Evidence-based Decision Making
Synthesis: Overview

Rui Mata, FS 2025

Version: April 28, 2025

Bild: KI-generiert

For more information visit
https://bernoulli.unibas.ch/
or scan QR code:

University of Basel

Faculty of
Business and Economics

Faculty of
Psychology

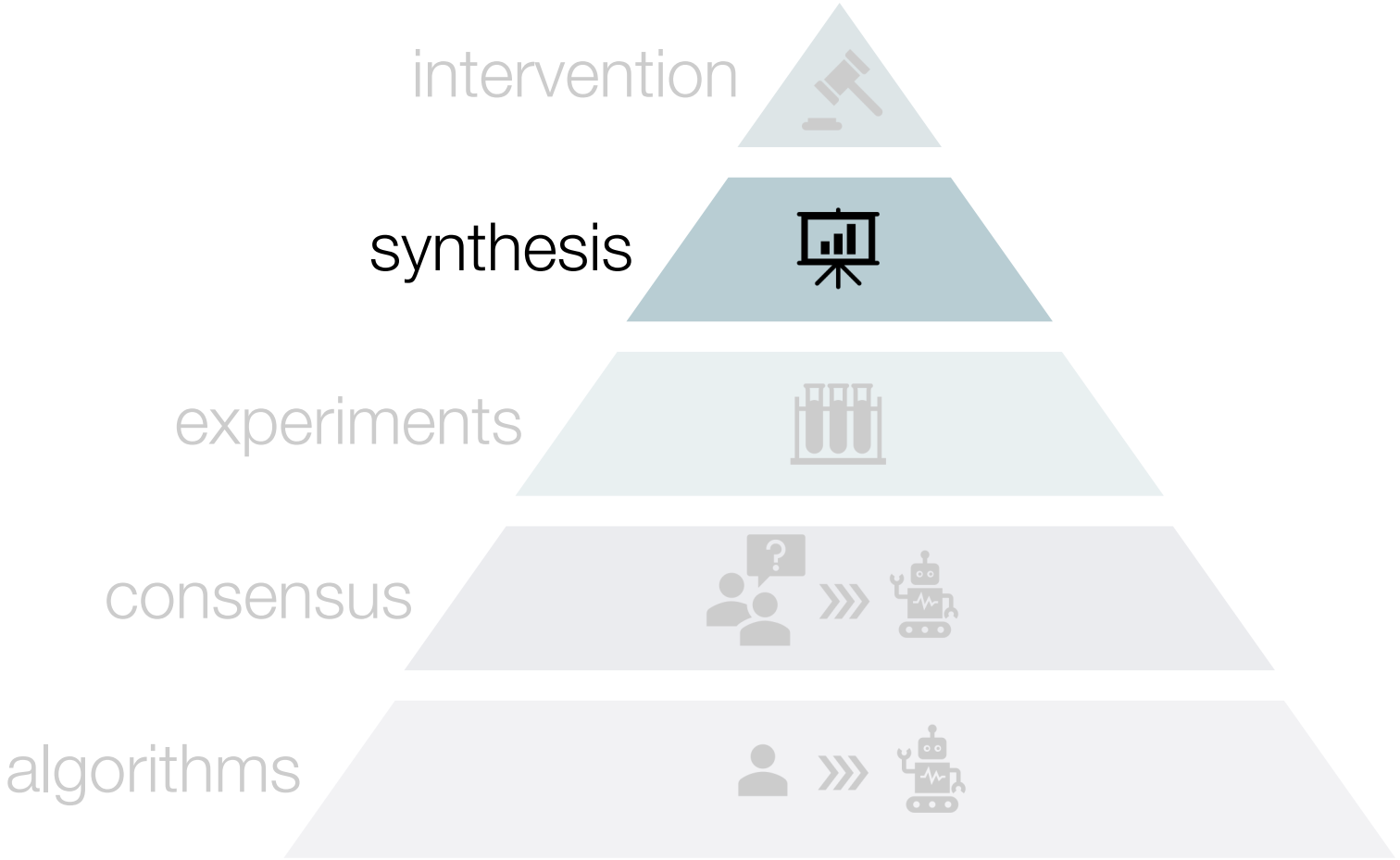
13th Bernoulli Lecture for the Behavioral Sciences

Is it time to question standard thinking on the economy, climate change, and human happiness?

