

Evidence-based Decision Making Synthesis

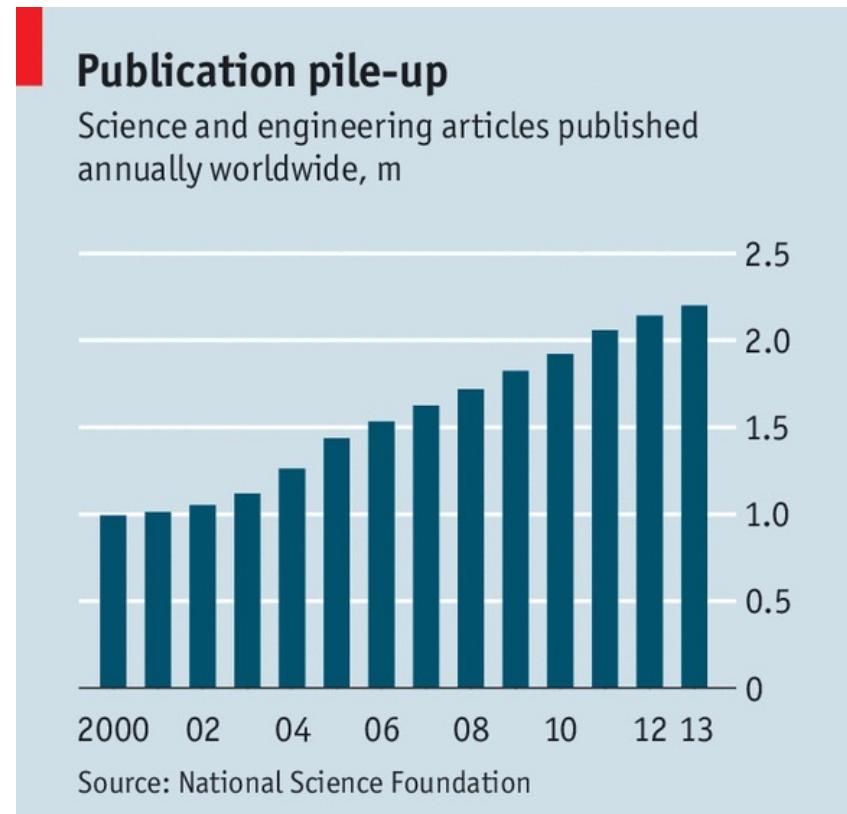
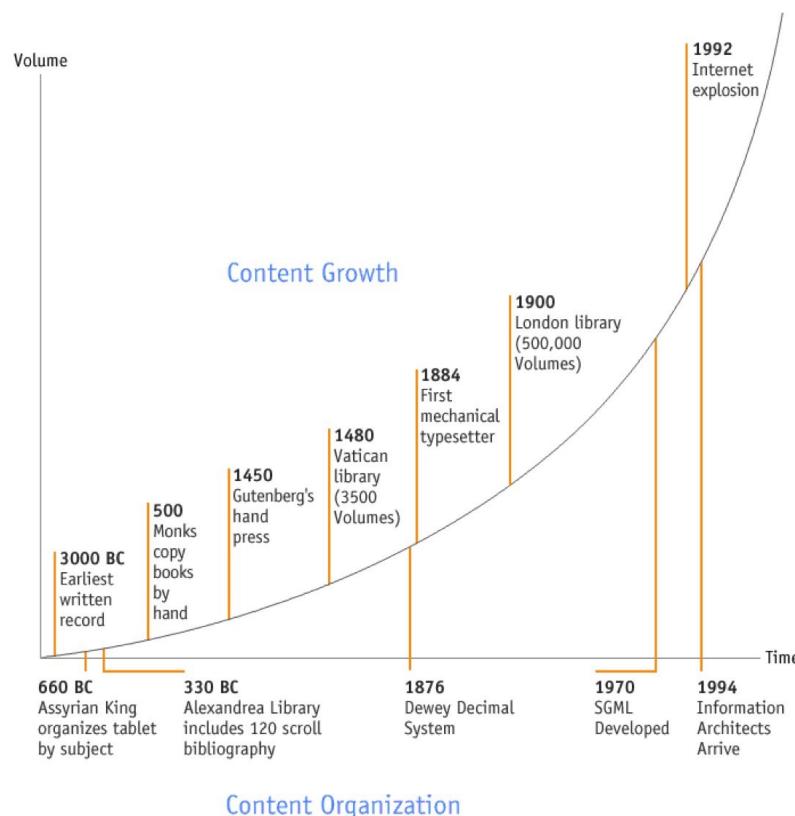
Rui Mata, FS 2023

Goals

- understand the relevance of research synthesis and be able to sketch its brief history
- define key terms associated with research synthesis (i.e., systematic review, meta-analysis, protocol)
- consider limitations of research syntheses

Why research synthesis matters...

Information Explosion



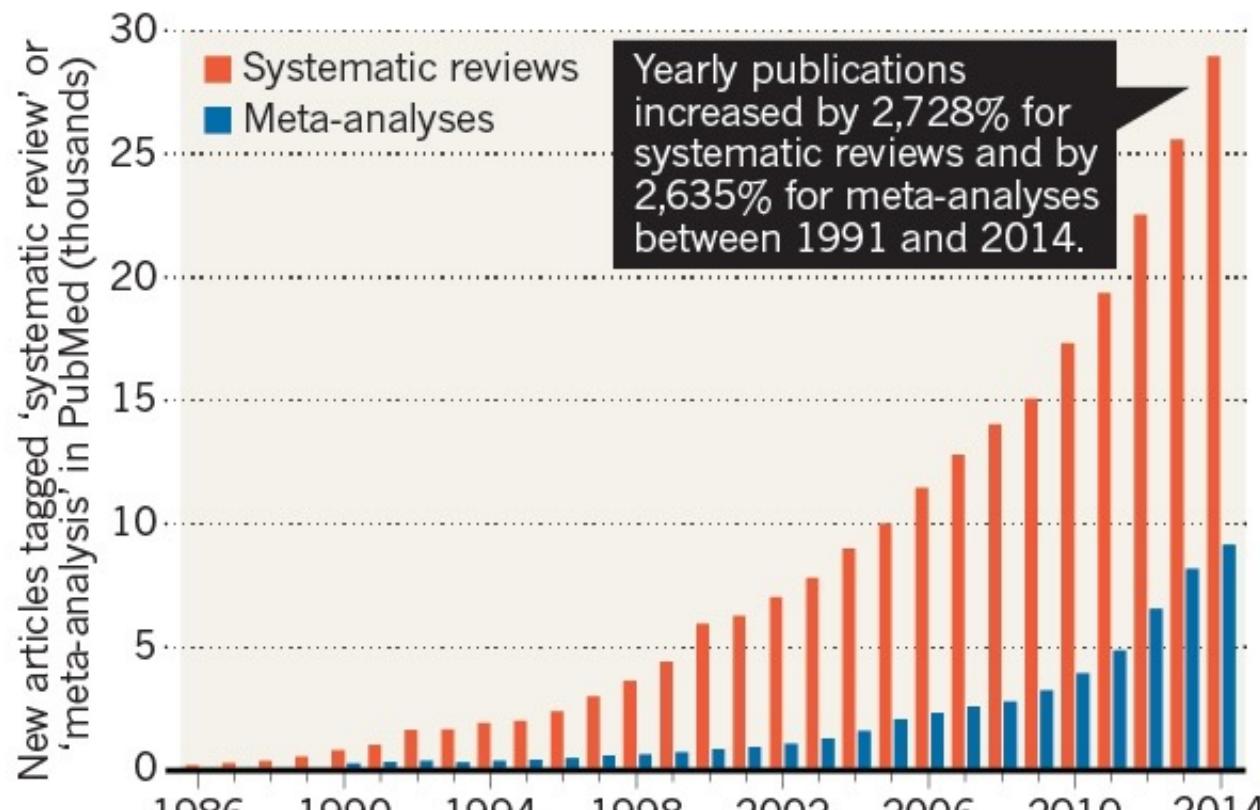
Economist.com

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

Why research synthesis matters...

