# Evidence-based Decision Making: Session 8

Rui Mata, FS 2022

# Session information

Sessions take place Tuesdays, 16.15–17.45. Currently, the course is planned to be held in person but a change to an online format is possible depending on the current epidemiological situation.

| # | Date | Topic | Slides |
|---|------|-------|--------|
| 1 | 22.02.2022 | The Scientific Method(s) | pdf |
| 2 | 01.03.2022 | Algorithms | pdf |
| 3 | 22.03.2022 | Algorithms | pdf |
| 4 | 29.03.2022 | Consensus | pdf |
| 5 | 05.04.2022 | Consensus | pdf |
| 6 | 12.04.2022 | Counterfactuals | pdf |
| 7 | 19.04.2022 | Counterfactuals | pdf |
| 8 | 26.04.2022 | Synthesis | pdf |
| 9 | 03.05.2022 | Synthesis | pdf |
| 10 | 10.05.2022 | Interventions | pdf |
| 11 | 17.05.2022 | Interventions | pdf |
| 12 | 24.05.2022 | Exam | |

# 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
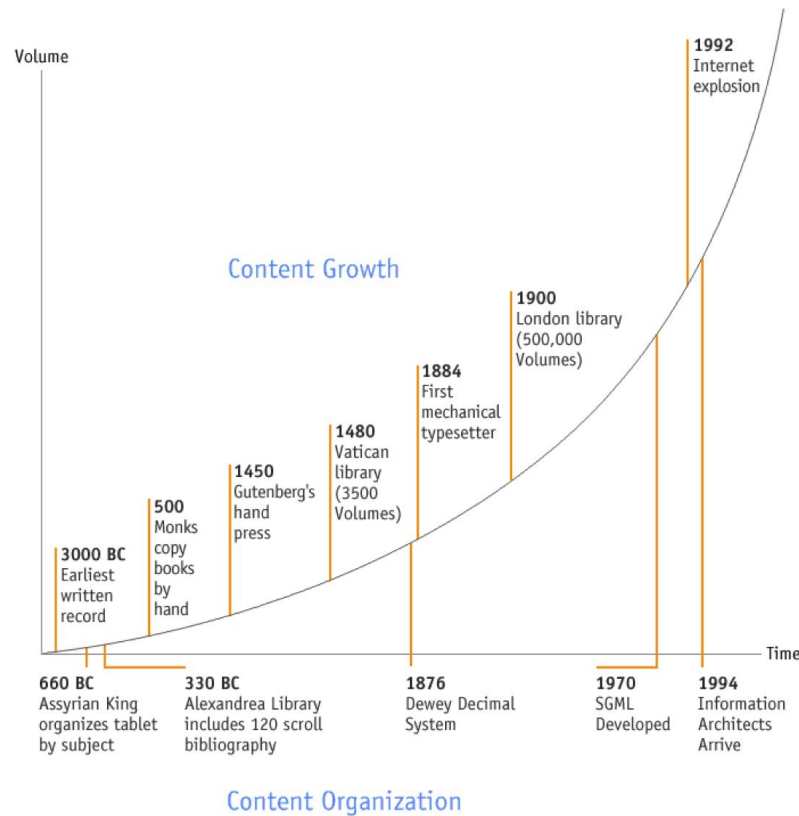


- rough estimates:
  - # of articles double every ~10 years
  - # of journals double every ~15 years