Prof. Dr. Andrew Oswald
Professor of Economics and Behavioural Science,
University of Warwick

The Lecture is free and open to the public.

Wednesday, May 7, 2025, 18:15-19:45
Bernoullianum, Grosser Hörsaal
Bernoullistr. 30, 4056 Basel


intervention
synthesis
experiments
consensus
algorithms

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

HOW WOULD WE KNOW IF VACCINES CAUSE AUTISM?

What kind of evidence (if any) would it take to convince you?


EARLY REPORT

Early report

Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children

A J Wakefield, S H Murch, A Anthony, J Linnell, D M Casson, M Malik, M Berelowitz, A P Dhillon, M A Thomson, P Harvey, A Valentine, S E Davies, J A Walker-Smith

RETRACTED

Summary

Introduction

Patients and methods

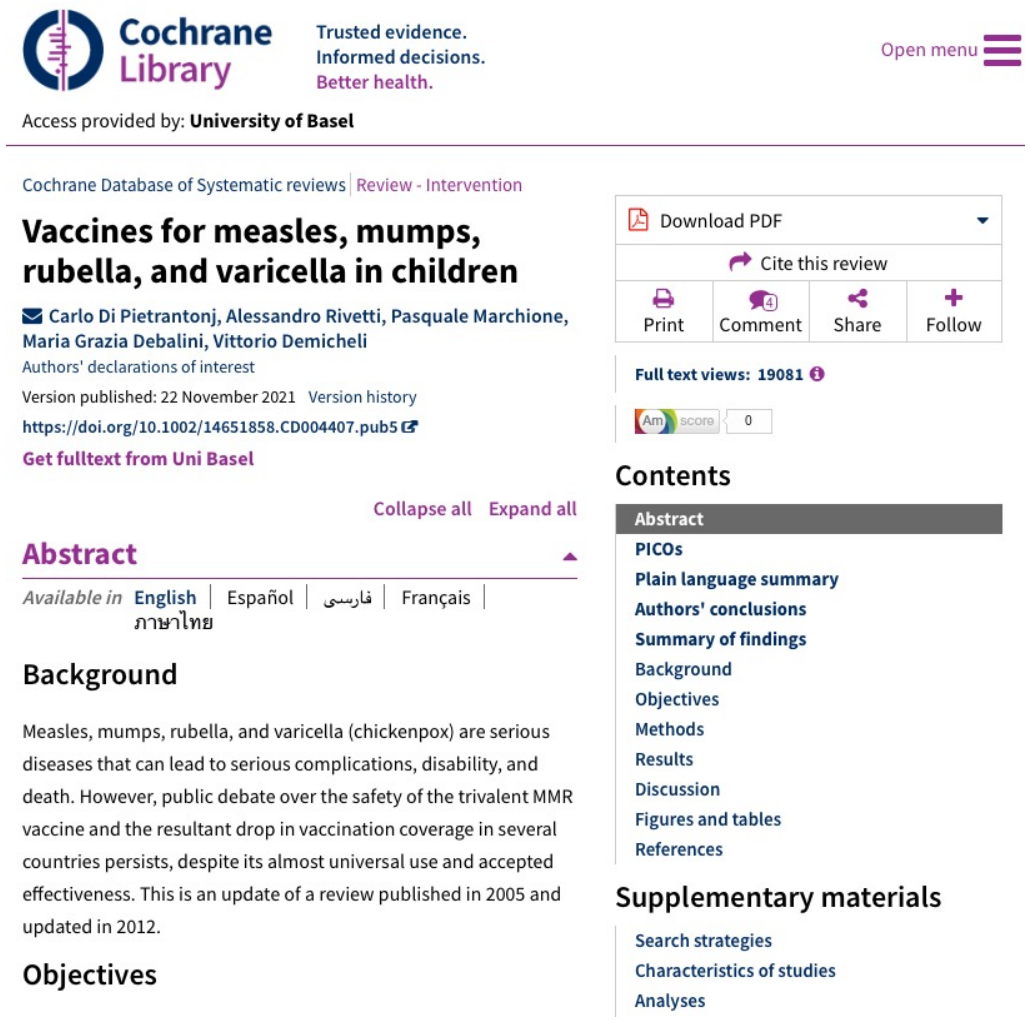
Laboratory investigations

THE LANCET

637

In 1998, a study led by Andrew Wakefield and published in *The Lancet* suggested a possible link between the MMR (measles, mumps, and rubella) vaccine and the onset of autism in children. Although based on only 12 cases, the study received widespread media attention and sparked public fear about vaccine safety. Subsequent investigations revealed serious ethical breaches, undisclosed financial conflicts of interest, and deliberate data manipulation. Extensive research has since shown no connection between the MMR vaccine and autism. The study was fully retracted in 2010, and Wakefield was stripped of his medical license. This case is now widely cited as an example of scientific fraud and its long-lasting impact on public trust in science and medicine.