META MASS PRODUCTION

The number of systematic reviews and meta-analyses published each year has proliferated since 1986.



A systematic review analyses and compiles all papers, and sometimes unpublished work, on a topic.
A meta-analysis is a systematic review that combines data from multiple papers.

©nature

<https://www.nature.com/news/mass-production-of-review-articles-is-cause-for-concern-1.20617>

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: Hedges & Olkin (1985), Light & Pillemer (1984)
- EBM movement: 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

1996: QUOROM (QUality Of Reporting Of Meta-analyses);
see also (CONSORT, Consolidated Standards of Reporting Trials)

1999: PRISMA (Preferred Reporting Items for Systematic
Reviews and Meta-analyses)

2015: PRISMA-P (Preferred Reporting Items for Systematic
Reviews and Meta-Analysis Protocols)

A brief history of research synthesis



THE COCHRANE
COLLABORATION

 THE COCHRANE LIBRARY
Independent high-quality evidence for health care decision making



How do you know if one healthcare intervention works better than another, or if it will do more harm than good?

The Cochrane Library enables those involved with healthcare decisions to keep up-to-date with all the latest evidence

Go to www.thecochranelibrary.com to discover this essential resource today

www.cochrane.org

1993

 THE CAMPBELL COLLABORATION

Systematic reviews of the effects of interventions in education, crime and justice, and social welfare, to promote evidence-based decision-making.

What helps?

What harms?

Based on what evidence?

www.campbellcollaboration.org

1999



THE CAMPBELL
COLLABORATION

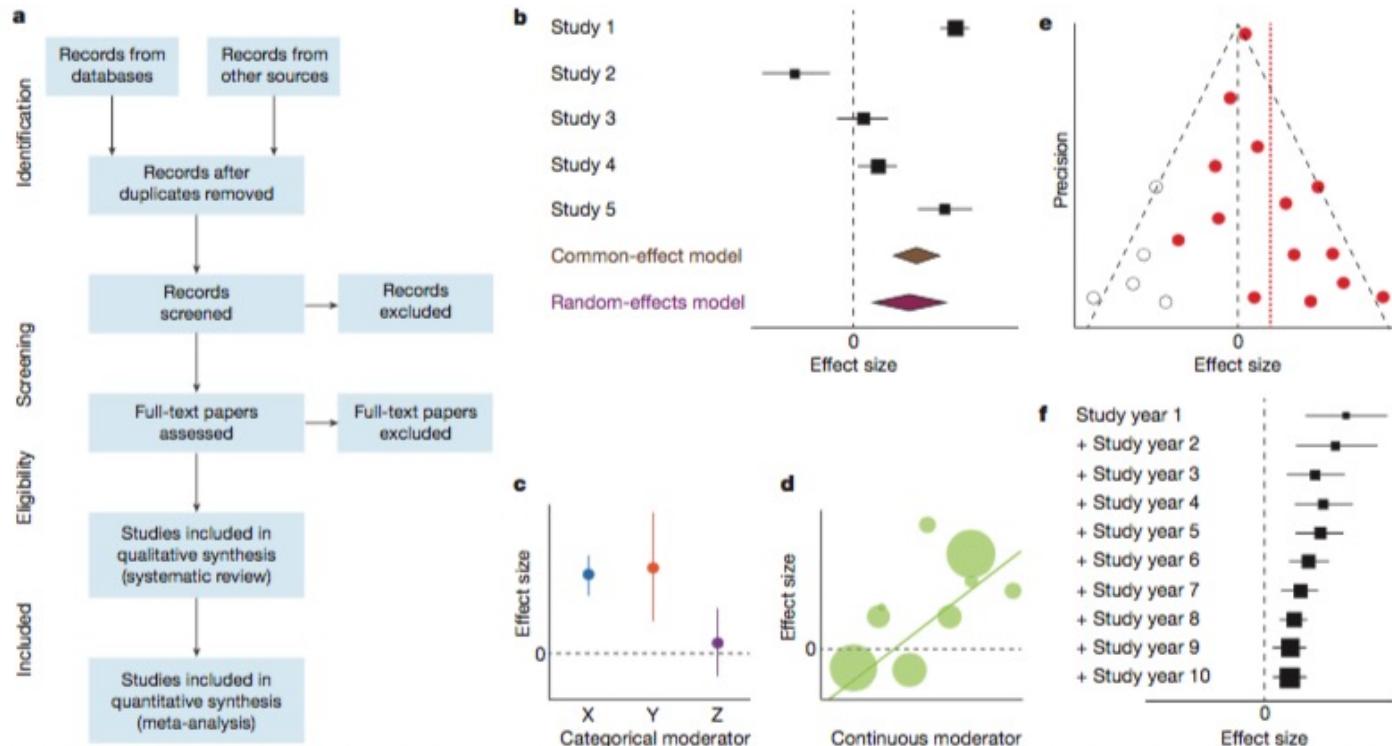
Definitions

Table 2 PRISMA-P terminology

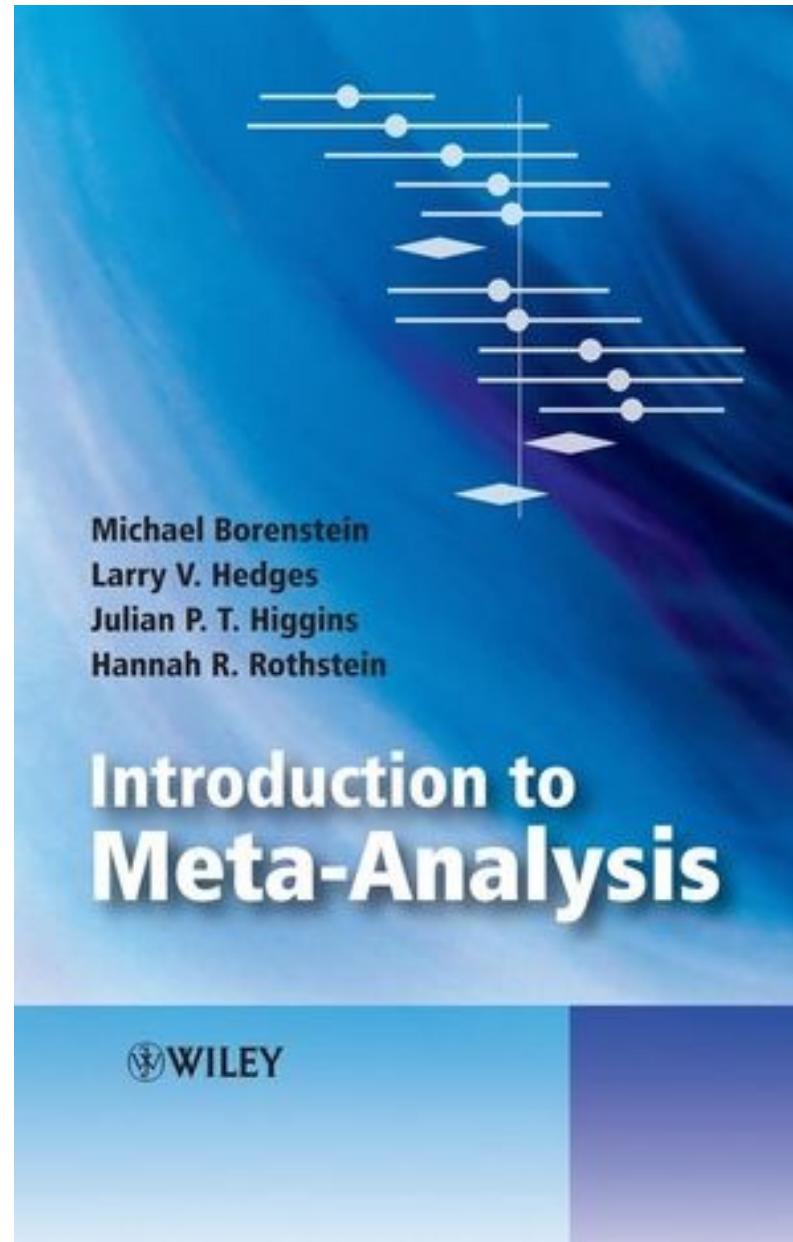
Term	Definition
Systematic review	A systematic review attempts to collate all relevant evidences that fits pre-specified eligibility criteria to answer a specific research question. It uses explicit, systematic methods to minimize bias in the identification, selection, synthesis, and summary of studies. 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., 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>

Happy 40th, 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>



Effect sizes

Effect size 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.

