent reviewers	14 (17 %)
One reviewer and one verifier	11 (13 %)
One reviewer only	6 (7 %)
Done but unclear number of reviewers	24 (29 %)
Not done	6 (7 %)
Not reported	21 (26 %)
Data synthesis	
Data synthesis	
Meta-analysis or clear reasons for not pooling results	18 (22 %)
Narrative/descriptive summary only	64 (78 %)

colleagues (2000) examined the impact of 20 rapid review products [43] and found that 14 had an influence on policy decision-making, four provided guidance, and two had no perceived impact. McGregor

Types of research synthesis: Umbrella reviews

“Systematic reviews and meta-analyses aim to synthesise the findings and investigate the biases. However, as the number of reviews of meta-analyses also increased, clinicians may also feel overwhelmed with too many of them. Umbrella reviews have been developed to overcome such a gap of knowledge. They are reviews of previously published systematic reviews or meta-analyses, and consist in the repetition of the meta-analyses following a uniform approach for all factors to allow their comparison.”

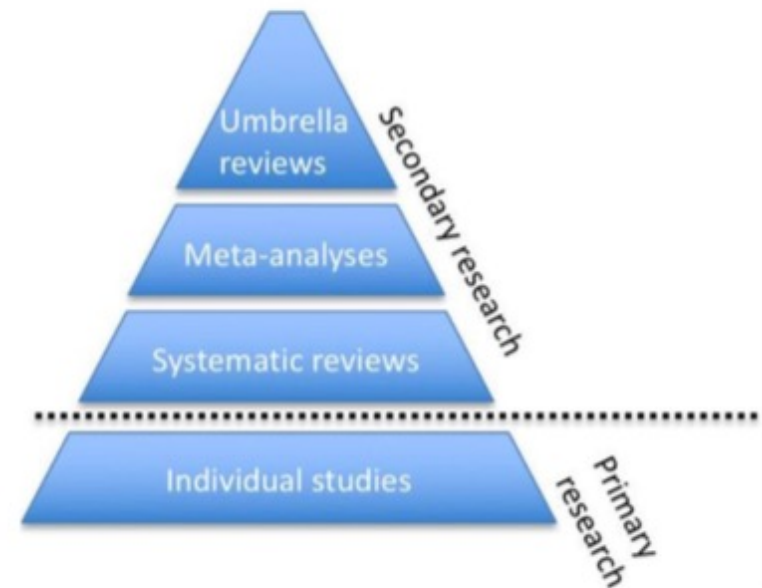


Figure 1 Hierarchy of evidence synthesis methods.

Fusar-Poli, P., & Radua, J. (2018). Ten simple rules for conducting umbrella reviews. *Evidence Based Mental Health, 21*(3), 95–100. <http://doi.org/10.1136/ebmental-2018-300014>

Types of research synthesis: Individual participant data

“Systematic reviews incorporating individual participant data (IPD) include the original data from each eligible study.”

Stewart LA, Tierney JF. To IPD or Not to IPD? Advantages and disadvantages of systematic reviews using individual patient data. *Evaluation and the Health Professions* 2002; 25: 76-97.

Tierney, J. F., Vale, C., Riley, R., Smith, C. T., Stewart, L., Clarke, M., & Rovers, M. (2015). Individual Participant Data (IPD) Meta-analyses of Randomised Controlled Trials: Guidance on Their Use. *PLOS Medicine*, 12(7), e1001855. <https://doi.org/10.1371/journal.pmed.1001855>

Type of Bias	Definition	Steps That Are Taken to Investigate and Minimise Bias			
		Usual with both AD and IPD approaches	Usual with IPD approach but may be possible with AD approach *	Only with IPD approach	
Study selection bias	Systematic differences between results of trials that are and are not selected for inclusion	Prospectively define eligibility criteria	✓		
		Clarify eligibility with trial protocol or trialist		✓	
Publication bias	Systematic differences between results of trials that are and are not published	Include all eligible trials irrespective of publication status		✓	
Data availability bias	Systematic difference between the results of trials for which data were and were not available	Include data for all eligible trials		✓	
		Investigate/discuss the impact of trials for which data were not available		✓	
Participant selection bias	Systematic differences between comparison groups in participant characteristics that can lead to differences in prognosis and/or responsiveness to treatment (Prevented by random allocation and allocation concealment)	Clarify the randomisation methods, i.e., sequence generation and allocation concealment with trial protocol or trialist		✓	
		Exclude "nonrandomised" trials		✓	
		Check for unusual allocation patterns or distributions of participant characteristics			✓
		Exclude trials with inappropriate allocation			✓
Performance and detection bias	Systematic differences between comparison groups in the care received or provided or in how outcomes are ascertained (Prevented by blinding study participants, care givers, and outcome assessors to the allocated treatment. Note this is not possible for all interventions, e.g., surgery, and is less important for objective outcomes, e.g., mortality)	Exclude nonrandomised participants from trial IPD		✓	
		Obtain more complete information on blinding and outcome assessment from trialist and/or protocol		✓	
Attrition bias	Systematic differences between comparison groups in the dropout or exclusion of participants (Prevented by the maintenance of all participants in the trial and trial analysis)	Include data on all randomised participants, irrespective of whether they were included in trial analyses		✓	
		Analyse all trials according to the allocated intervention ("intention to treat")		✓	
		Check for "missing" participants and unusual patterns of dropout or exclusion			✓
Outcome reporting or availability bias	Systematic differences between results of reported/available and unreported/unavailable outcomes (Prevented by making results for all study outcomes available)	Prespecify any reasonable participant exclusions and apply consistently across trials		✓	
		Check which outcomes were collected in a trial with protocol and/or trialist		✓	
		Include data for all relevant outcomes		✓	

Summary

- **Importance of synthesis:** research synthesis can be helpful in dealing with information explosion and is crucial to quantification of summary effects and quality assessment which are key elements of any cumulative science.
- **History:** research synthesis underwent progressive standardisation through the development of terminology, institutions (Cochrane collaboration), and guidelines (e.g., PRISMA) with the goal of increasing transparency and reduce bias (e.g., transparent exclusion criteria, protocols); while standardization is always work in progress, the logic (e.g., ensuring comprehensiveness and reproducibility, reduce bias) remains the same.
- **Aggregation:** the key statistical ingredient of quantitative research synthesis is weighted aggregation in which the information from several estimates is aggregated as a function of the confidence in each study (precision)
- **Kinds of synthesis:** there are different types of research synthesis available that serve different goals: systematic reviews w/ qualitative summary, meta-analyses, scoping reviews, rapid reviews, umbrella reviews, individual participant data, etc.