

# Introduction to meta-analysis

Trusted evidence.  
Informed decisions.  
Better health.



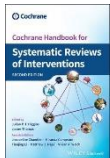
# Steps of a Cochrane Review

1. define the question
2. plan eligibility criteria
3. plan methods
4. search for studies
5. apply eligibility criteria
6. collect data
7. assess studies for risk of bias
8. **analyse and present results**
9. interpret results and draw conclusions
10. improve and update review



# Session outline

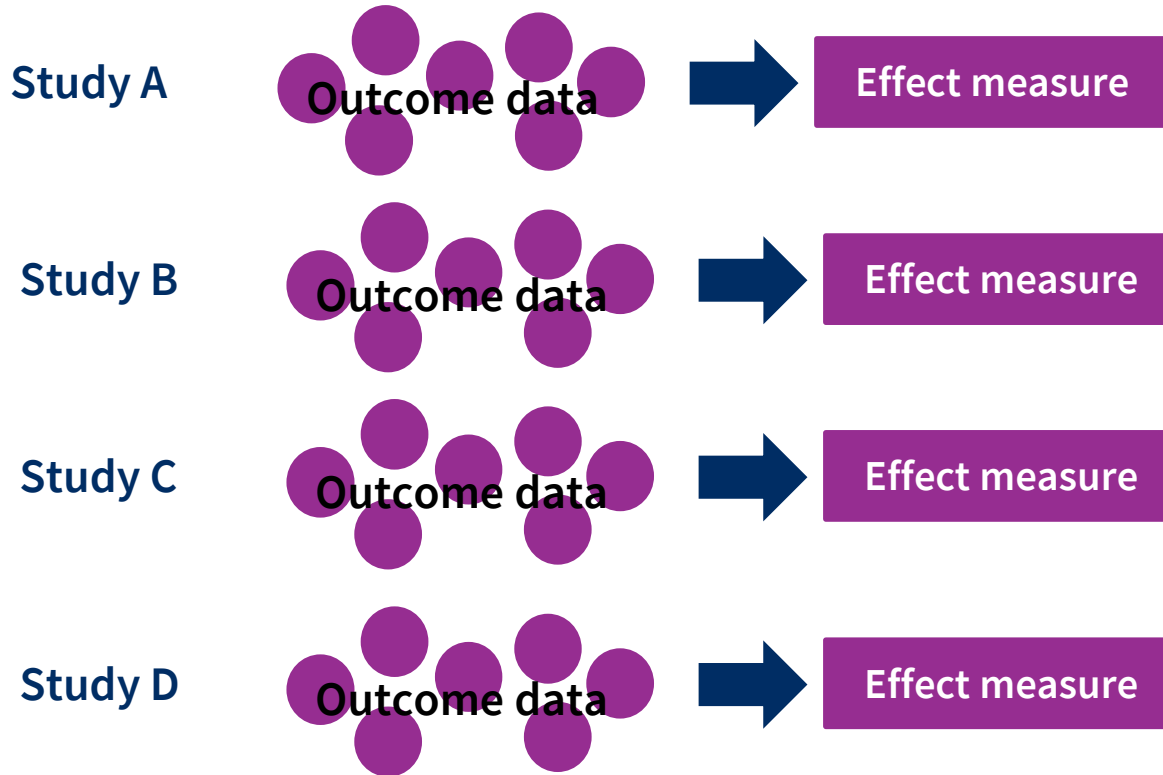
- **principles of meta-analysis**
- steps in a meta-analysis
- presenting your results



See Chapter 10 of the Handbook



### Study level

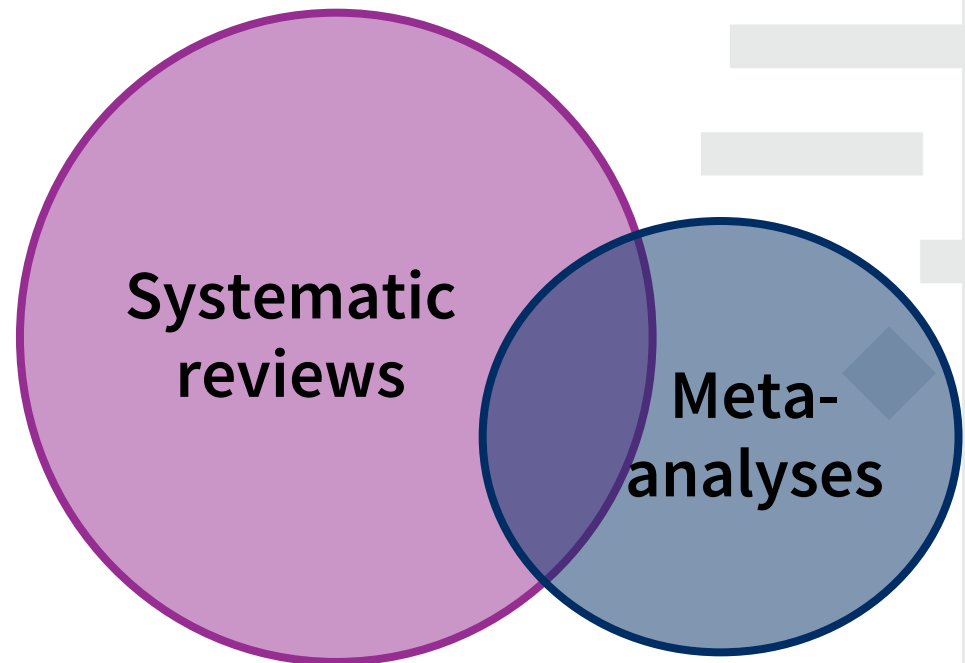


### Review level



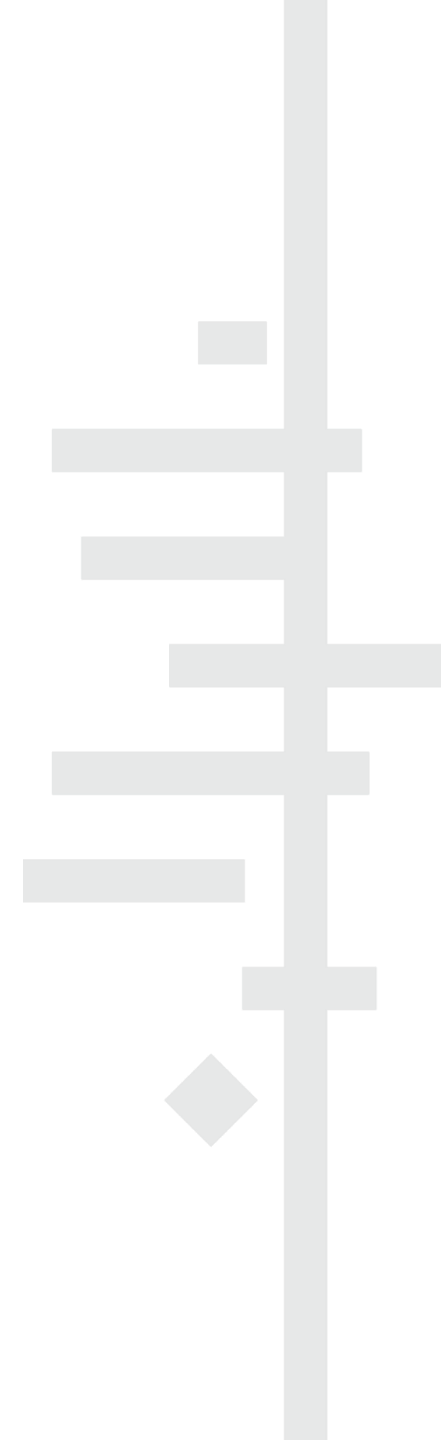
# What is a meta-analysis?