Bornstein et al. (2009) give a roadmap of formulas and examples for different effect sizes as do others

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

Meta-analysis (based on mean differences)

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

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

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,

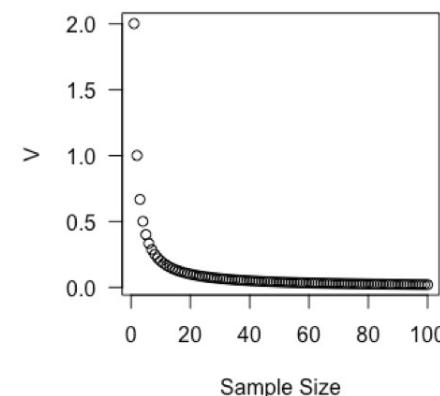
$$S_{\text{within}} = \sqrt{\frac{(n_1 - 1)S_1^2 + (n_2 - 1)S_2^2}{n_1 + n_2 - 2}} \quad (4.19)$$

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)

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

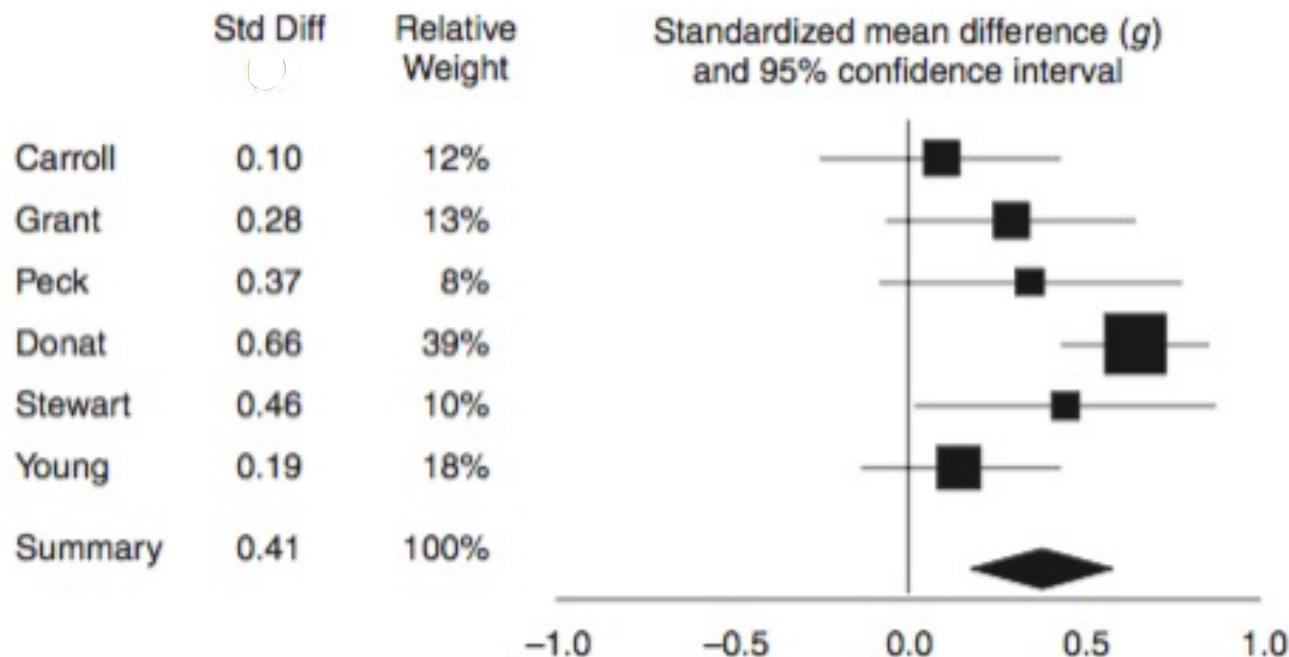
$$V_M = \frac{1}{\sum_{i=1}^k W_i}, \quad (11.4)$$

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.

Meta-analysis



Meta-analysis in practice...

The metafor Package
A Meta-Analysis Package for R

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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/>

Summary

- research synthesis can be helpful in dealing with information explosion and quantification of effects of interest
- the history of research synthesis is defined by a progressive standardisation through the development of terminology (i.e., systematic review, meta-analysis), guidelines (e.g., PRISMA), and procedures with the goal of increasing clarity, transparency, and reduce bias (e.g., transparent exclusion criteria, protocols)
- 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)

Summary (of previous session)

- research synthesis can be helpful in dealing with information explosion and quantification of effects of interest
- the history of research synthesis is defined by a progressive standardisation through the development of terminology (i.e., systematic review, meta-analysis), guidelines (e.g., PRISMA), and procedures with the goal of increasing clarity, transparency, and reduce bias (e.g., transparent exclusion criteria, protocols)
- 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)

Goals

- Discuss the use of guidelines (PRISMA and PRISMA-P) and their importance
- Not all research synthesis is created equal: types of research synthesis
- Discuss limitations of research synthesis
- Discuss (positive) examples of research synthesis

Definitions

Table 1 PROSPERO and PRISMA-P

Definition and objective	
PROSPERO: International Prospective Register of Systematic Reviews	An online portal through which to register the intention to conduct a systematic review, with health-related outcomes, before it is initiated [16]. One of the main goals of PROSPERO is to make the intent of systematic reviews known before they are conducted in order to reduce the unplanned duplication of systematic reviews [15]. In addition, by requiring the documentation of <i>a priori</i> methods, the register facilitates increased transparency in the review process by allowing readers of systematic reviews to compare methods, outcomes, and analyses carried out with those planned in advance and judge whether such changes impact the results of a review.
PRISMA-P: Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols	A guideline to help authors prepare protocols for planned systematic reviews and meta-analyses that provides them with a minimum set of items to be included in the protocol. A protocol is intended to provide the rationale for the review and pre-planned methodological and analytic approach, prior to embarking on a review. Investigators should prepare a review protocol in advance of registering it in PROSPERO so that details requiring further consideration may be thought through in advance, avoiding the need for multiple amendments to registration information. PRISMA-P items have been derived largely from the PRISMA checklist and items of the PROSPERO register, in order to facilitate seamless registration.

<https://www.crd.york.ac.uk/PROSPERO/>

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>

PRISMA and PRISMA-P Guidelines

Box 2 |: Helping to develop the research question(s): the PICOS approach

Formulating relevant and precise questions that can be answered in a systematic review can be complex and time consuming. A structured approach for framing questions that uses five components may help facilitate the process. This approach is commonly known by the acronym “PICOS” where each letter refers to a component: the patient population or the disease being addressed (P), the interventions or exposure (I), the comparator group (C), the outcome or endpoint (O), and the study design chosen (S).¹⁸⁶ Issues relating to PICOS affect several PRISMA items (items 6, 8, 9, 10, 11, and 18).