https://en.wikipedia.org/wiki/Lancet_MMR_autism_fraud



Cochrane Library
Trusted evidence.
Informed decisions.
Better health.

Open menu

Access provided by: **University of Basel**

Cochrane Database of Systematic reviews | Review - Intervention

Vaccines for measles, mumps, rubella, and varicella in children

Carlo Di Pietrantonj, Alessandro Rivetti, Pasquale Marchione, Maria Grazia Debalini, Vittorio Demicheli

Authors' declarations of interest

Version published: 22 November 2021 Version history

https://doi.org/10.1002/14651858.CD004407.pub5

Get fulltext from Uni Basel

Collapse all Expand all

Abstract

Available in English | Español | فارسی | Français | ภาษาไทย

Background

Measles, mumps, rubella, and varicella (chickenpox) are serious diseases that can lead to serious complications, disability, and death. However, public debate over the safety of the trivalent MMR vaccine and the resultant drop in vaccination coverage in several countries persists, despite its almost universal use and accepted effectiveness. This is an update of a review published in 2005 and updated in 2012.

Objectives

Download PDF

Cite this review

Print | Comment | Share | Follow

Full text views: 19081

Am score 0

Contents

- Abstract
- PICOs
- Plain language summary
- Authors' conclusions
- Summary of findings
- Background
- Objectives
- Methods
- Results
- Discussion
- Figures and tables
- References

Supplementary materials

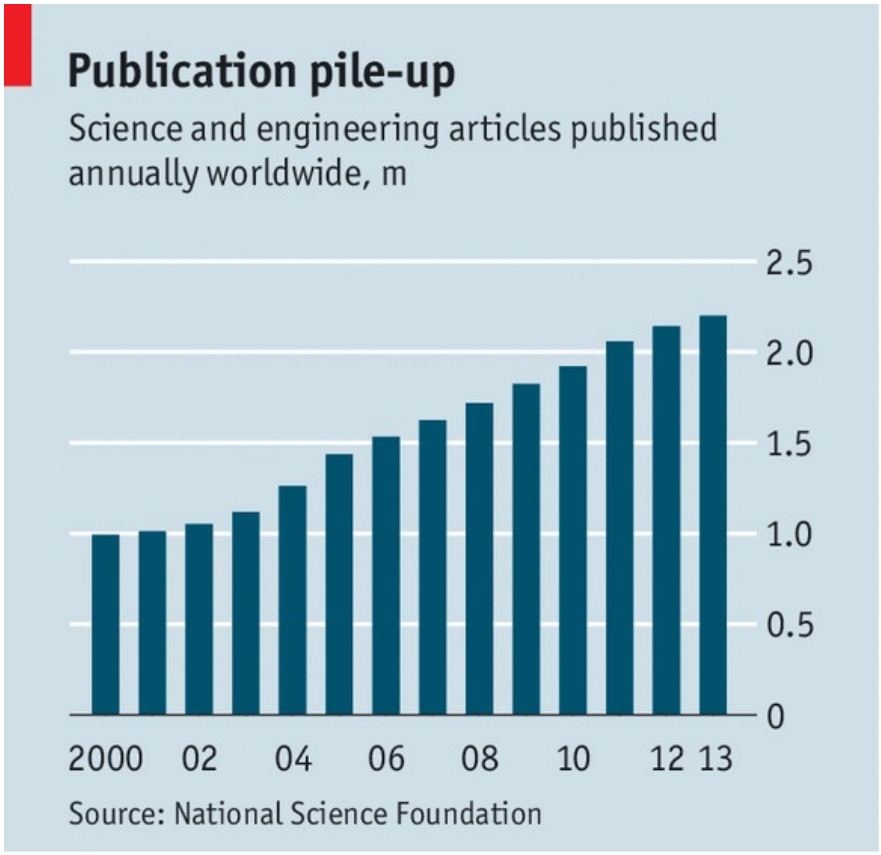
- Search strategies
- Characteristics of studies
- Analyses

