Online Advanced Methods for Cost-Effectiveness Analysis

Presentation 3: Populating decision models: effectiveness evidence
3.4: Meta-analysis: Fixed- and random-effects pairwise meta-analysis

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Objectives

- Understanding forest plots
- Fixed-effect approach and its assumptions
- Concept of heterogeneity, how it can affect a meta-analysis and how can we test for its presence
- Random-effects approach and its assumptions

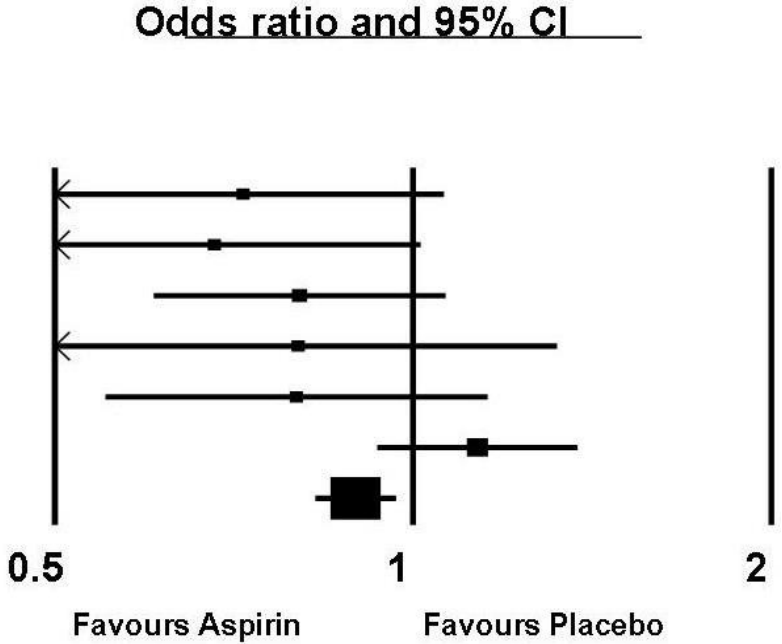
Example: Meta-analysis of RCTs of the effect of aspirin in preventing death after myocardial infarction

Study	Aspirin group		Placebo group	
	Deaths	Total	Deaths	Total
MRC-1	49	615	67	624
CDP	44	758	64	771
MRC-2	102	832	126	850
GASP	32	317	38	309
PARIS	85	810	52	406
AMIS	246	2267	219	2257
ISIS-2	1570	8587	1720	8600

Source: Fleiss. The statistical basis of meta-analysis. *Stat Methods Med. Res.* 1993; 2: 121-145

Forest plot of odds ratios – example

Study name	Odds ratio	Lower limit	Upper limit
MRC-1	0.72	0.49	1.06
CDP	0.68	0.46	1.01
MRC-2	0.80	0.61	1.06
GASP	0.80	0.49	1.32
PARIS	0.80	0.55	1.15
AMIS	1.13	0.93	1.37
ISIS-2	0.89	0.83	0.97