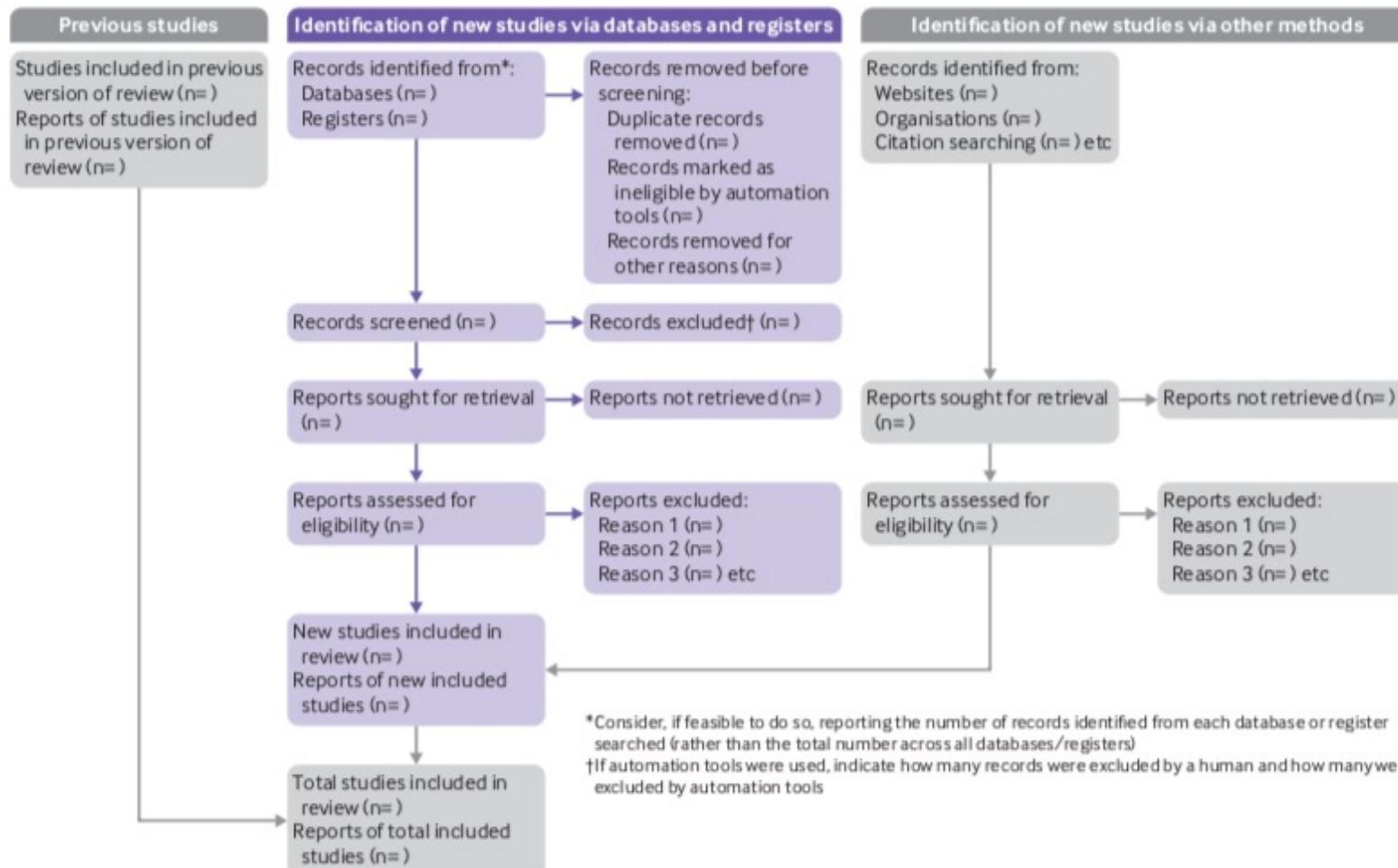
- **P**—Providing information about the population requires a precise definition of a group of participants (often patients), such as men over the age of 65 years, their defining characteristics of interest (often disease), and possibly the setting of care considered, such as an acute care hospital.
- **I**—The interventions (exposures) under consideration in the systematic review need to be transparently reported. For example, if the reviewers answer a question regarding the association between a woman’s prenatal exposure to folic acid and subsequent offspring’s neural tube defects, reporting the dose, frequency, and duration of folic acid used in different studies is likely to be important for readers to interpret the review’s results and conclusions. Other interventions (exposures) might include diagnostic, preventive, or therapeutic treatments; arrangements of specific processes of care; lifestyle changes; psychosocial or educational interventions; or risk factors.
- **C**—Clearly reporting the comparator (control) group intervention(s)—such as usual care, drug, or placebo—is essential for readers to fully understand the selection criteria of primary studies included in the systematic review, and might be a source of heterogeneity investigators have to deal with. Comparators are often poorly described. Clearly reporting what the intervention is compared with is important and may sometimes have implications for the inclusion of studies in a review—many reviews compare with “standard care,” which is otherwise undefined; this should be properly addressed by authors.
- **O**—The outcomes of the intervention being assessed—such as mortality, morbidity, symptoms, or quality of life improvements—should be clearly specified as they are required to interpret the validity and generalisability of the systematic review’s results.
- **S**—Finally, the type of study design(s) included in the review should be reported. Some reviews include only reports of randomised trials, whereas others have broader design criteria and include randomised trials and certain types of observational studies. Still other reviews, such as those specifically answering questions related to harms, may include a wide variety of designs ranging from cohort studies to case reports. Whatever study designs are included in the review, these should be reported.

Independently from how difficult it is to identify the components of the research question, the important point is that a structured approach is preferable, and this extends beyond systematic reviews of effectiveness. Ideally the PICOS criteria should be formulated *a priori*, in the systematic review’s protocol, although some revisions might be required because of the iterative nature of the review process. Authors are encouraged to report their PICOS criteria and whether any modifications were made during the review process. A useful example in this realm is the appendix of the “systematic reviews of water fluoridation” undertaken by the Centre for Reviews and Dissemination.¹⁸⁷

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>

PRISMA 2020



Page, M. J., McKenzie, J. E., Bossuyt, P. M., Boutron, I., Hoffmann, T. C., Mulrow, C. D., et al. (2021). The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. *Bmj*, 372, n71. <http://doi.org/10.1136/bmj.n71>

PRISMA and PRISMA-P Guidelines: Benefits

Table 4 Proposed stakeholders, actions, and potential benefits for supporting adherence to PRISMA-P

Stakeholder	Proposed action	Potential benefits
Funders	Promote or mandate adherence to PRISMA-P or use PRISMA-P as a template for systematic review proposals for grant applications	Improved quality, completeness, and consistency of systematic review proposal submissions Standardized protocol content will improve peer review efficiency and investigator understanding of requirements
Systematic review authors/ groups/organizations	Use/adhere to PRISMA-P during protocol development	Improved quality, completeness, and consistency of protocol content
	groups/organizations	Enables reviewers to anticipate and avoid future changes to review methods (i.e., outcomes)
		Increased awareness of minimum content for protocol reporting
		Improved completeness of reporting of completed reviews
PROSPERO (and other review registries)	Encourage the development of PRISMA-P-based protocols	Improved quality of registry entries
Practice guideline developers	Use PRISMA-P to gauge the completeness of protocols and facilitate detection of selective reporting when considering reviews for guideline inclusion	Improved consistency across registry entries, protocols, and systematic reviews
Policymakers	Advocate use of PRISMA-P by those funding and carrying out systematic reviews	Enables easy comparison across protocols, registry entries, and completed systematic reviews
Journal editors	Encourage compliance to PRISMA-P for authors submitting protocols for publication	May yield better quality, more complete, and more consistent reviews to inform decision-making
	Offer PRISMA-P as a template to assist in protocol writing for publication	Improved quality, completeness, and consistency of protocols over those published in journals not endorsing PRISMA-P
		Increased efficiency in protocol peer and author understanding of journal requirements
		Improved transparency and interpretation of reviews by readers
Educators	Use PRISMA-P as a training tool	Simplified teaching and grading of protocols
	Encourage adherence in students submitting protocols for coursework	Improved quality, completeness, and consistency of protocol content
Students	Develop protocols for coursework or research using PRISMA-P	Improved understanding of the minimum protocol content
		Well-trained systematic reviewer going into the workforce

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 Results of individual 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 Conclusions	25	Discuss the limitations of the scoping review process.
	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.”