# Why research synthesis matters…



**META MASS PRODUCTION**

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

Yearly publications increased by 2,728% for systematic reviews and by 2,635% for meta-analyses between 1991 and 2014.
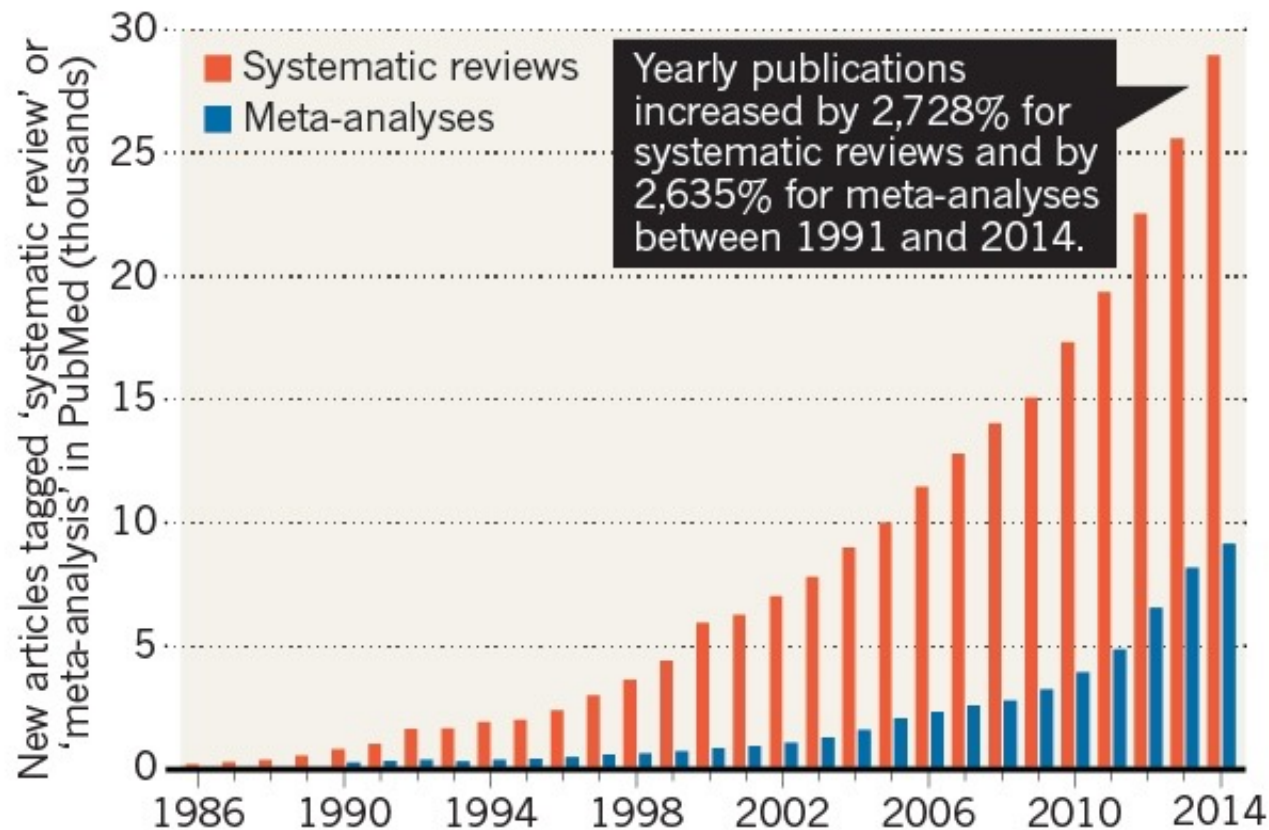
A systematic review analyses and compiles all papers, and sometimes unpublished work, on a topic. A meta-analysis is a systematic review that combines data from multiple papers.

©nature

# 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)

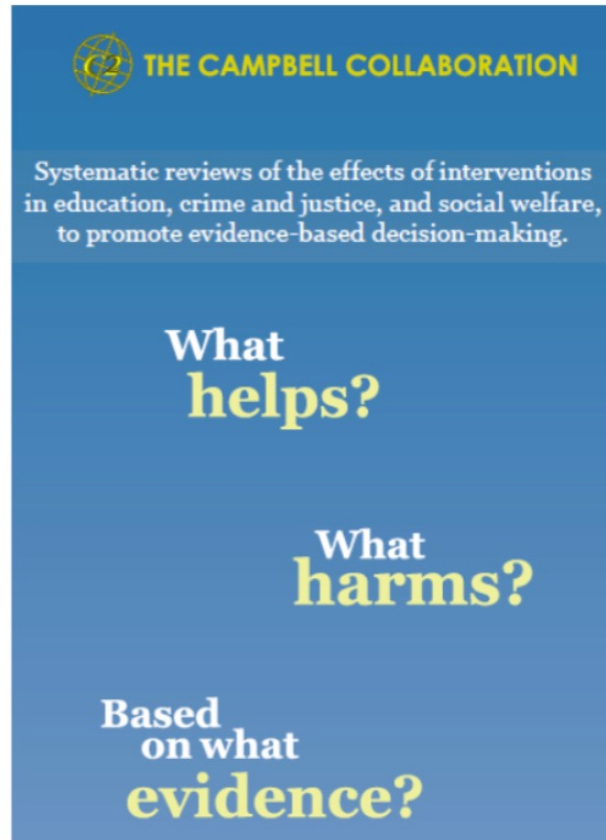1999: PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses)