Di Pietrantonj et al. reviewed the effectiveness and safety of the MMR (measles, mumps, rubella) vaccine in children up to 15 years old. It included 138 studies covering over 23 million children. The researchers searched multiple major databases up to May 2019 and included randomized controlled trials, cohort studies, case-control studies, and other observational designs. Outcomes measured were vaccine effectiveness (preventing disease) and a wide range of potential adverse effects. The authors also assessed the certainty of evidence. The review concluded that MMR vaccines are highly effective and safe, with no evidence supporting an association with autism (moderate confidence) or other serious long-term harms.

Di Pietrantonj, C., Rivetti, A., Marchione, P., Debalini, M. G., & Demicheli, V. (2021). Vaccines for measles, mumps, rubella, and varicella in children. Cochrane Database of Systematic Reviews, 2021(11). https://doi.org/10.1002/14651858.CD004407.pub5

Why research synthesis matters…

Synthesis as a way to deal with information explosion



- 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

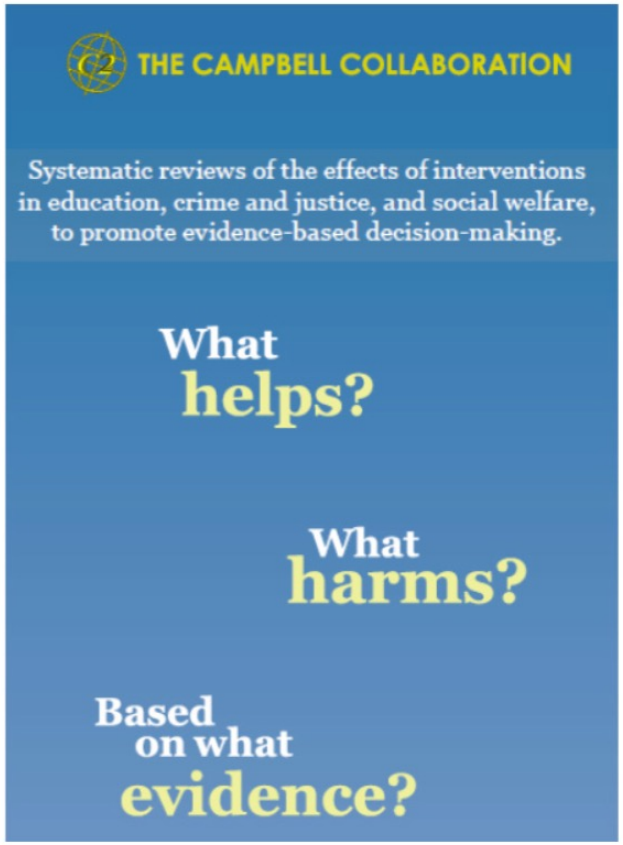
- Origin of term “meta-analysis” (Glass, 1976)
- Textbooks: Light & Pillemer (1984), Hedges & Olkin (1985)
- Evidence-based libraries: Cochrane, Campbell
- Guidelines, guidelines, guidelines (CONSORT, PRISMA)…

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

THE COCHRANE COLLABORATION



THE CAMPBELL COLLABORATION

www.cochrane.org

www.campbellcollaboration.org

1993

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 *a priori* methodological and analytical approach of the review

PRISMA-P Group, Moher, D., Shamseer, L., Clarke, M., Ghersi, 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.

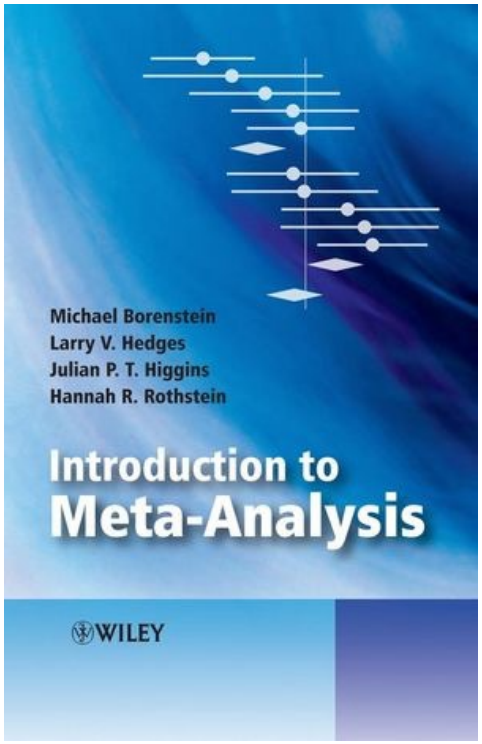


Table 3.1 Roadmap of formulas in subsequent chapters.