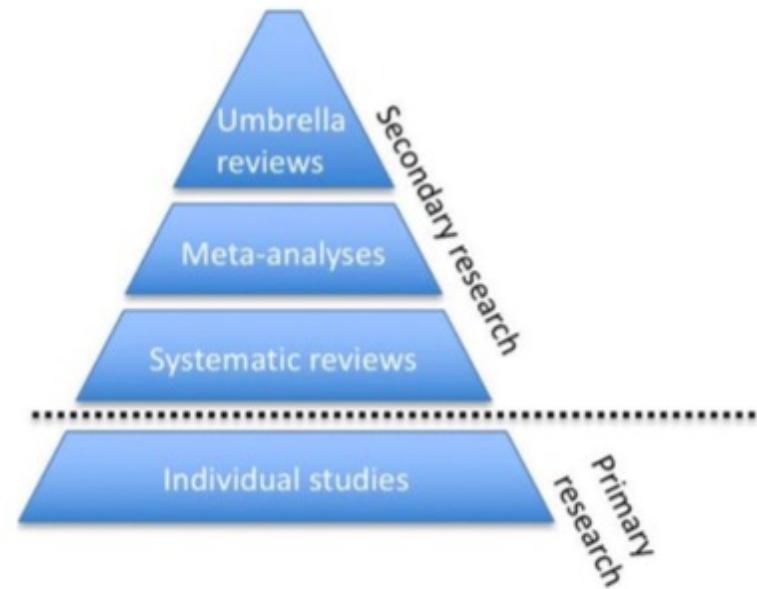


Figure 1 Hierarchy of evidence synthesis methods.

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 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	✓ ✓	

A long history of critique of research synthesis

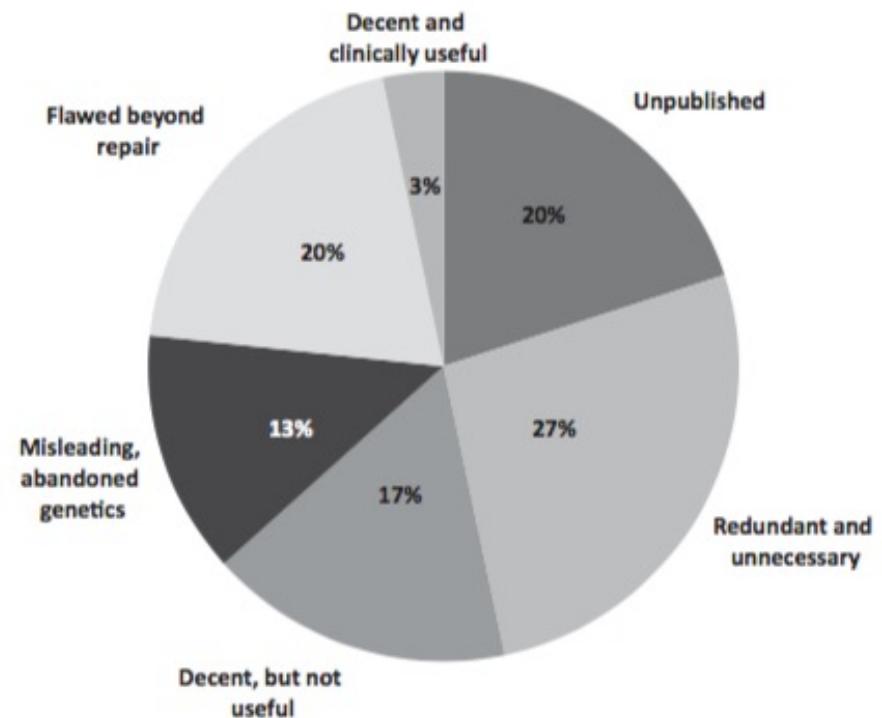
- Garbage-in, garbage out (“mega-silliness”, Eysenck, 1978)
- “Instead of promoting evidence-based medicine and health care, these instruments often serve mostly as easily produced publishable units or marketing tools” (Ioannidis, 2016)

A long history of critique of research synthesis

Policy Points:

- Currently, there is massive production of unnecessary, misleading, and conflicted systematic reviews and meta-analyses. Instead of promoting evidence-based medicine and health care, these instruments often serve mostly as easily produced publishable units or marketing tools.
- Suboptimal systematic reviews and meta-analyses can be harmful given the major prestige and influence these types of studies have acquired.
- The publication of systematic reviews and meta-analyses should be realigned to remove biases and vested interests and to integrate them better with the primary production of evidence.

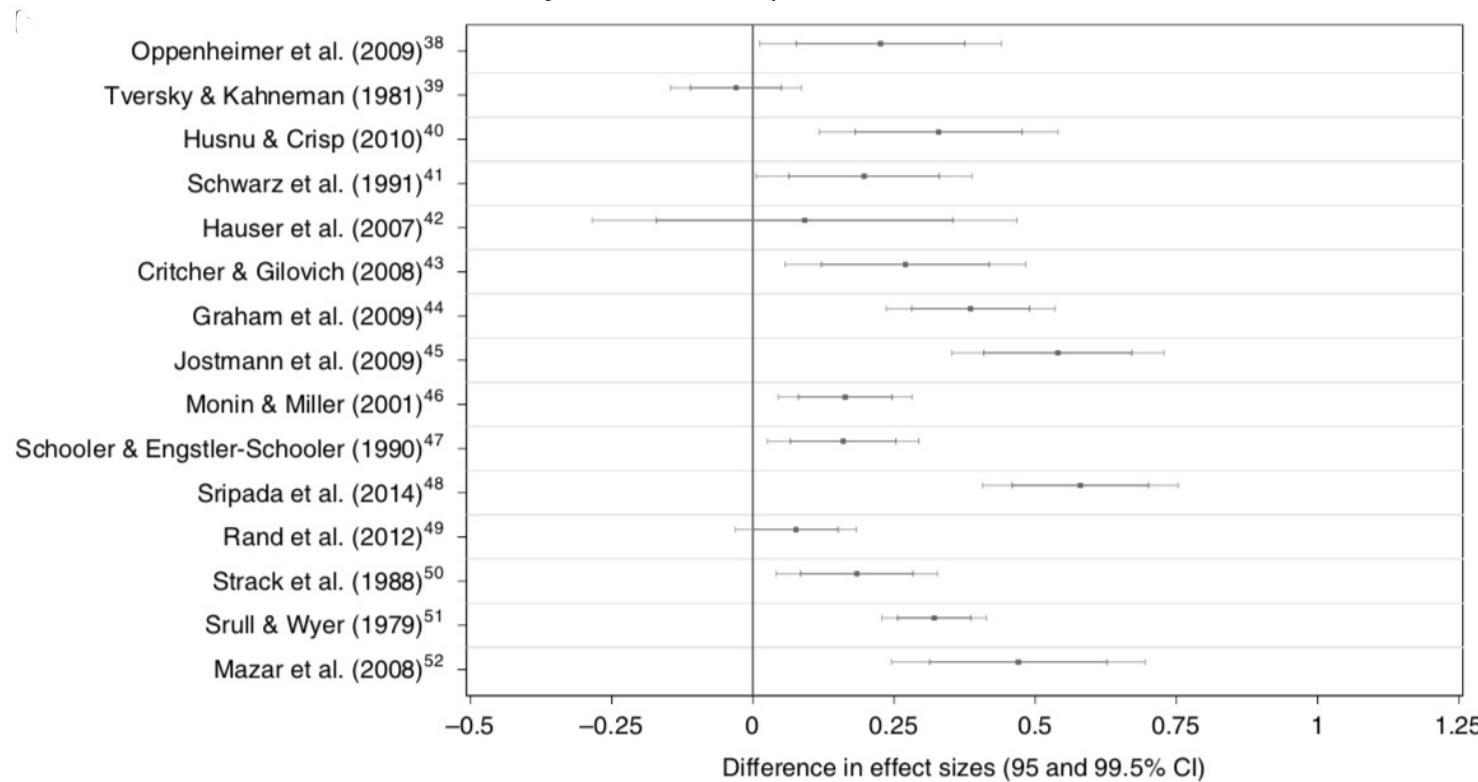
Figure 4. A Summary Overview of Currently Produced Meta-analyses



