Systematic Review & Meta-analysis (2)

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Meta-analysis (MA)
Use of statistical techniques in a systematic review (SR) to integrate the results of included studies to conduct statistical inference

Key Points

1. MA should not be used as a synonym for SR

2. An MA should be done in the context of an SR

3. An MA should not be assumed to always be an appropriate step in an SR. The decision to conduct an MA is neither purely analytical nor statistical in nature.

Primary Studies


A randomized trial to test the effectiveness of art therapy for children with asthma


Breathing retraining for African-American adolescents with asthma: a pilot study of a school-based randomized controlled trial

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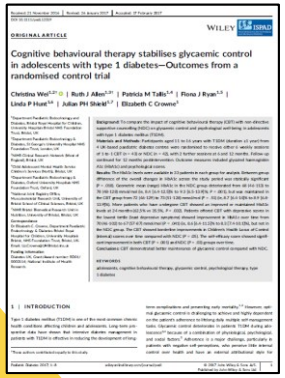

Cognitive behavioural therapy stabilises glycaemic control in adolescents with type 1 diabetes—Outcomes from a randomised control trial

Effect sizes

Y_1

Y_2

Y_k

Weights

x W_1

x W_2

x W_k

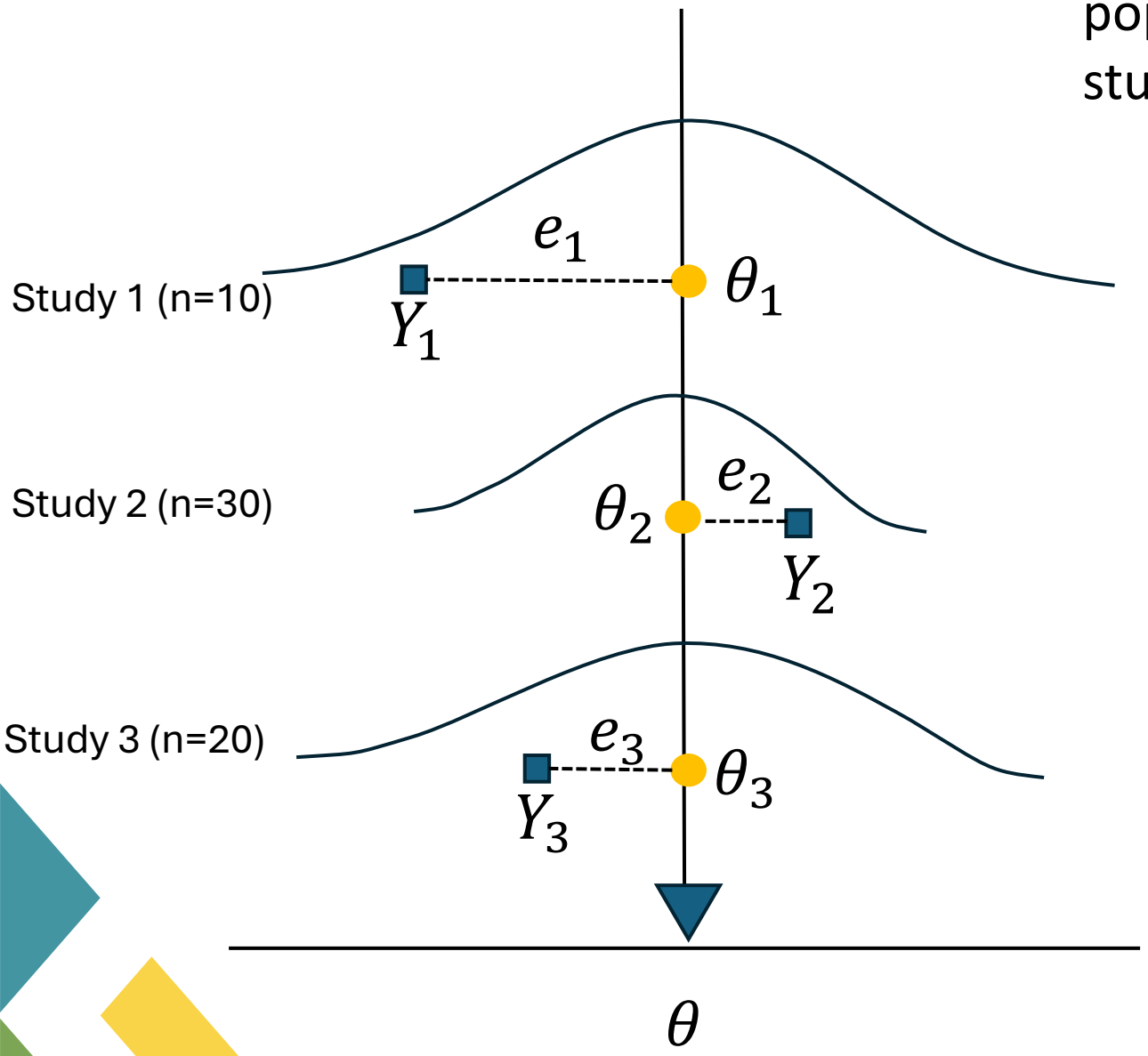
Meta-analysis

Weighted average

$$\theta = \frac{\sum_{i=1}^{k} W_i Y_i}{\sum_{i=1}^{k} W_i}$$

- **fixed-effect** model
- **random-effects** model

Fixed-effect model



The observed effect Y_i for any study is given by the population mean plus the **sampling error** in that study: $Y_i = \theta + e_i$

Weight assigned to each study $W_i = \frac{1}{V_{Y_i}}$

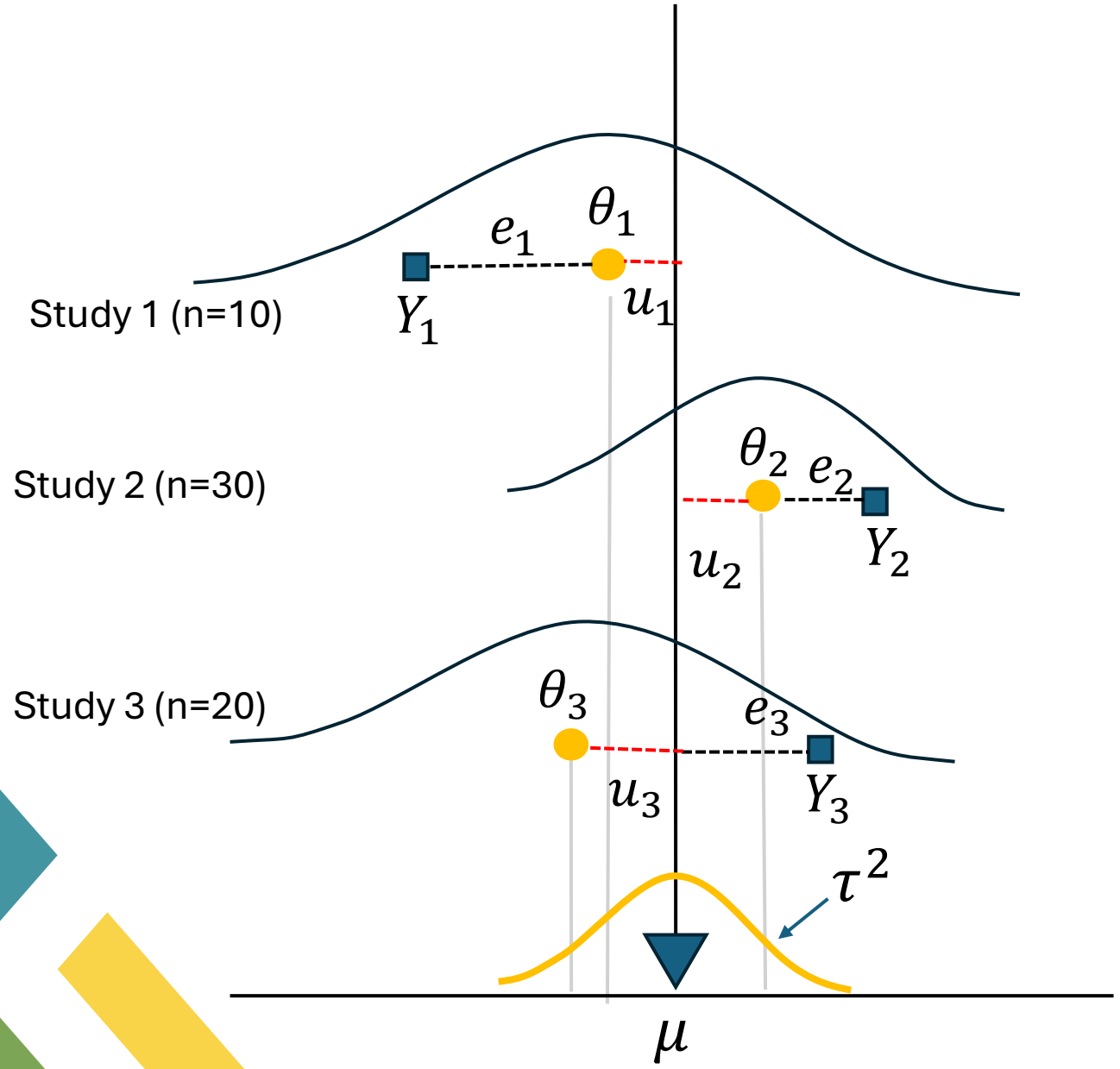
Summary effect:

$$\theta_F = \frac{\sum_{i=1}^{k} W_i Y_i}{\sum_{i=1}^{k} W_i}$$

Variance of the summary effect

$$V_{\theta_F} = \frac{1}{\sum_{i=1}^{k} W_i}$$

Random-effects model



The observed effect Y_i for any study is given by $Y_i = \theta_i + e_i = \mu + u_i + e_i$

The variance of Y_i for any study is given by $V^*_{Y_i} = V_{Y_i} + \tau^2$ Between-study variance

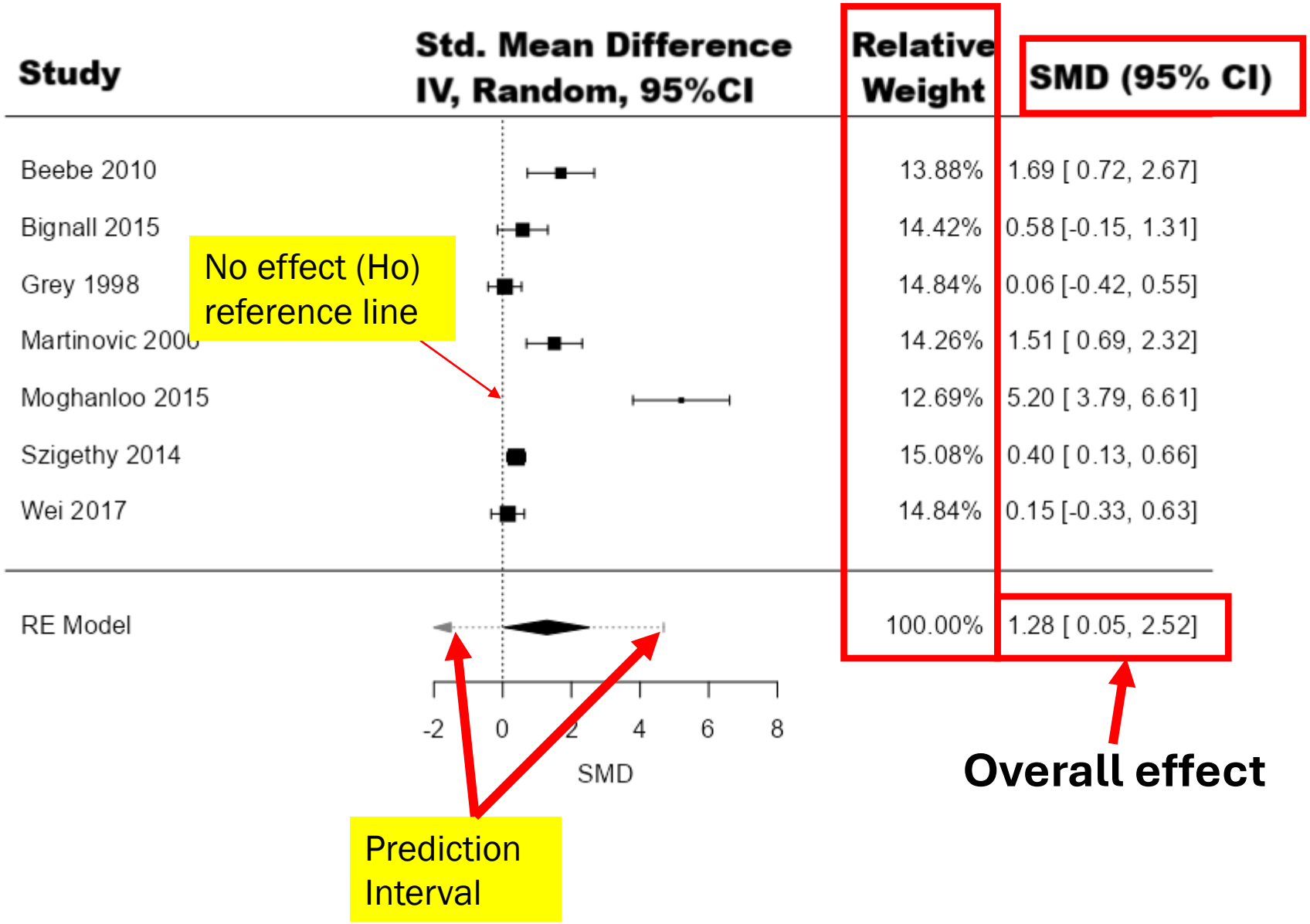
Weight assigned to each study

$$W_i^* = \frac{1}{V^*_{Y_i}} = \frac{1}{V_{Y_i} + \tau^2}$$

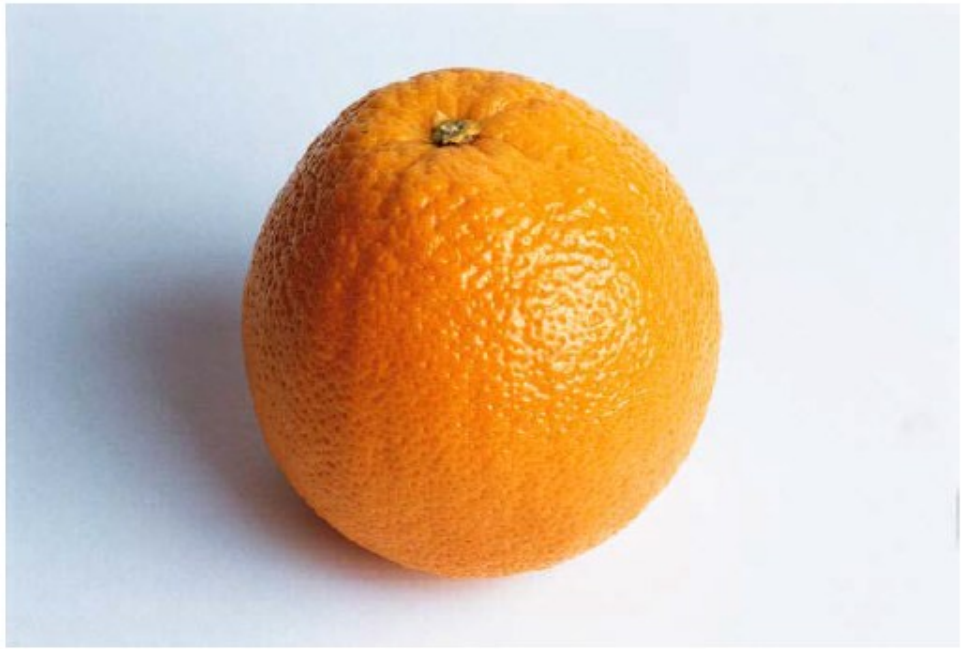
Summary effect and variance:

$$\theta_R = \frac{\sum_{i=1}^{k} W_i^* Y_i}{\sum_{i=1}^{k} W_i^*} \qquad V_{\theta_R} = \frac{1}{\sum_{i=1}^{k} W_i^*}$$

Forest plot


Study
Std. Mean Difference
IV, Random, 95%CI
Relative Weight
SMD (95% CI)
Beebe 2010
13.88%
1.69 [0.72, 2.67]
Bignall 2015
14.42%
0.58 [-0.15, 1.31]
Grey 1998
14.84%
0.06 [-0.42, 0.55]
Martinovic 2006
14.26%
1.51 [0.69, 2.32]
Moghanloo 2015
12.69%
5.20 [3.79, 6.61]
Szigethy 2014
15.08%
0.40 [0.13, 0.66]
Wei 2017
14.84%
0.15 [-0.33, 0.63]
RE Model
100.00%
1.28 [0.05, 2.52]
-2
0
2
4
6
8
SMD
No effect (Ho) reference line
Prediction Interval
Overall effect

“Heterogeneity is Your Friend” (J. Berlin)



Fruit salad may, or may not, be tasty and interesting
Which are the apples and oranges, and how do they differ?

Definitions of Heterogeneity From a Health Care Perspective

Different types of heterogeneity:

- **Clinical heterogeneity:** Variability in participants, interventions and outcomes

- **Methodological heterogeneity:** Variability in study design and risk of bias

- **Statistical heterogeneity:** Variability in treatment effects, resulting from clinical and/or methodological diversity

Statistical heterogeneity is present if the observed treatment effects are more different from each other than would be expected due to chance alone

Discuss Clinical/Methodological or “Substantive” Heterogeneity Prior To Analysis

- **Think first:** Are included studies similar with respect to treatment effect? Study design, subjects, treatments, etc. may affect results.