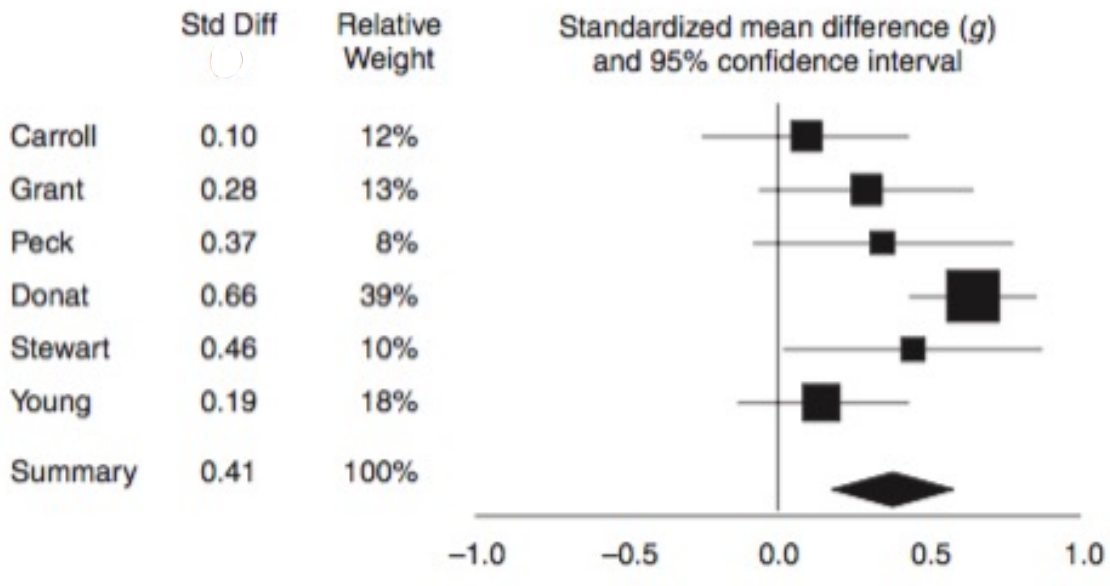
Effect sizes based on means (Chapter 4)
Raw (unstandardized) mean difference (*D*)
Based on studies with independent groups
Based on studies with matched groups or pre-post designs
Standardized mean difference (*d* or *g*)
Based on studies with independent groups
Based on studies with matched groups 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 (δ) from studies that used two independent groups as

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

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

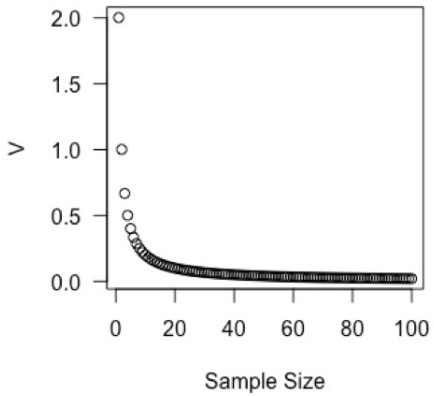
$$S_{within} = \sqrt{\frac{(n_1 - 1)S_1^2 + (n_2 - 1)S_2^2}{n_1 + n_2 - 2}} \quad (4.19)$$

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)

Bornstein et al. (2009, Chapter 4)

