# Meta-analysis and Analysis of Pooled Data

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# Meta-analysis

- In statistics, a meta-analysis combines the results of several studies that address a set of related research hypotheses
- Based on a common measure of effect size, for which a weighted average might be the output of a meta-analyses

# Analysis of pooled data

- Based on individual patient data
- Integrated summary of safety and efficacy based on pooled data

# Meta-analysis based on literature review

- Identify variables of interest
- Identify studies for inclusion
- Literature search (references, key words)
- Obtain effect size for each study
- Meta-analysis results (weighted mean, Confidence intervals, heterogeneity)

# Types of effect size

- Mean Difference
- Odds-Ratio
- Hazard ratio
- Risk-ratio

# From single study to population effect size

Studies vary in size

- An effect size based on 100 subjects is assumed to be a more "precise"estimate of the population effect size than an effect size based on 10 subjects
- Larger studies should carry more "weight"in a meta-analysis than smaller studies

**Simple approach:** weight each study effect size by its sample size

**Better approach:** weight each study effect size by the inverse variance

# From single study to population effect size

- The standard error (SE) is a direct index of the precision of the effect size
- The smaller the SE, the more precise is the effect size
- The optimal weights for meta-analysis are:

$$w = \frac{1}{SE^2} \quad \text{, where} \quad SE = \frac{SD}{\sqrt{N}}$$

The Weighted Mean Effect Size

$$\overline{ES} = \frac{\sum (w \times ES)}{\sum w}$$

# Homogeneity analysis

- Homogeneity analysis tests whether the assumption that all of the effect sizes are estimating the same population mean is a reasonable assumption
- If homogeneity is rejected, the distribution of effect sizes is assumed to be heterogeneous
  - Single weighted mean effect size not a good descriptor of the distribution
  - There are real between study differences, that is, studies estimate different population mean effect sizes
  - Fit a random effects model

# The random effects model

- Fixed effects model assumes that all of the variability between effect sizes is due to sampling error
- Random effects model assumes that the variability between effect sizes is due to sampling error plus variability in the population of effects
- The weighting of each study becomes the inverse of the sampling variance plus a constant that represents the variability across the population effects

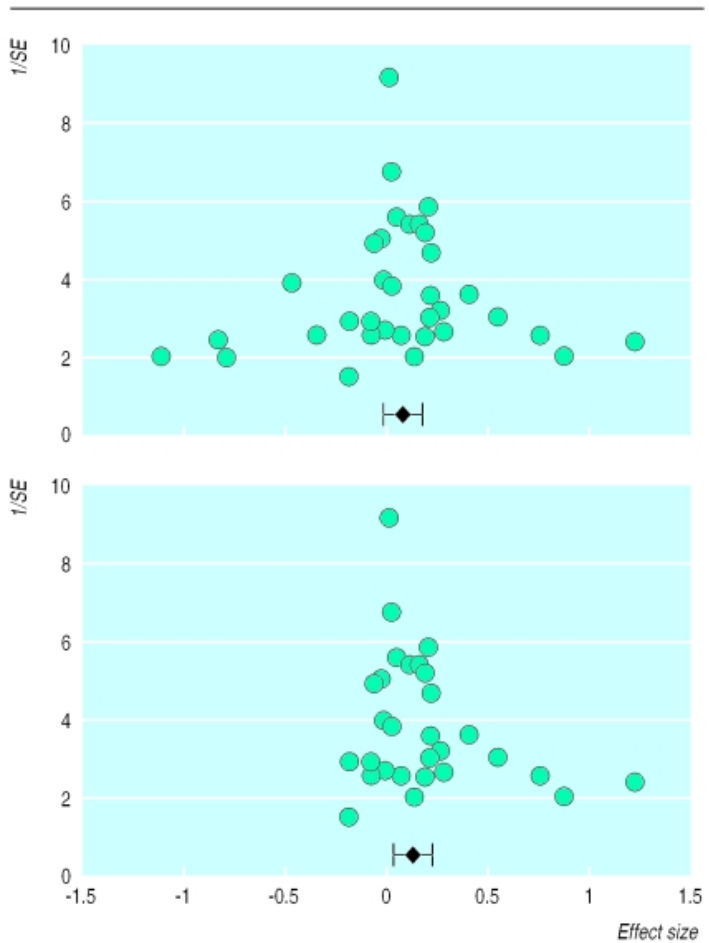
$$w_i = \frac{1}{SE_i^2 + \hat{\nu}_\theta}$$

# Comparison of random effect with fixed effect results

- The biggest difference you will notice is in the significance levels and confidence intervals
  - Confidence intervals will get wider
  - Effects that were significant under a fixed effect model may no longer be significant
- Random effects models are therefore more conservative

# Publication bias, funnel plots

Typical funnel plot generated from 35 simulated studies (top) and same data with five missing studies showing a typical manifestation of publication bias (bottom).




Sutton A J et al. BMJ 2000;320:1574-1577

# Summary of clinical efficacy