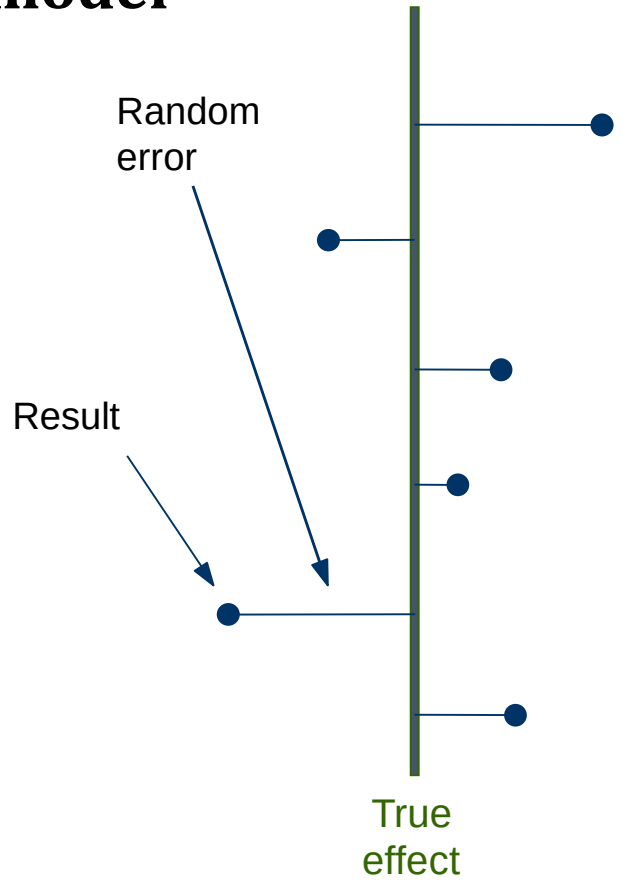


Meta-Analysis, Fixed effects model

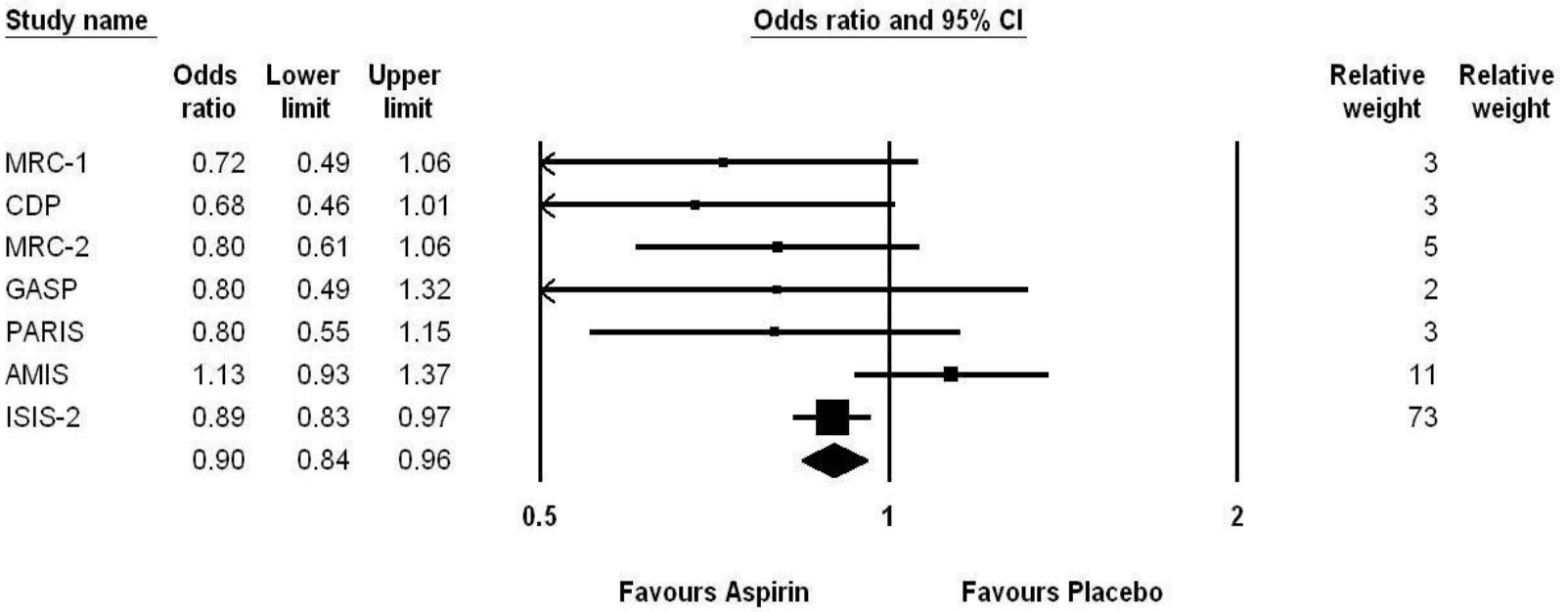
- Statistical homogeneity
- Formally, MA FE assumes:

$$Y_i \sim \text{Normal}(\theta, V_i)$$

- We estimate the common true effect, θ



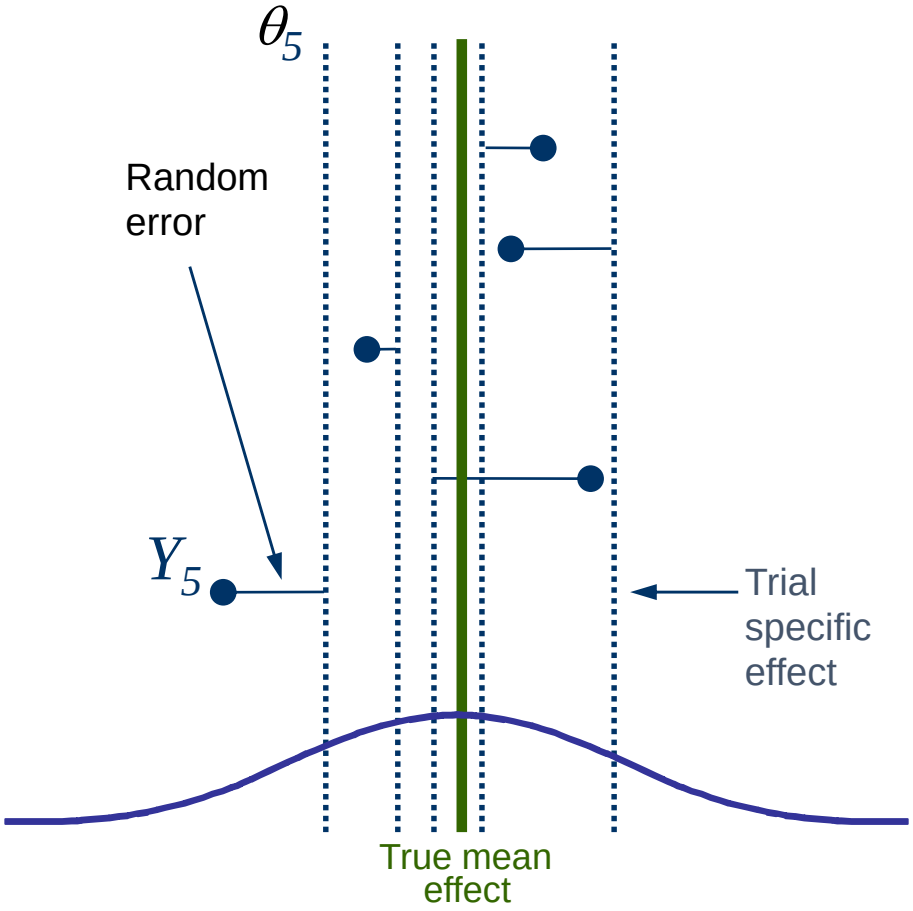
Fixed effect results – example results



Heterogeneity

- Fixed effect model assumes all the trials are estimating exactly the same treatment effect
- Is this reasonable?
  - Trials may differ in design and conduct in many ways including the characteristics of the patients or intervention (e.g. dose of drug)
- Statistical tests exist to assess its existence:
  - Cochran's Q test (aka χ^2): heterogeneity exists if p-value small (<0.1)
  - Higgins' I^2: how much of the total variability is due to heterogeneity? 0% (no) to 100% (much) scale

Random effects model



Model:

- within studies

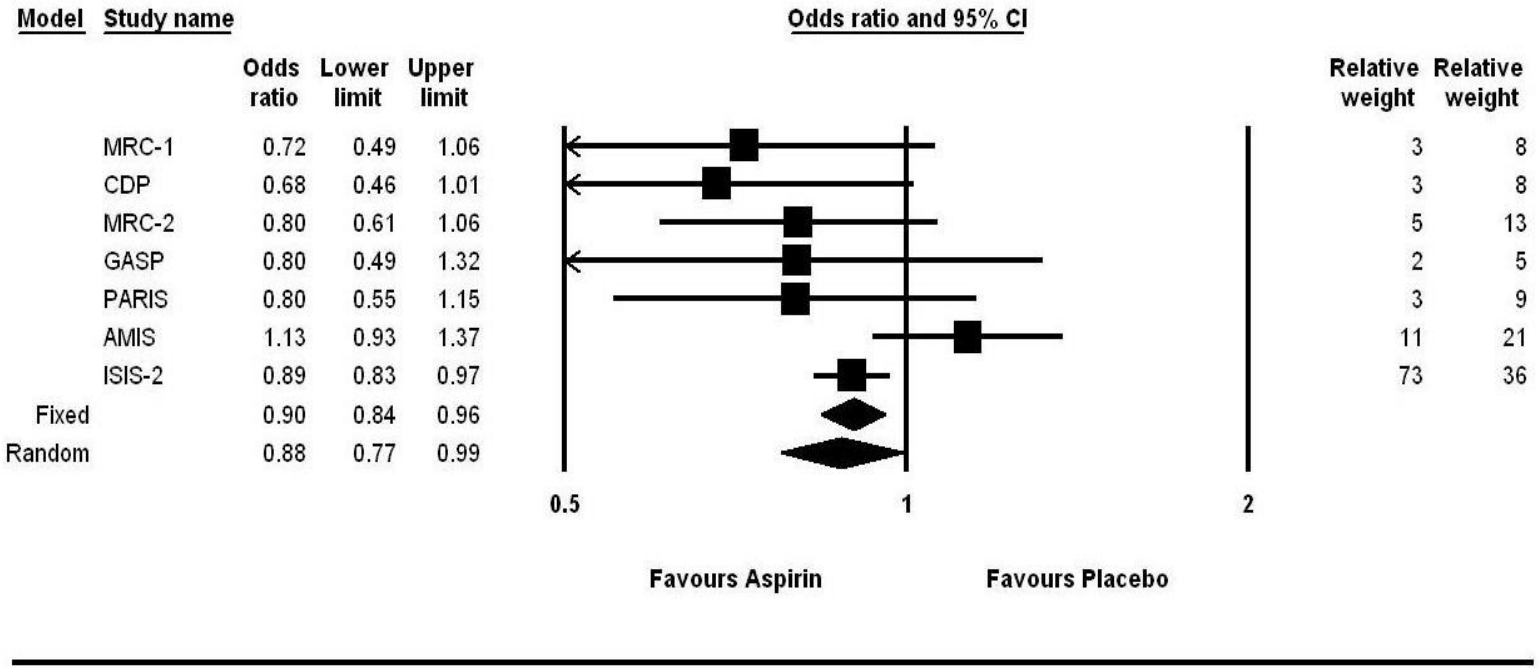
$$Y_i \sim \text{Normal}(\theta_i, V_i)$$

- across studies

$$\theta_i \sim \text{Normal}(\theta, t^2)$$

- There is a distribution of effect θ
- $\text{Weight}_i = 1 / (V_i + t^2)$

Comparison – fixed and random effects – example results



Exploring heterogeneity?

- What causes between study heterogeneity?
  - Clinical heterogeneity, e.g. differences in patients, disease severity, medical history
  - Methodological heterogeneity, e.g. differences in study intervention/conduct, e.g. randomisation, endpoints and time points
  - Chance
- Random effects model only account for it – they do not explain it
- Subgroup analyses/meta-regression methods can help to explain heterogeneity which may provide further insight into the treatment effect

Summary points

- Fixed-effect and random-effects approaches make different assumptions regarding the true effect estimate
- Study diversity may lead to heterogeneity: differences in true effect
- Existence of heterogeneity may be tested and heterogeneity can be quantified