Ioannidis, J. P. A. (2016). The Mass Production of Redundant, Misleading, and Conflicted Systematic Reviews and Meta-analyses. *The Milbank Quarterly*, 94(3), 485–514. <http://doi.org/10.1111/1468-0009.12210>

Limitations of Research Synthesis

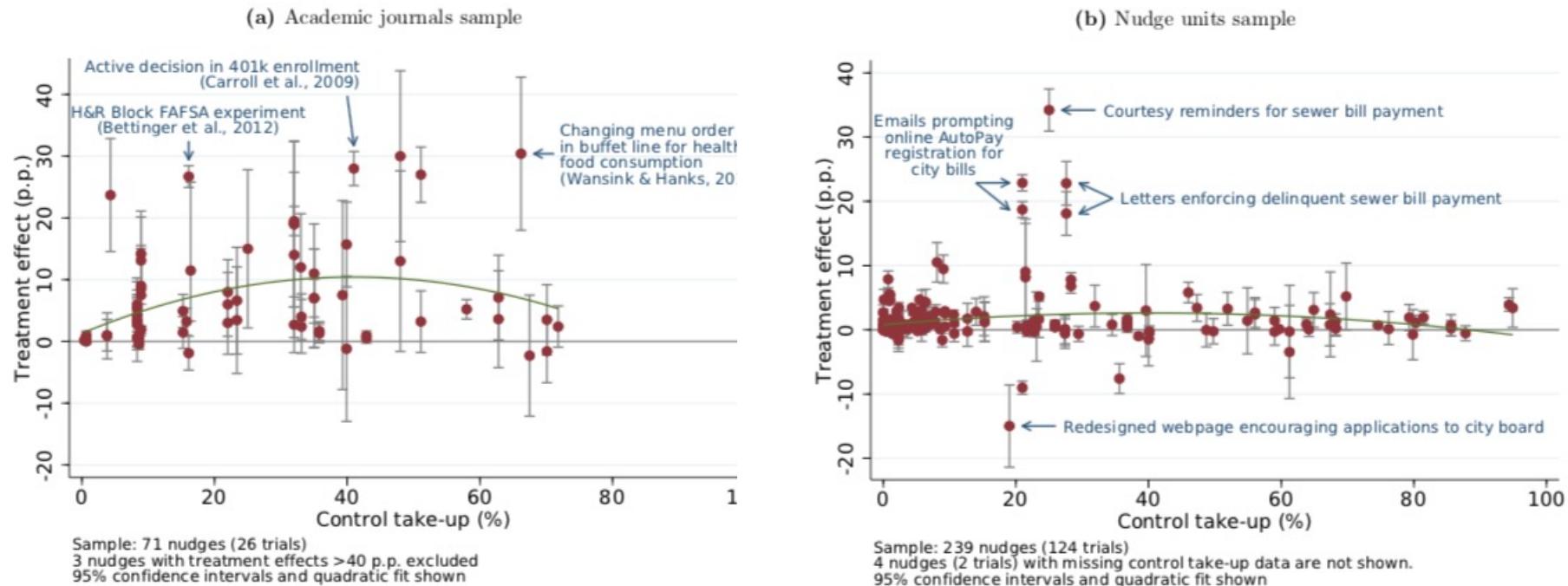
Difference between meta-analytic and replication studies effect size for 15 studies



"We find that meta-analytic effect sizes are significantly different from replication effect sizes for 12 out of the 15 meta-replication pairs. These differences are systematic and, on average, meta-analytic effect sizes are almost three times as large as replication effect sizes. We also implement three methods of correcting meta-analysis for bias, but these methods do not substantively improve the meta-analytic results." - these findings suggest that meta-analysis may not be able to adjust inflated effect sizes that arise from publication bias/selective reporting.

Kvarven, A., Strømland, E., & Johannesson, M. (2020). Comparing meta-analyses and preregistered multiple-laboratory replication projects. *Nature Human Behaviour*, 4(4), 423–434.
<http://doi.org/10.1038/s41562-019-0787-z>

Limitations of Research Synthesis



We assemble a unique data set including all trials run by two of the largest Nudge Units in the United States, including 126 RCTs covering over 23 million individuals. We compare these trials to a separate sample of nudge trials published in academic journals from two recent meta-analyses. In papers published in academic journals, the average impact of a nudge is very large – an 8.7 percentage point take-up increase over the control. In the Nudge Unit trials, the average impact is still sizable and highly statistically significant, but smaller at 1.4 percentage points. We show that a large share of the gap is accounted for by publication bias.”

Limitations of Research Synthesis

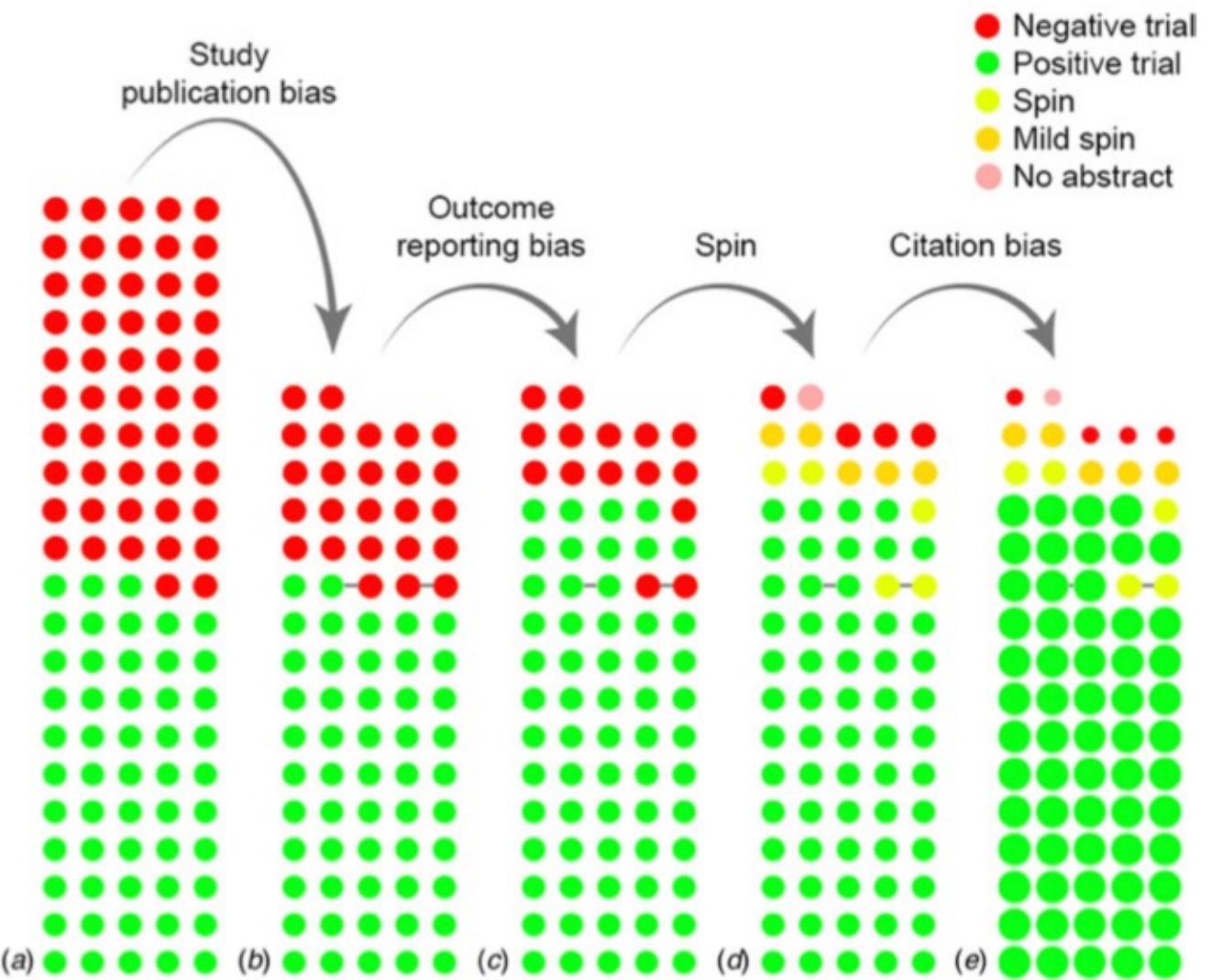


Fig. 1. The cumulative impact of reporting and citation biases on the evidence base for antidepressants. (a) displays the initial, complete cohort of trials, while (b) through (e) show the cumulative effect of biases. Each circle indicates a trial, while the color indicates the results or the presence of spin. Circles connected by a grey line indicate trials that were published together in a pooled publication. In (e), the size of the circle indicates the (relative) number of citations received by that category of studies.