- combines the results from two or more studies
- estimates an ‘average’ or ‘common’ effect
- optional part of a systematic review



# Why perform a meta-analysis?

- quantify treatment effects and their uncertainty
- increase power
- increase precision
- explore differences between studies
- settle controversies from conflicting studies
- generate new hypotheses



# When not to do a meta-analysis

- **mixing apples with oranges**
  - each included study must address the same question
    - consider comparison and outcomes
    - requires your subjective judgement
  - combining a broad mix of studies answers broad questions
  - answer may be meaningless and genuine effects may be obscured if studies are too diverse

# When not to do a meta-analysis

- **garbage in – garbage out**
  - a meta-analysis is only as good as the studies in it
  - if included studies are biased:
    - meta-analysis result will also be incorrect
    - will give more credibility and narrower confidence interval
  - if serious reporting biases present:
    - unrepresentative set of studies may give misleading result



# When can you do a meta-analysis?

- more than one study has measured an effect
- the studies are sufficiently similar to produce a meaningful and useful result
- the outcome has been measured in similar ways
- data are available in a format we can use



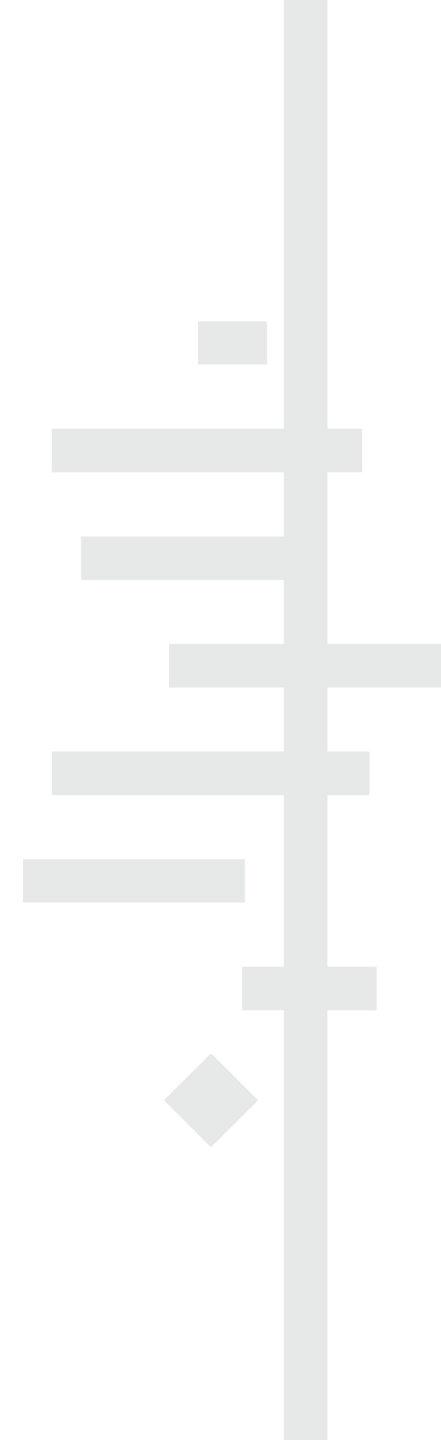
# Session outline

- principles of meta-analysis
- **steps in a meta-analysis**
- presenting your results



# Steps in a meta-analysis

- identify comparisons to be made
- identify outcomes to be reported and statistics to be used
- collect data from each relevant study
- combine the results to obtain the summary of effect
- explore differences between the studies
- interpret the results



# Selecting comparisons

**Hypothetical review:** Caffeine for daytime drowsiness

caffeinated coffee

vs

decaffeinated coffee

- break your topic down into pair-wise comparisons
- each review may have one or many
- use your judgement to decide what to group together, and what should be a separate comparison

# Selecting outcomes & effect measures

**Hypothetical review:** Caffeine for daytime drowsiness

caffeinated coffee

vs

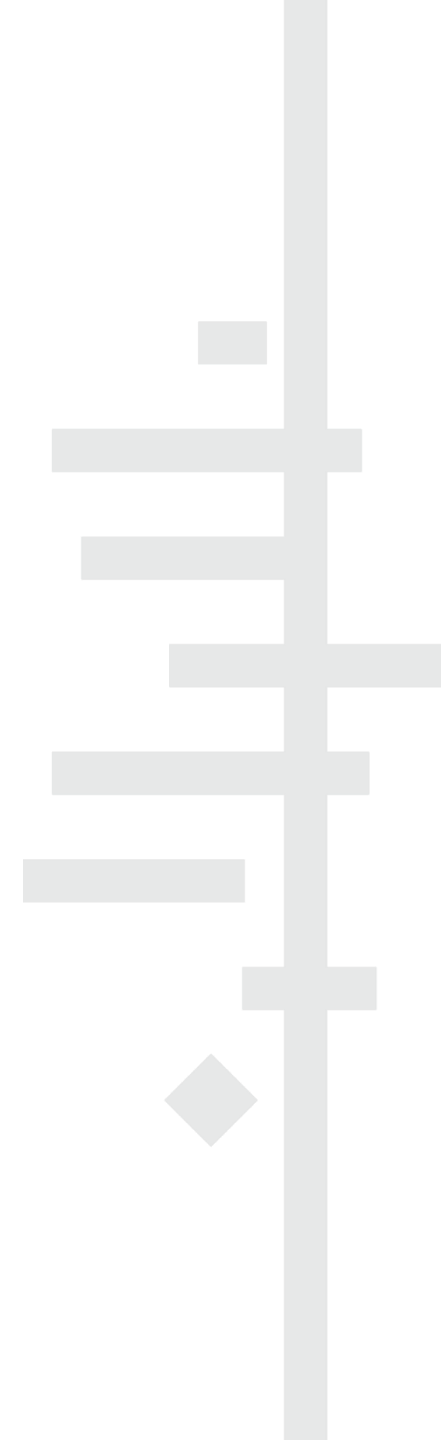
decaffeinated coffee

- asleep at end of trial (RR)
- irritability (MD/SMD)
- headaches (RR)