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

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

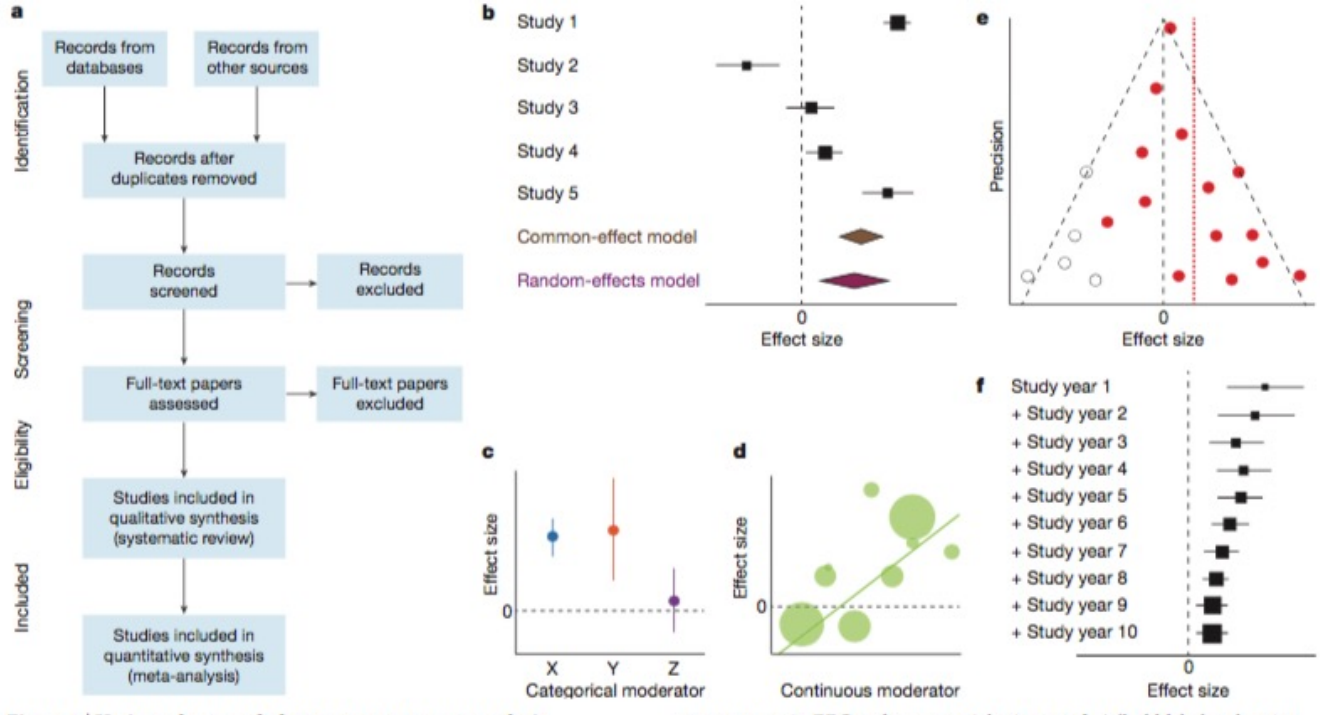
and the estimated standard error of the summary effect is then the square root of the variance,

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

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.