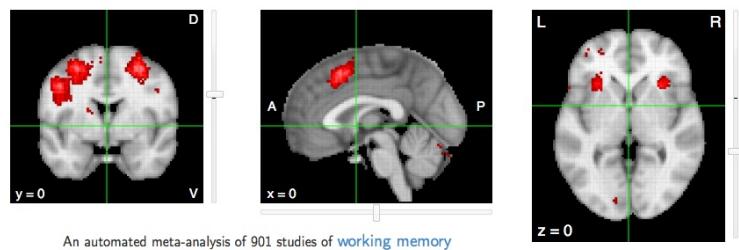
De Vries, Y. A., Roest, A. M., De Jonge, P., Cuijpers, P., Munafò, M. R., & Bastiaansen, J. A. (2018). The cumulative effect of reporting and citation biases on the apparent efficacy of treatments: The case of depression. *Psychological Medicine*, 48(15), 2453–2455. <http://doi.org/10.1017/S0033291718001873>

Future: Automatization of Research Synthesis

Neurosynth

Neurosynth is a platform for large-scale, automated synthesis of functional magnetic resonance imaging (fMRI) data.

It takes thousands of published articles reporting the results of fMRI studies, chews on them for a bit, and then spits out images that look like this:



Database Status

413429 activations reported in [11406 studies](#)

Interactive, downloadable meta-analyses of [3107 terms](#)

Functional connectivity and coactivation maps for over [150,000 brain locations](#)

<http://neurosynth.org>

Human Behaviour-Change Project

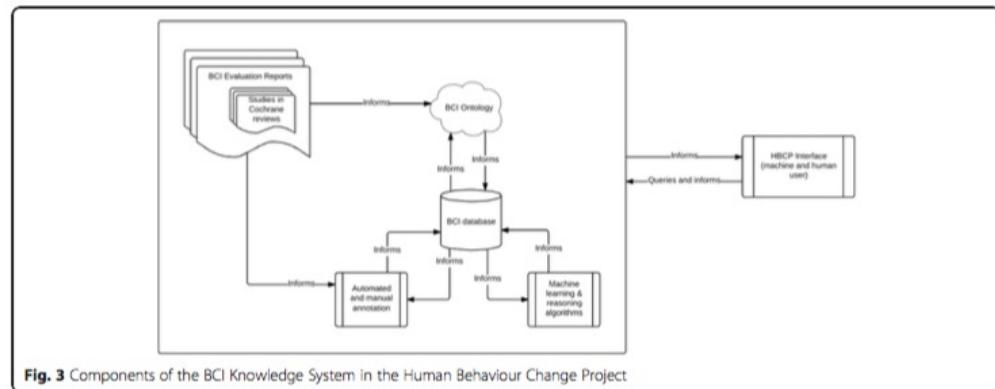
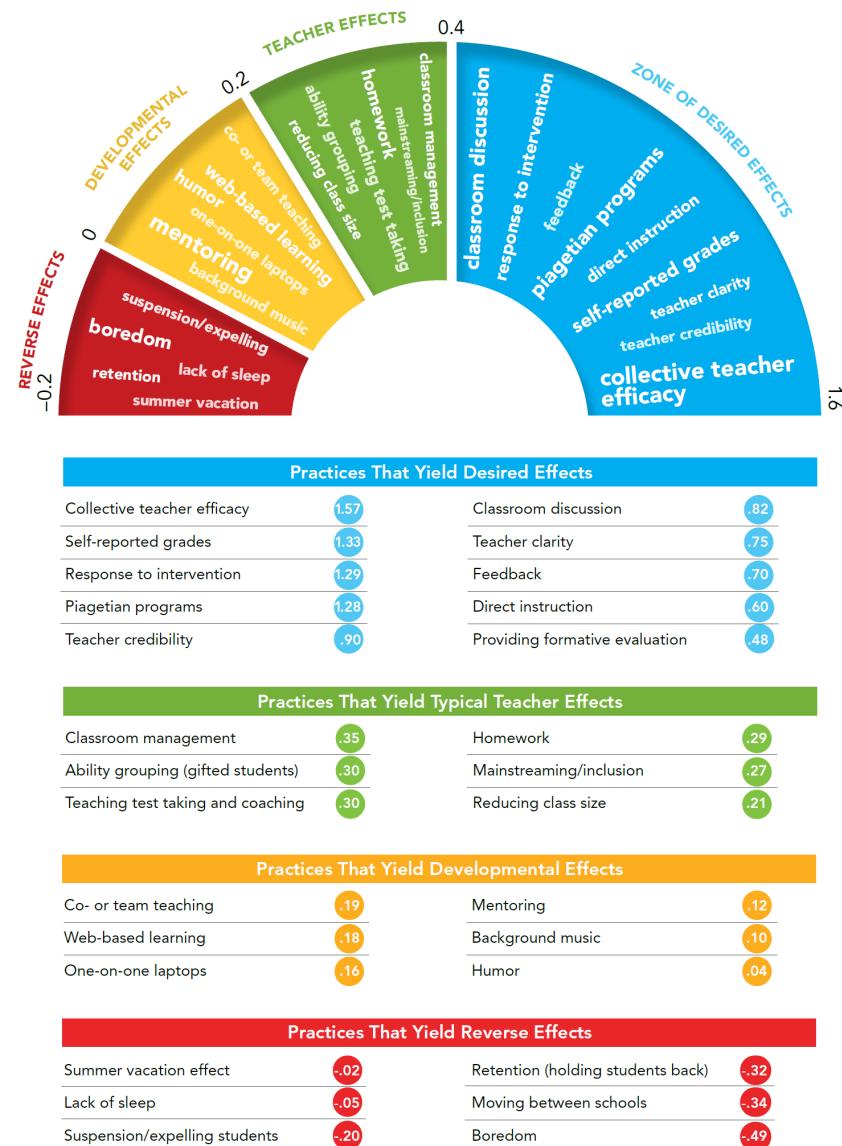
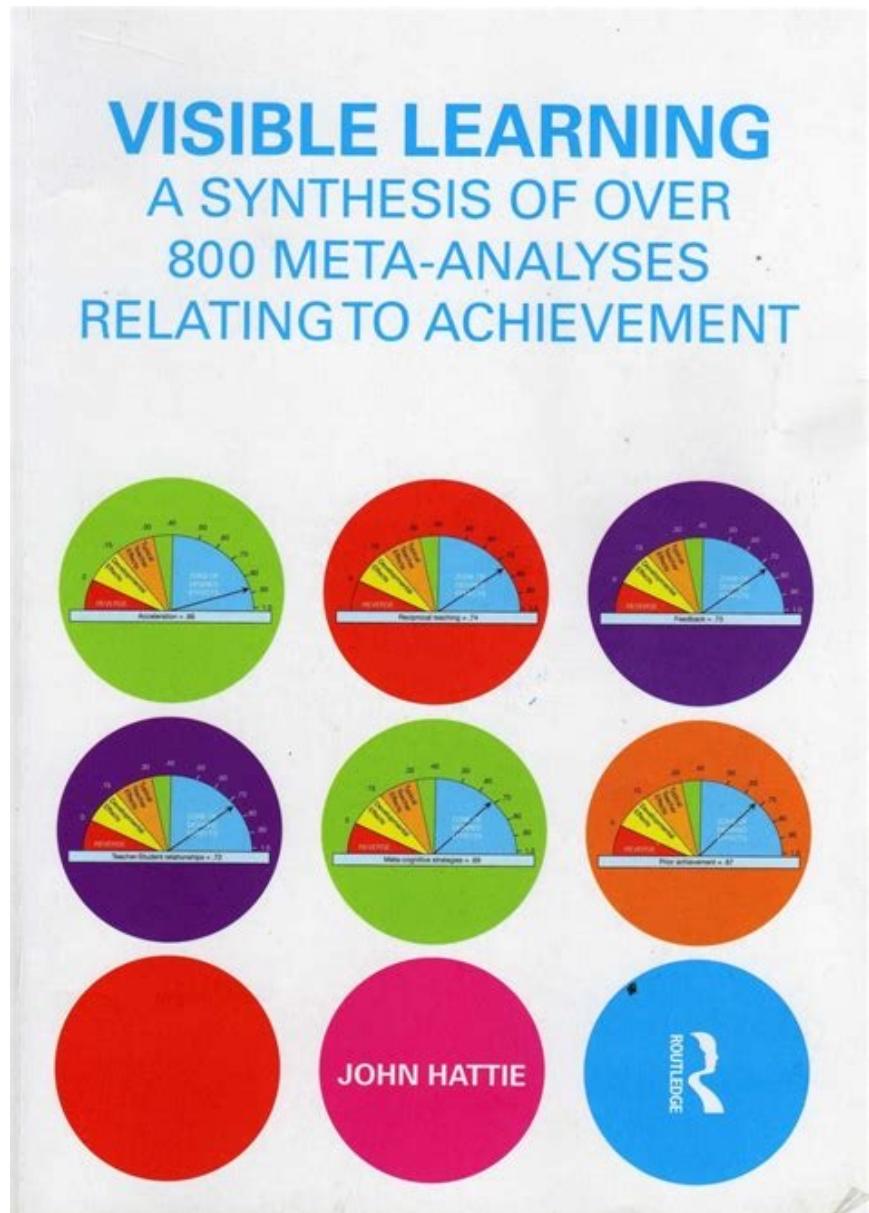