- for each comparison, select outcomes
- for each outcome, select an effect measure
  - may depend on the available data from included studies

# Calculating the summary result

- collect a summary statistic from each contributing study
- how do we bring them together?
  - treat as one big study – add intervention & control data?
    - breaks randomisation, will give the wrong answer
  - simple average?
    - weights all studies equally – some studies closer to the truth
  - weighted average



# Weighting studies

- more weight to the studies which give more information
  - more participants, more events, narrower confidence interval
  - calculated using the effect estimate and its variance
- inverse-variance method:

$$\text{weight} = \frac{1}{\text{variance of estimate}} = \frac{1}{SE^2}$$

$$\text{pooled estimate} = \frac{\text{sum of (estimate} \times \text{weight)}}{\text{sum of weights}}$$

## For example

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Headache	Caffeine	Decaf	Weight
<b>Amore-Coffea 2000</b>	2/31	10/34	
<b>Deliciozza 2004</b>	10/40	9/40	
<b>Mama-Kaffa 1999</b>	12/53	9/61	
<b>Morrocona 1998</b>	3/15	1/17	
<b>Norscafe 1998</b>	19/68	9/64	
<b>Oohlahlazza 1998</b>	4/35	2/37	
<b>Piazza-Allerta 2003</b>	8/35	6/37	

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## For example

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Headache	Caffeine	Decaf	Weight
Amore-Coffea 2000	2/31	10/34	6.6%
Deliciozza 2004	10/40	9/40	21.9%
Mama-Kaffa 1999	12/53	9/61	22.2%
Morrocona 1998	3/15	1/17	2.9%
Norscafe 1998	19/68	9/64	26.4%
Oohlahlazza 1998	4/35	2/37	5.1%
Piazza-Allerta 2003	8/35	6/37	14.9%

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# Meta-analysis options

- for dichotomous or continuous data
  - inverse-variance
    - straightforward, general method
- for dichotomous data only
  - Mantel-Haenszel (default)
    - good with few events – common in Cochrane reviews
    - weighting system depends on effect measure
  - Peto
    - for odds ratios only
    - good with few events and small effect sizes (OR close to 1)



# Meta-analysis options

**i** Name

Headache

Data source

Custom input

Data type

Dichotomous

Intervention group 1

Caffeinated coffee

Intervention group 2

Decaffeinated coffee

## Statistical settings

Statistical method

Inverse variance

Effect measure

Risk ratio

Analysis model

Fixed effect

Totals

Totals and subtotals

Test for subgroup differences

Swap event and non-event

Study confidence interval

95%

Total confidence interval

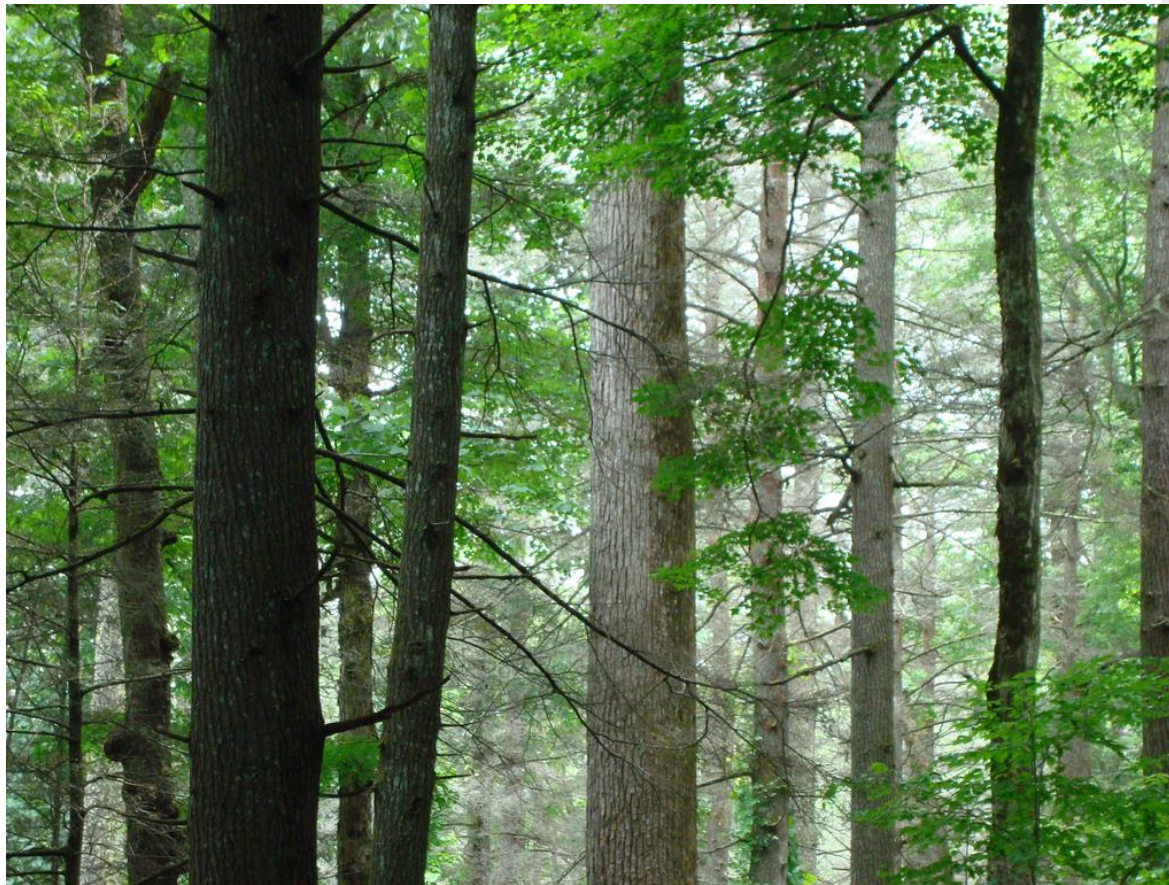
95%

# Session outline

- principles of meta-analysis
- steps in a meta-analysis
- **presenting your results**