- **Include in protocol:** Sources of heterogeneity that you might stratify analysis on, or that you might include as independent variables in a meta-regression

- **Do statistics later:** **Q statistic** to test the hypothesis that the true (population) treatment effect is equal in all studies; and/or **I-squared (I2)** statistic; and **prediction interval (PI)**

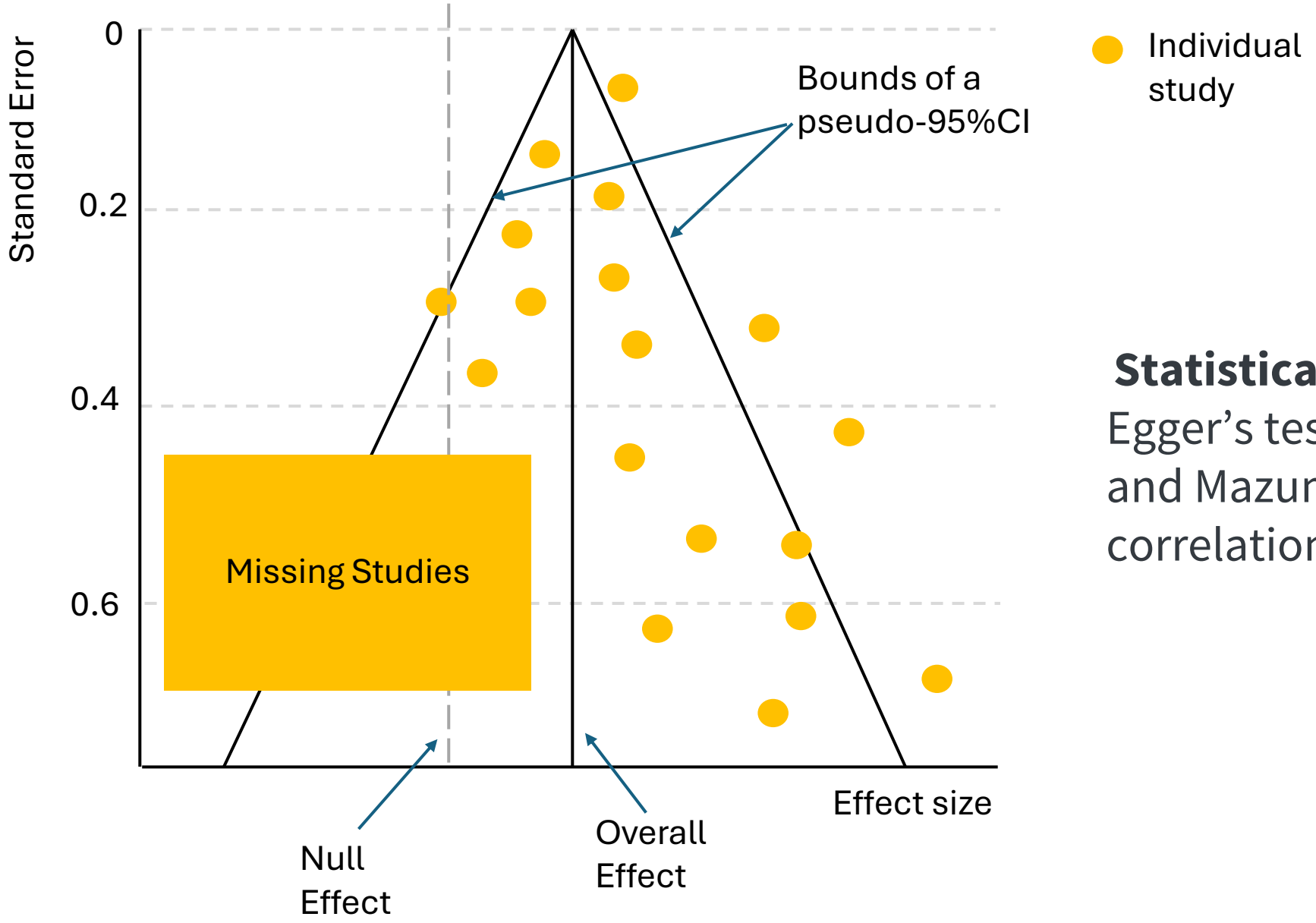
- **Remember:** Tests for heterogeneity have low statistical power

Small-study effects in meta-Analysis

"Small-study effects" is a generic term for the phenomenon that **smaller studies** sometimes show different, often larger, treatment effects than large ones.

Funnel-plot symmetry

Funnel-plot asymmetry



Statistical tests:
Egger's test or the Begg and Mazumdar rank correlation ($p<0.05$)

Potential sources of asymmetry in funnel plots

- Publication bias (the likelihood of a study being published—particularly a small study—increases if it shows a stronger, statistically significant, and favorable effect.
- Outcome reporting bias (selective reporting of the most favourable outcomes)
- Poor methodological design of small studies