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

# A brief history of research synthesis
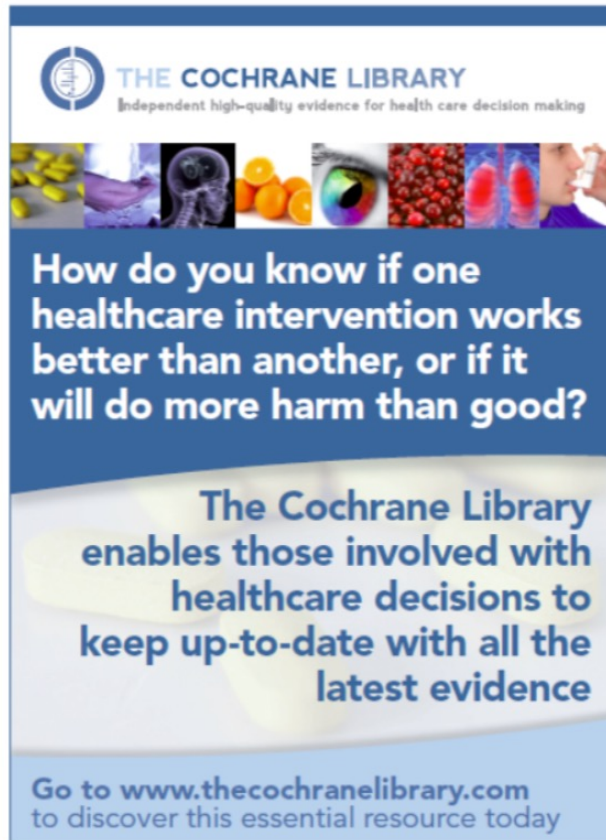


www.cochrane.org

www.campbellcollaboration.org

1993

1999

# Definitions

**Table 2 PRISMA-P terminology**

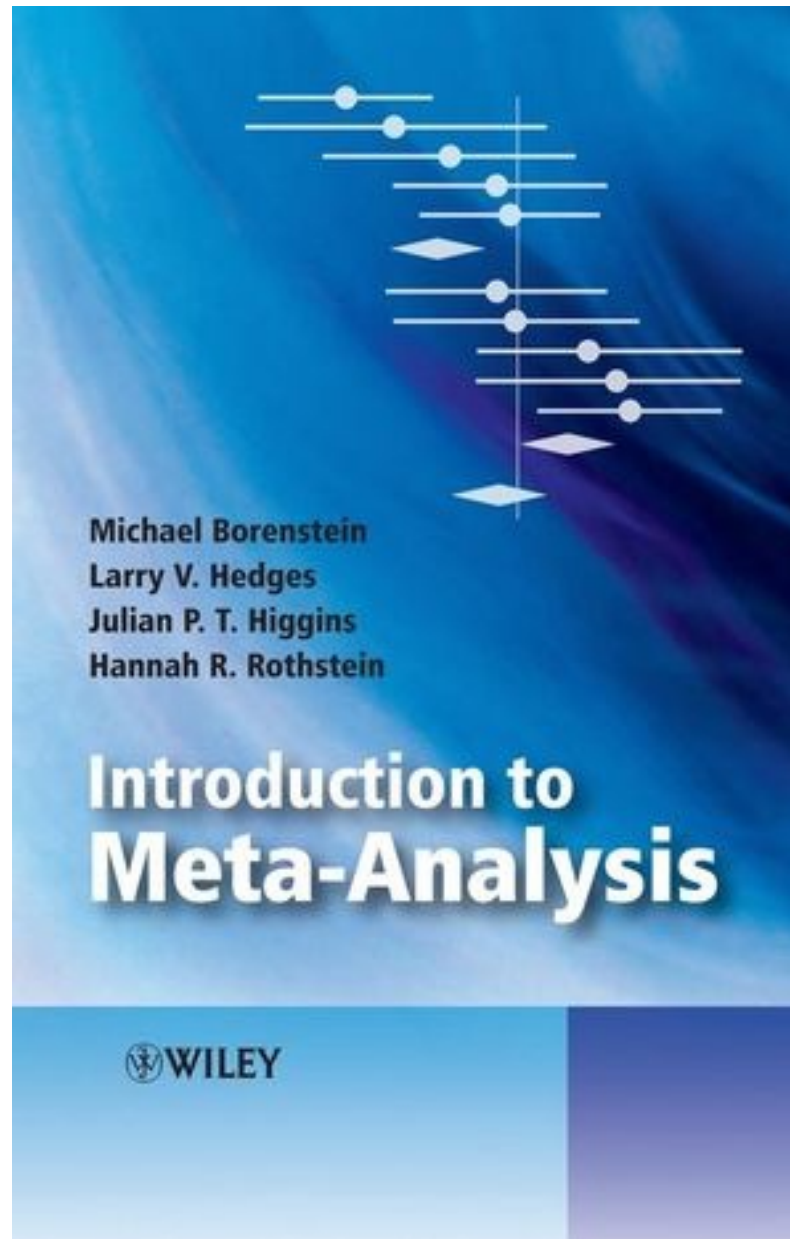| Term | Definition |
| --- | --- |
| Systematic review | A systematic review attempts to collate all relevant evidences that fits pre-specified eligibility criteria to answer a specific research question. It uses explicit, systematic methods to minimize bias in the identification, selection, synthesis,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