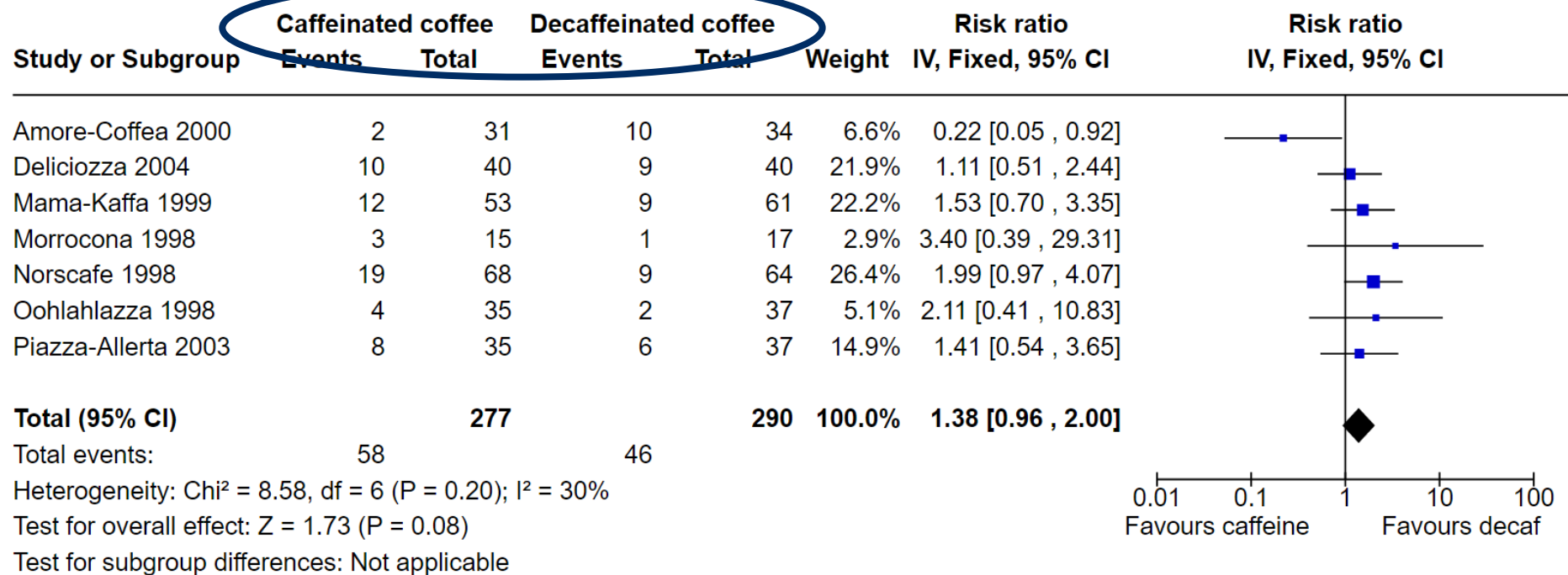


# A forest of lines



# Forest plots

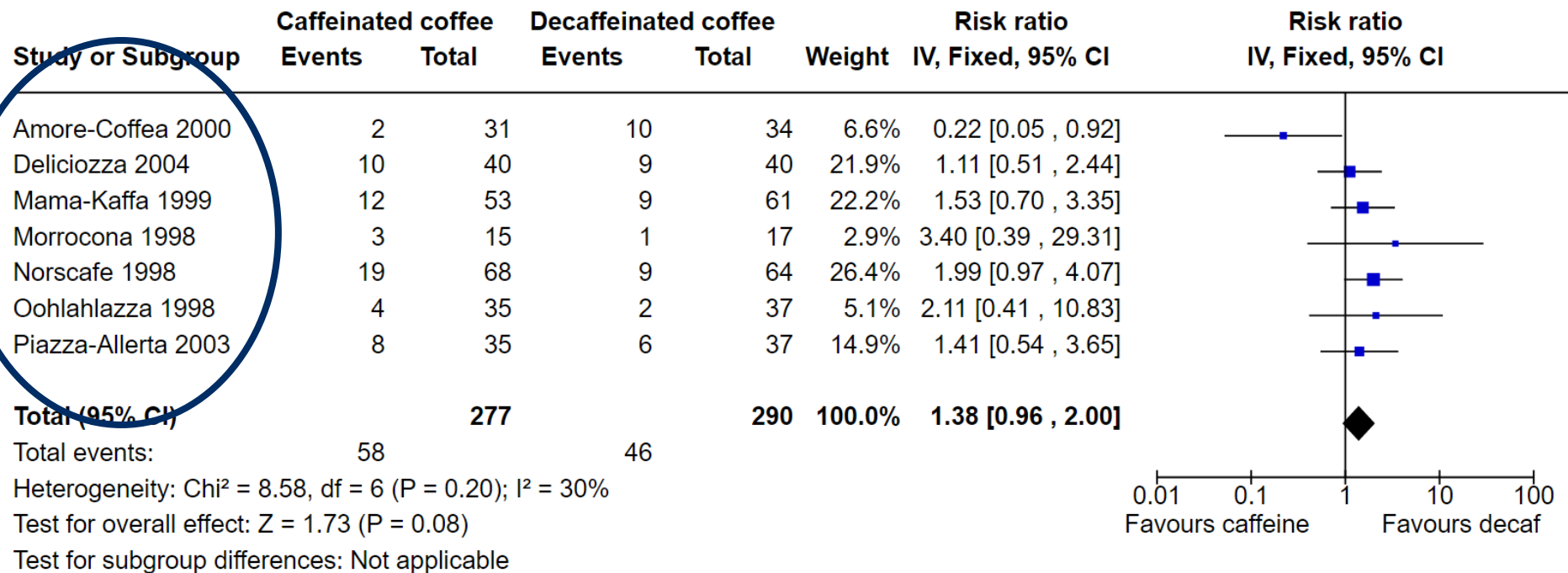
## Headache at 24 hours



- headings explain the comparison

# Forest plots

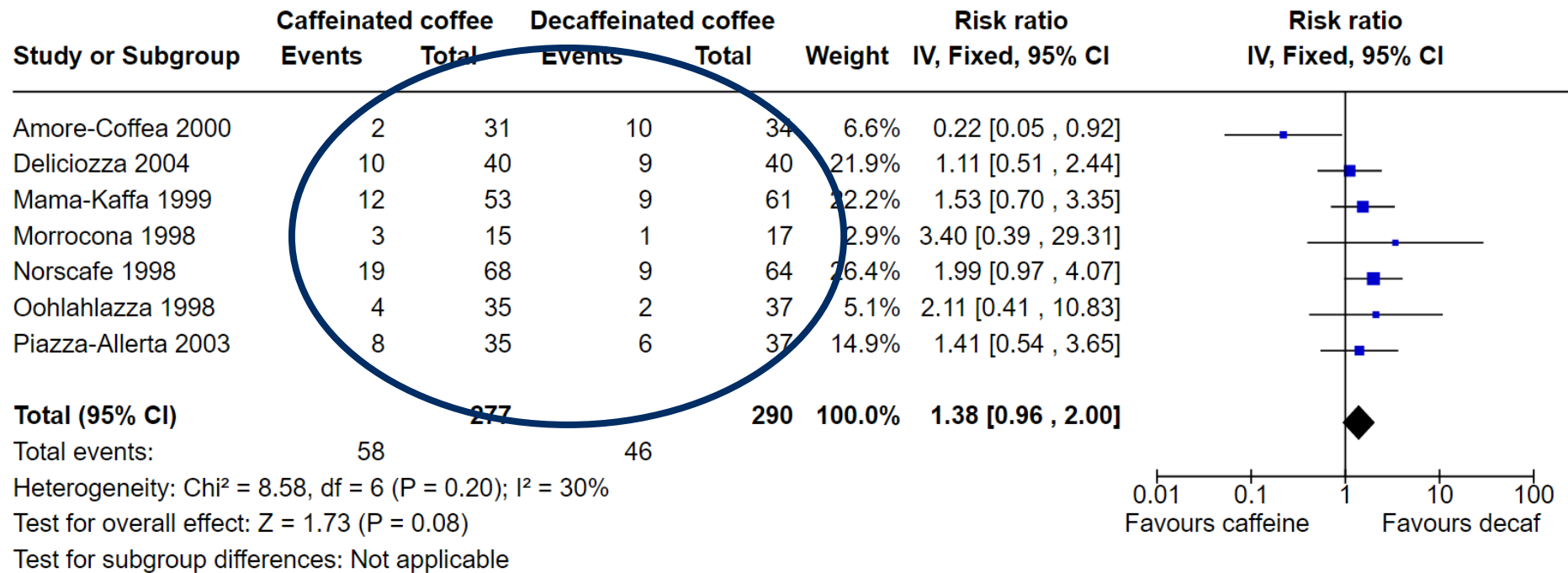
## Headache at 24 hours



- list of included studies

# Forest plots

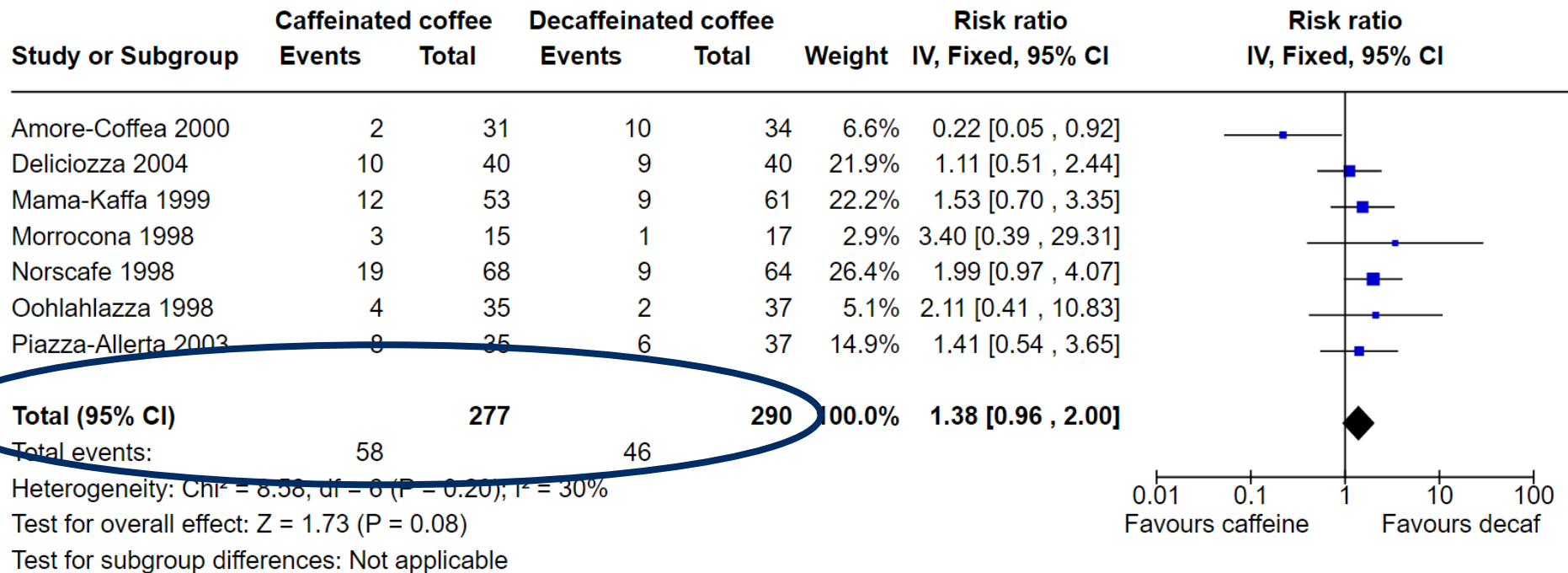
## Headache at 24 hours



- raw data for each study

# Forest plots

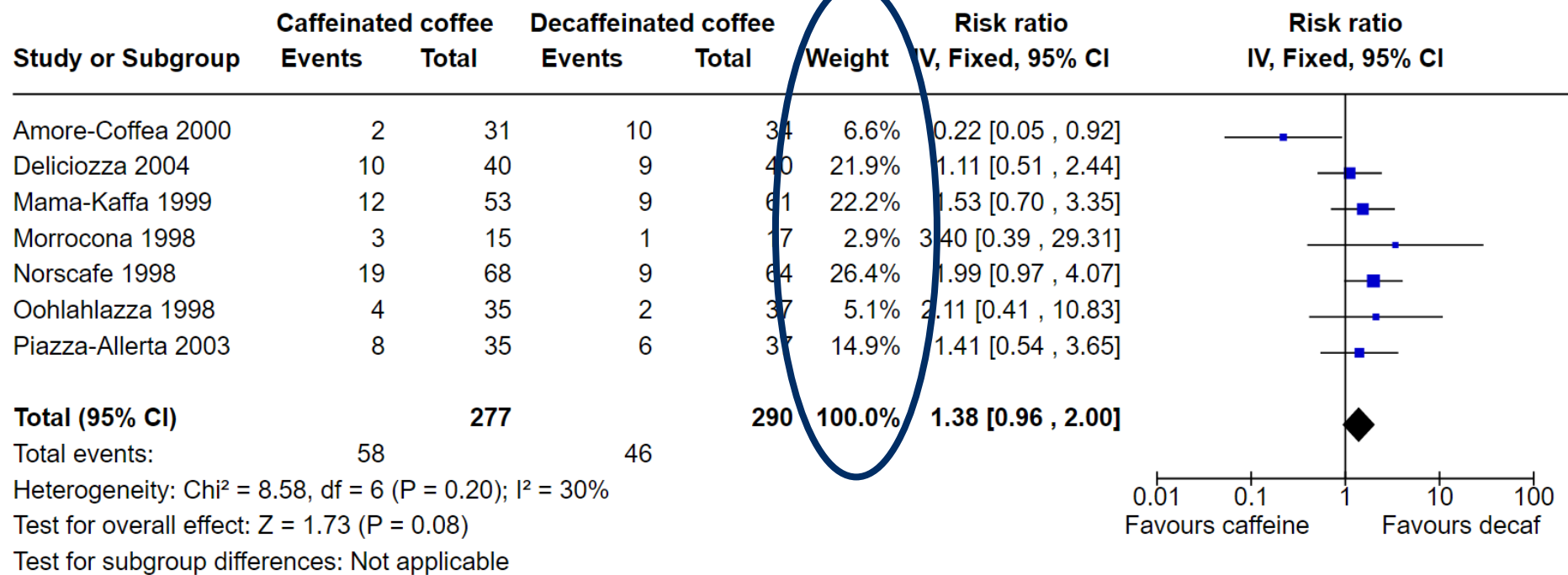
## Headache at 24 hours



- total data for all studies

# Forest plots

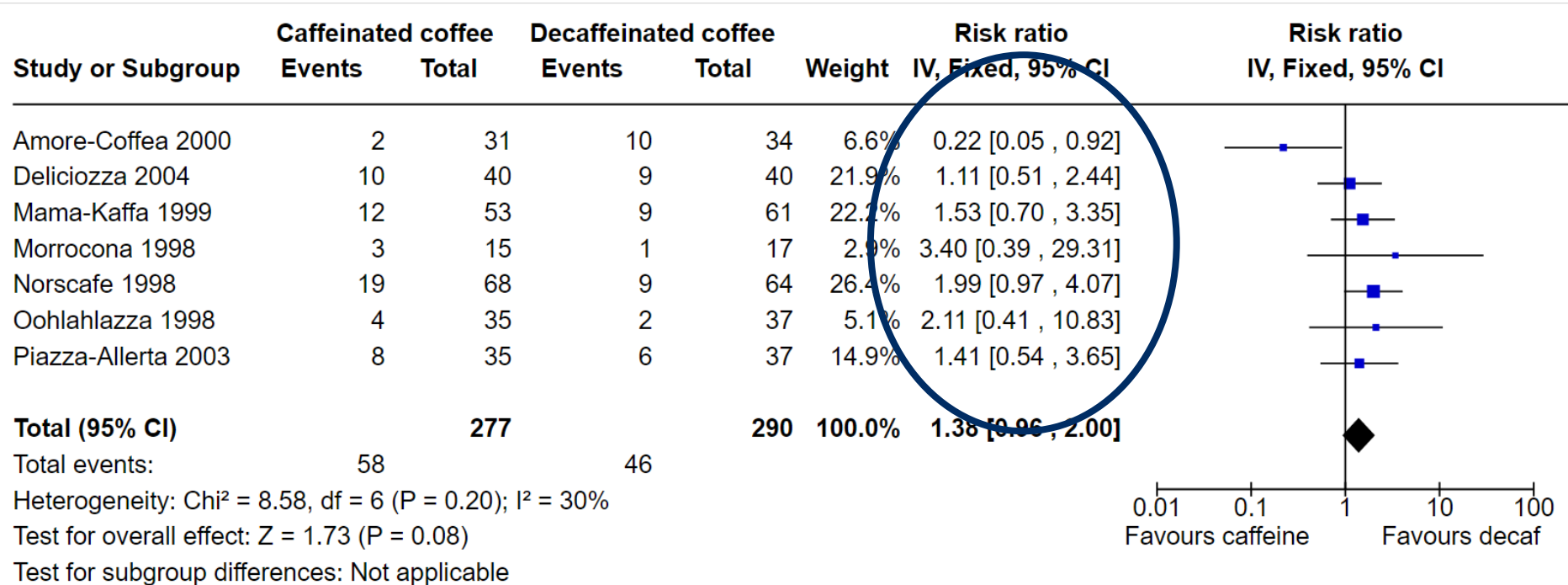
## Headache at 24 hours



- weight given to each study

# Forest plots

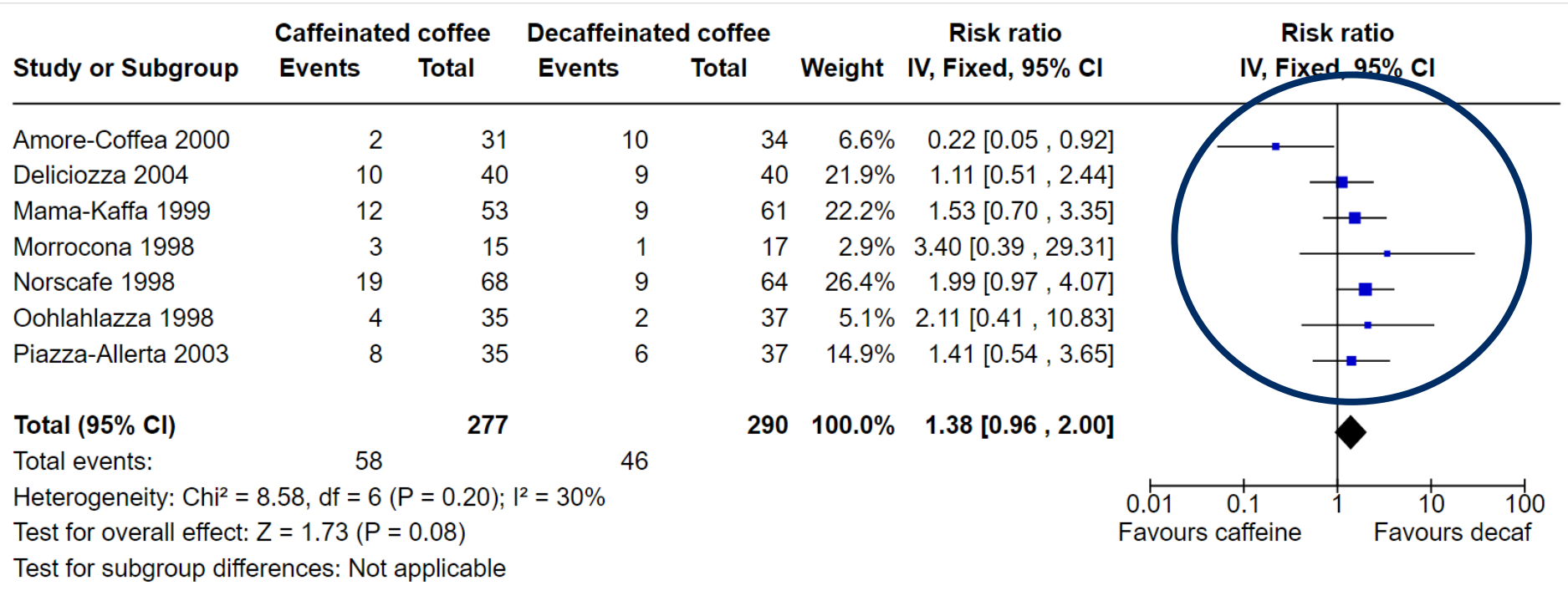
## Headache at 24 hours



- effect estimate for each study, with CI

# Forest plots

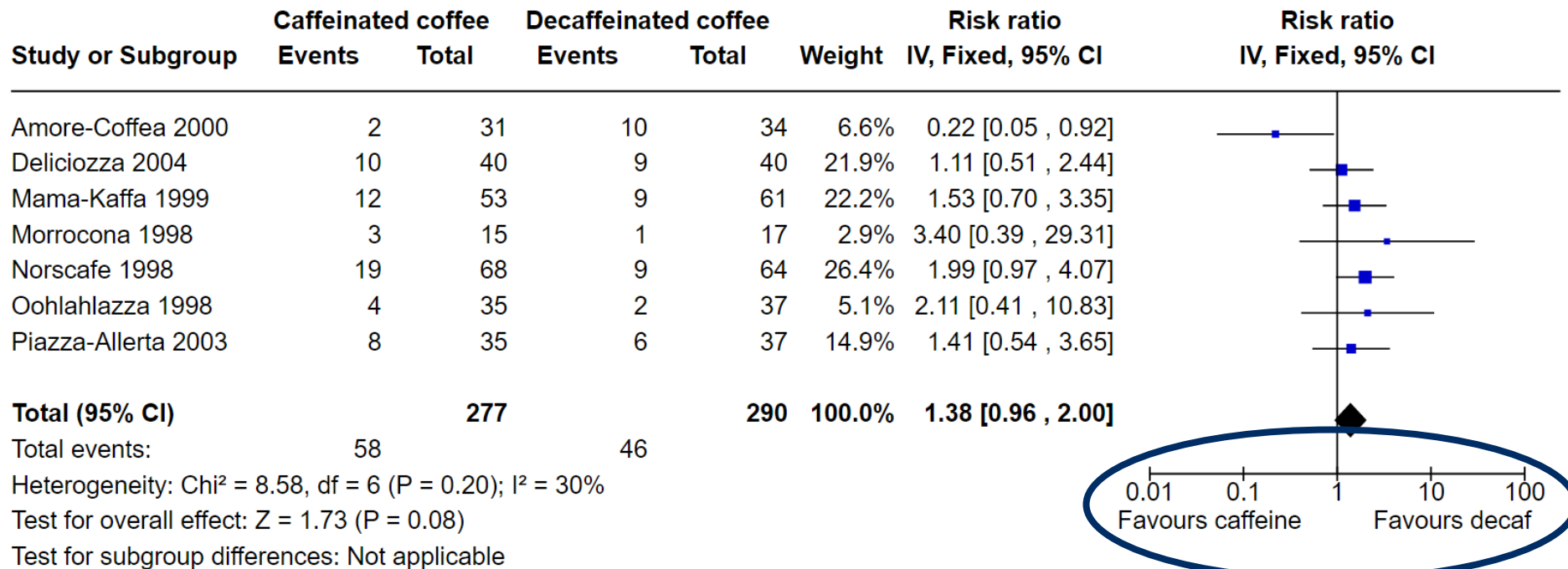