Fig. 3 Components of the BCI Knowledge System in the Human Behaviour Change Project

Yarkoni, T., Poldrack, R. A., Nichols, T. E., Van Essen, D. C., & Wager, T. D. (2011). Large-scale automated synthesis of human functional neuroimaging data. *Nature Methods*, 8(8), 665–670. <http://doi.org/10.1038/nmeth.1635>

Michie, S., Thomas, J., Johnston, M., Mac Aonghusa, P., Shawe-Taylor, J., Kelly, M. P., et al. (2017). The Human Behaviour-Change Project: harnessing the power of artificial intelligence and machine learning for evidence synthesis and interpretation, *Implementation Science*, 1–12. <http://doi.org/10.1186/s13012-017-0641-5>

[insert here your favorite example]



Variables Associated With Achievement in Higher Education: A Systematic Review of Meta-Analyses

Michael Schneider and Franzis Preckel
University of Trier

The last 2 decades witnessed a surge in empirical studies on the variables associated with achievement in higher education. A number of meta-analyses synthesized these findings. In our systematic literature review, we included 38 meta-analyses investigating 105 correlates of achievement, based on 3,330 effect sizes from almost 2 million students. We provide a list of the 105 variables, ordered by the effect size, and summary statistics for central research topics. The results highlight the close relation between social interaction in courses and achievement. Achievement is also strongly associated with the stimulation of meaningful learning by presenting information in a clear way, relating it to the students, and using conceptually demanding learning tasks. Instruction and communication technology has comparably weak effect sizes, which did not increase over time. Strong moderator effects are found for almost all instructional methods, indicating that how a method is implemented in detail strongly affects achievement. Teachers with high-achieving students invest time and effort in designing the microstructure of their courses, establish clear learning goals, and employ feedback practices. This emphasizes the importance of teacher training in higher education. Students with high achievement are characterized by high self-efficacy, high prior achievement and intelligence, conscientiousness, and the goal-directed use of learning strategies. Barring the paucity of controlled experiments and the lack of meta-analyses on recent educational innovations, the variables associated with achievement in higher education are generally well investigated and well understood. By using these findings, teachers, university administrators, and policymakers can increase the effectiveness of higher education.

Keywords: academic achievement, meta-analysis, tertiary education, instruction, individual differences

Supplemental materials: <http://dx.doi.org/10.1037/bul0000098.sup>

Table 3

Absolute Frequencies of Data Points and Percentage of Variables by Effect Size (Ordered by the Combined Frequency of Medium and Large Effects)

	Absolute frequency of data points			% of variables			
	Students ^a	Effect sizes	Variables	No effect	Small effect	Medium effect	Large effect
Overall	1,920,239	3,330	105	12	36	36	15
Instruction variables	208,711	1,595	42	5	26	45	24
Social interaction	26,860	123	5	0	0	40	60
Stimulating meaningful learning	49,272	229	9	0	22	56	22
Assessment	41,493	316	8	0	25	50	25
Presentation	46,157	354	9	0	33	33	33
Technology	29,022	401	6	17	33	50	0
Extracurricular training programs	15,907	172	5	20	40	40	0
Student variables	1,711,528	1,735	63	18	43	30	10
Intelligence and prior achievement	74,711	95	4	0	0	50	50
Strategies	133,757	343	18	11	28	50	11
Motivation	137,880	390	12	17	42	25	17
Personality	1,093,174	694	16	31	44	25	0
Context	272,006	213	13	15	77	8	0

Note. No effect = $|d| < .11$; small effect = $.11 \leq |d| < .35$; medium effect = $.35 \leq |d| < .66$; large effect = $|d| \geq .66$.

^aEstimated by replacing missing values of a meta-analysis by the median value of all meta-analyses.



Methodological resources and training

- ❖ Cochrane Handbook for Systematic Reviews of Interventions
- ❖ Methodological Expectations of Cochrane Intervention Reviews (MECIR)
- ❖ Methods Network newsletter
- ❖ Cochrane Methods Symposia
- ❖ Annual Cochrane Methods Report
- ❖ Cochrane Methodology Register

We are currently building these pages to provide a portal to a variety of resources that will identify published methodological work of interest to those involved in conducting Cochrane Reviews.

Cochrane has a long history since its beginning to develop methods and methods-related tools to improve and advance systematic review methods. Development of methods involves conducting research into methods through empirical research, simulation studies and systematic reviews of methods studies e.g. the [Methodology Review Group](#).

Finding methodological research in current databases is challenging and led to Cochrane members (Mike Clarke, Sally Hopewell and Anne Eisinga) setting up the [Cochrane Methodology Register](#). Unfortunately, this database was archived in 2012 but remains accessible.

This page will also highlight [articles of topical methodological interest](#). Our current seventeen [Methods Groups](#) highlight key methodological papers of interest year by year.

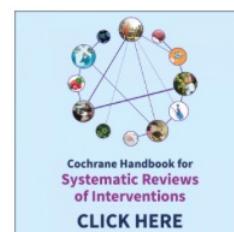
The Bias Methods Group have developed a [methods group strategy document](#)

If you have any suggestions for content for these pages or you can't find the resources you require please contact us by [email](#).

Methods Support Unit web clinic

A monthly web clinic for Cochrane authors, editors and staff

Stay connected with our Methods Network newsletter



Cochrane Handbook for Systematic Reviews of Interventions
[CLICK HERE](#)

<https://methods.cochrane.org/resources-list>

Summary

- Standardization is work in progress: Guidelines keep getting updated but the logic (e.g., ensure comprehensiveness and reproducibility, reduce bias) remains the same.
- Different types of research synthesis for different goals and contexts: systematic reviews w/ qualitative summary, meta-analyses, scoping reviews, rapid reviews, umbrella reviews, individual participant data, etc....
- Research synthesis is not a panacea and cannot provide accurate estimates of effects in the face of large reporting biases (publication bias & file-drawer problem)