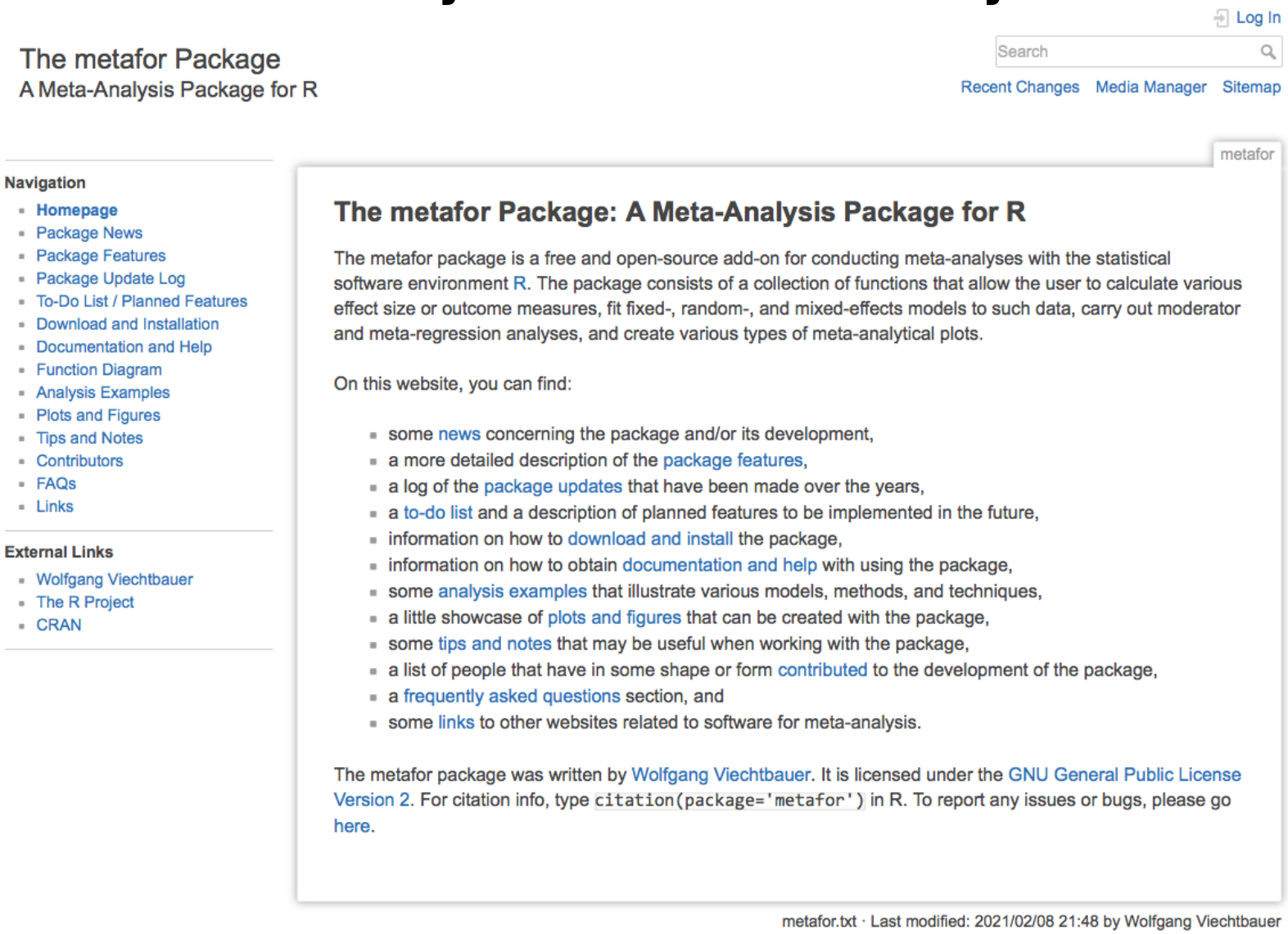
Bornstein et al. (2009, Chapter 11)

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



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

Tricco, A. C., Antony, J., Zarin, W., Strifler, L., Ghassemi, M., Ivory, J., et al. (2015). A scoping review of rapid review methods. *BMC Medicine*, *13*(1), 224. http://doi.org/10.1186/s12916-015-0465-6

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."

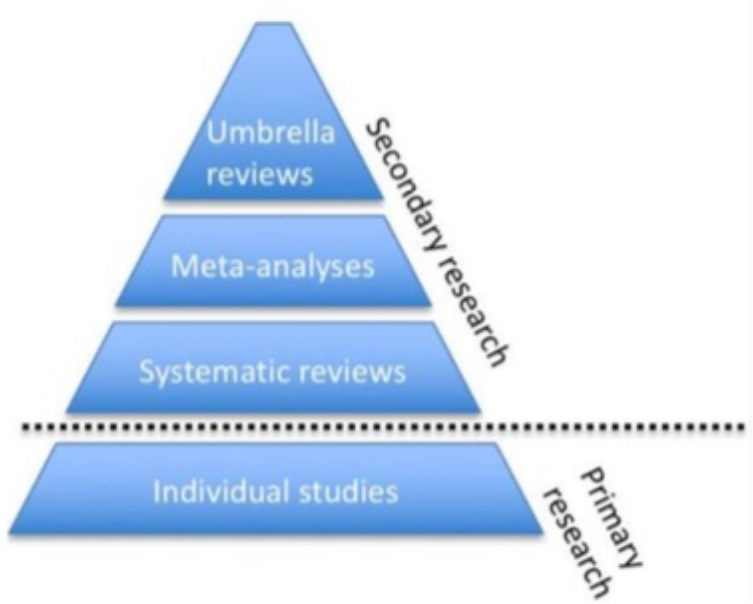


Figure 1 Hierarchy of evidence synthesis methods.

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			✓
		Exclude nonrandomised participants from trial IPD			✓
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)	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			✓
		Prespecify any reasonable participant exclusions and apply consistently across trials			✓
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)	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 and important for our confidence in policy decisions (e.g., vaccination).
- **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.