## Headache at 24 hours



- effect estimate for each study, with CI

# Forest plots

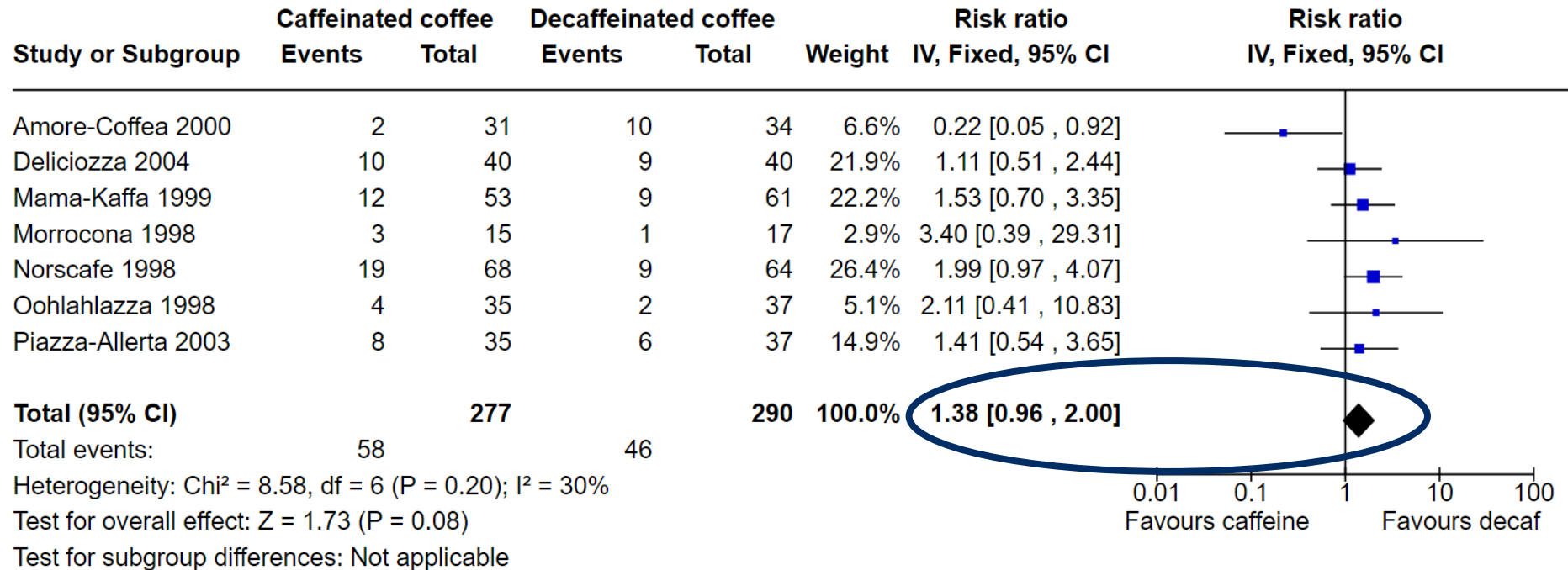
## Headache at 24 hours



- scale and direction of benefit

# Forest plots

## Headache at 24 hours



- pooled effect estimate for all studies, with CI

# Confidence intervals

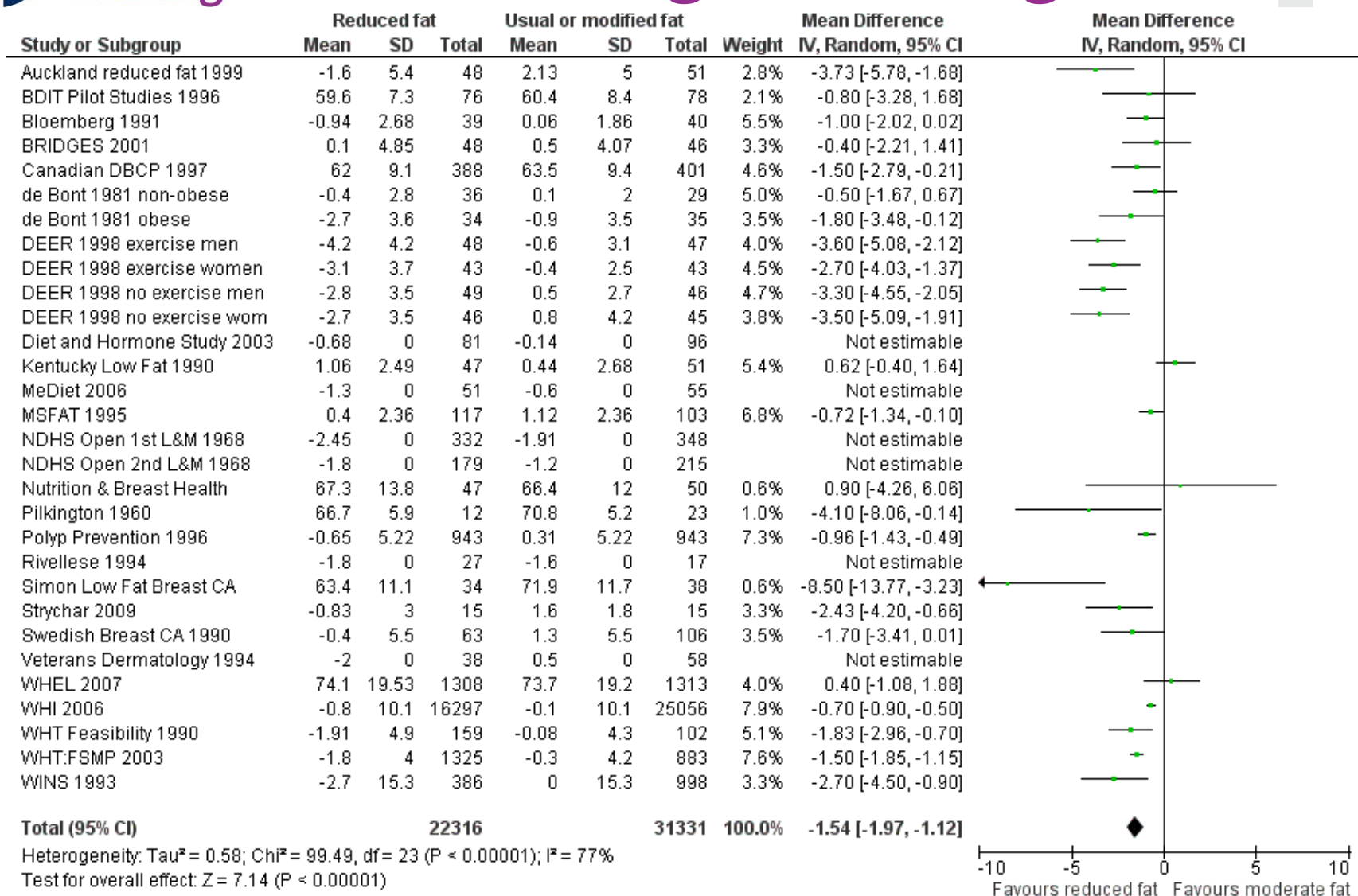
- Always present estimate with a confidence interval (CI)
- Effect estimate from study sample – best guess of effect
- Estimating effect in greater population - uncertainty
- 95% CIs are calculated to describe uncertainty around the effect estimate
- Describes a range of values we can be 95% certain includes the true effect
- Precision
  - Narrow CI (e.g. 0.70 to 0.80) indicates that the effect size is known precisely
  - Wide CI (e.g. 0.60 to 0.93) indicates greater uncertainty