# Happy 40th, meta-analysis!
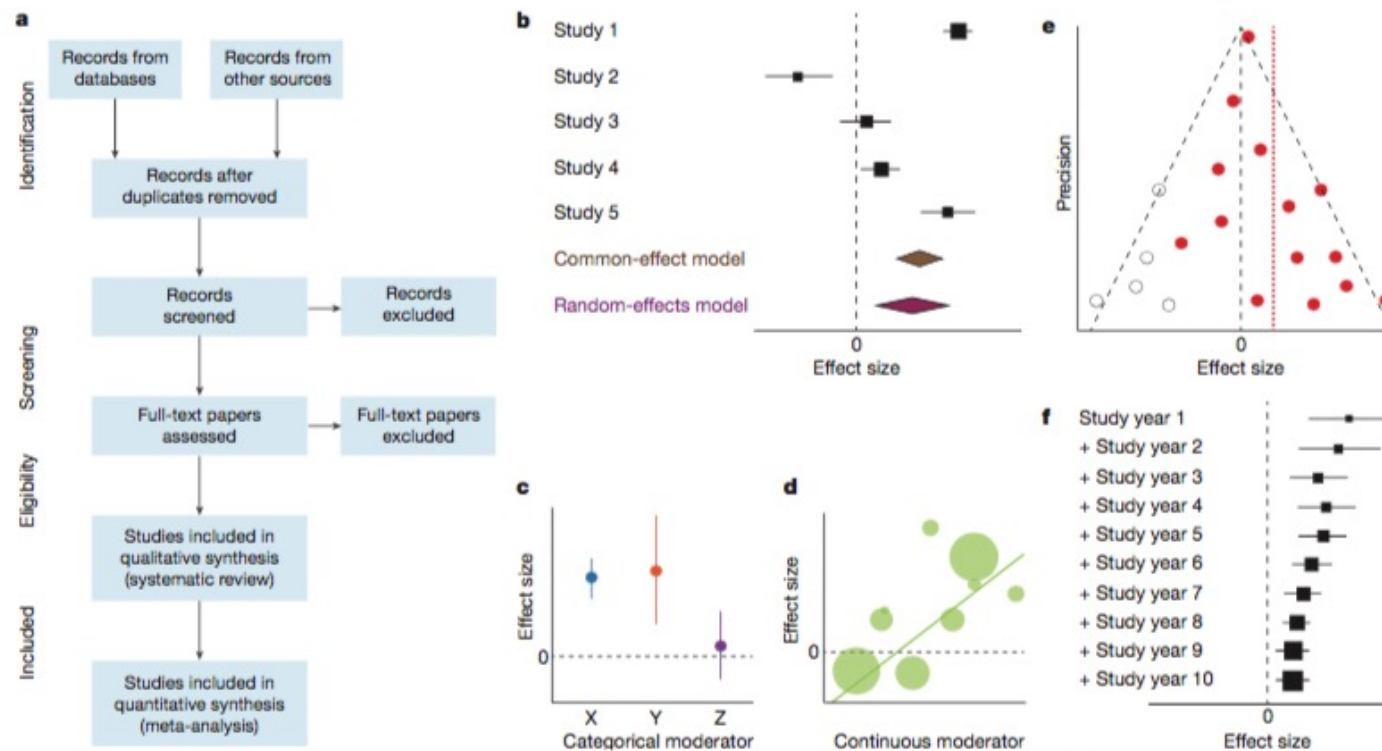
Gurevitch, J., Koricheva, J., Nakagawa, S., & Stewart, G. (2018). Meta-analysis and the science of research synthesis. *Nature, 555*, 175. http://doi.org/10.1038/nature25753