  - Very wide CI (e.g. 0.50 to 1.10) indicates that we have very little knowledge about the effect

# Confidence intervals

- Largely affected by sample size
  - Larger sample = narrower 95% CIs in individual studies
  - In meta-analysis, more studies will lead to a narrower CI if results are similar
  - If results are conflicting, more studies may lead to a wider CI
- Significance
  - if the CI includes the null value
    - rarely means evidence of no effect
    - effect cannot be confirmed or refuted by the available evidence
  - consider what level of change is clinically important



# Considering clinical significance



# Presenting data in your review

- present outcomes in consistent order throughout
  - Abstract, Methods, Results, data
- forest plots
  - key forest plots linked as figures
    - usually primary outcomes
  - all forest plots will be published as supplementary data
  - avoid forest plots with only one study
- may also add other data tables
  - results of single studies
    - summary data for each group, effect estimates, confidence intervals
  - non-standard data



# What to include in the protocol

- how will you decide whether a meta-analysis is appropriate?
- meta-analysis model to be used



## Take home message

- there are several advantages to performing a meta-analysis but it is not always possible (or appropriate)
- plan your analysis carefully, including comparisons, outcomes and meta-analysis methods
- forest plots display the results of meta-analyses graphically
- interpret your results with caution



## References

- Deeks JJ, Higgins JPT, Altman DG (editors). **Chapter 10: Analysing data and undertaking meta-analyses.** In: Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). *Cochrane Handbook for Systematic Reviews of Interventions* version 6.2 (updated February 2021). Cochrane, 2021. Available from [www.training.cochrane.org/handbook.S](http://www.training.cochrane.org/handbook.S)
- Schünemann HJ, Higgins JPT, Vist GE, Glasziou P, Akl EA, Skoetz N, Guyatt GH. **Chapter 14: Completing ‘Summary of findings’ tables and grading the certainty of the evidence.** In: Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). *Cochrane Handbook for Systematic Reviews of Interventions* version 6.2 (updated February 2021). Cochrane, 2021. Available from [www.training.cochrane.org/handbook](http://www.training.cochrane.org/handbook).

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