Michael Borenstein
Larry V. Hedges
Julian P. T. Higgins
Hannah R. Rothstein

# Introduction to
# Meta-Analysis

WILEY

# 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 ($\delta$) from studies that used two independent groups as

$$d = \frac{\bar{X}_1 - \bar{X}_2}{S_{within}}. \tag{4.18}$$

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,

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

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

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

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)).
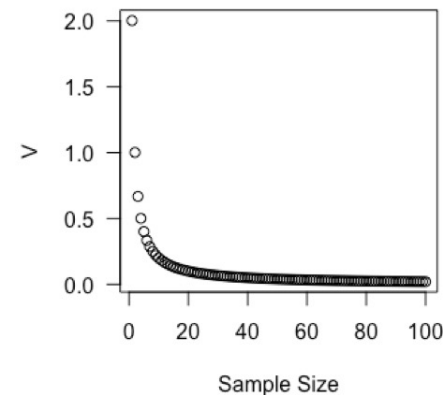


The effect size will often be a standardised value that represents the magnitude of the effect; the variance of the effect size captures the precision of the estimate and will be largely a function of the sample size (see figure)

Bornstein et al. (2009, Chapter 4)

13

# 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

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

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

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

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

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

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)

# Meta-analysis



| | Std Diff | Relative Weight | Standardized mean difference (g) and 95% confidence interval |
|---|---|---|---|
| Carroll | 0.10 | 12% | |
| Grant | 0.28 | 13% | |
| Peck | 0.37 | 8% | |
| Donat | 0.66 | 39% | |
| Stewart | 0.46 | 10% | |
| Young | 0.19 | 18% | |
| Summary | 0.41 | 100% | |
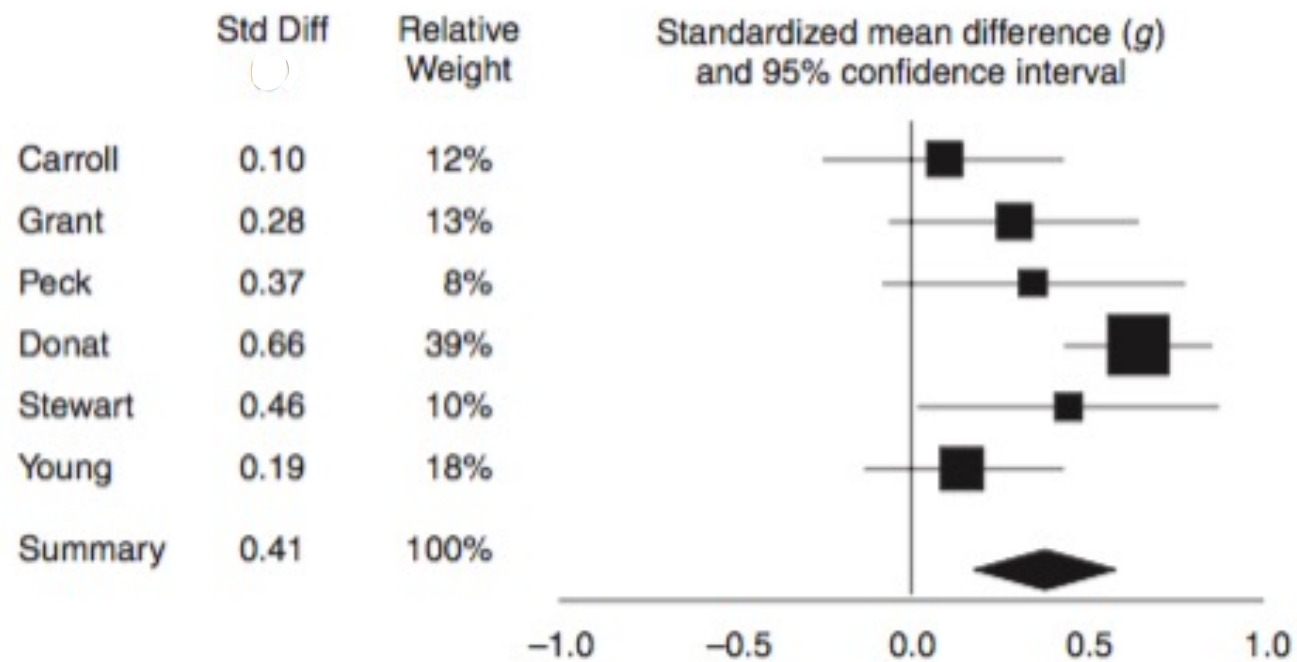
# Meta-analysis in practice…



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)