

# Statistical methods and other new material in Handbook 5

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## New statistics in RevMan 5



In a nutshell

- New method for dichotomous data: inverse-variance
- Test for difference between subgroups
- Ability to swap events for dichotomous outcomes
- Display of heterogeneity variance

## Statistical methods - RevMan 4.2

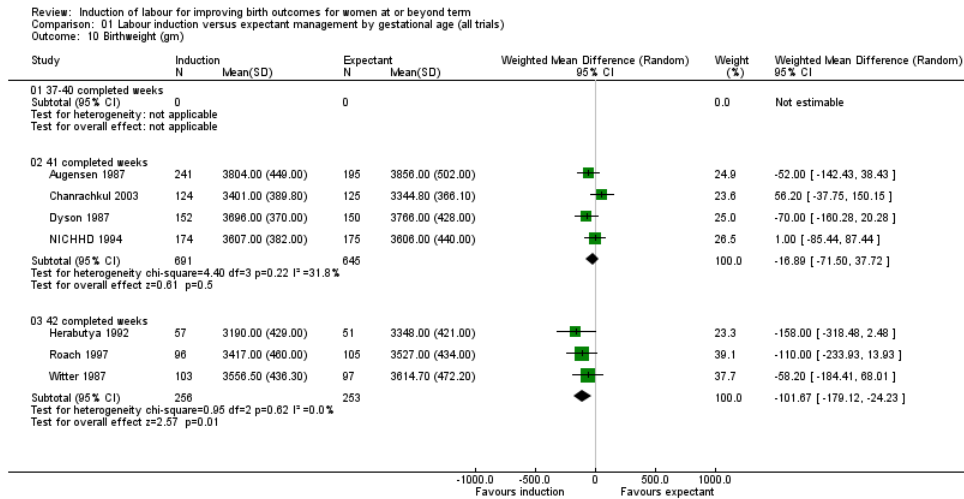
|           | Fixed |                 |                  | Random          |                  |
|-----------|-------|-----------------|------------------|-----------------|------------------|
|           | Peto  | Mantel-Haenszel | Inverse variance | Mantel-Haenszel | Inverse variance |
| OR        | Y     | Y               | -                | Y               | -                |
| RR        | n/a   | Y               | -                | Y               | -                |
| RD        | n/a   | Y               | -                | Y               | -                |
| MD        | n/a   | n/a             | Y                | n/a             | Y                |
| SMD       | n/a   | n/a             | Y                | n/a             | Y                |
| GIV       | n/a   | n/a             | Y                | n/a             | Y                |
| O-E and V | Y     | n/a             | n/a              | n/a             | n/a              |

## Statistical methods - RevMan 5

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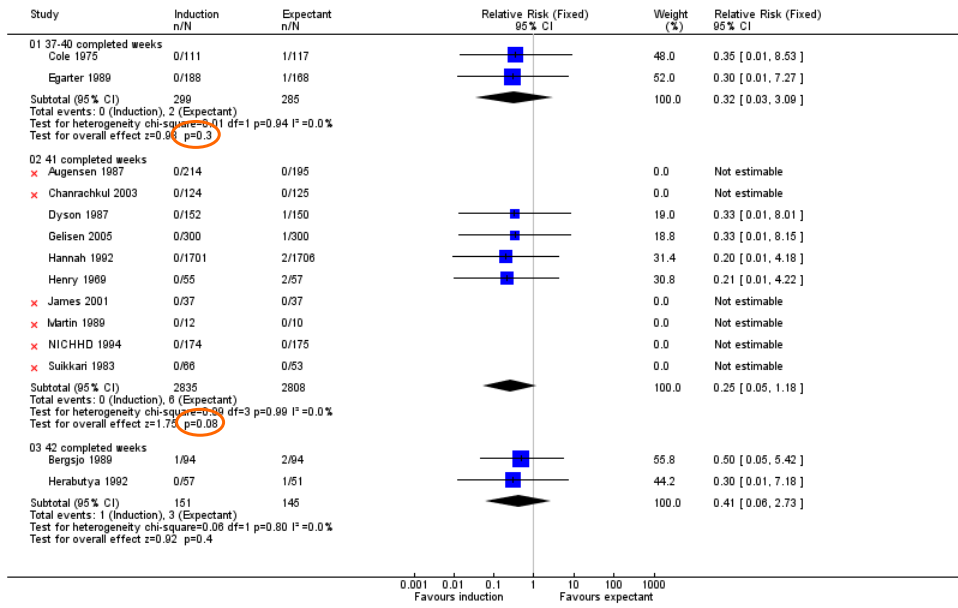
# Why?

- For 'completeness'
  - Inverse-variance method easiest to teach
- But mainly:
- To allow test for difference between subgroups

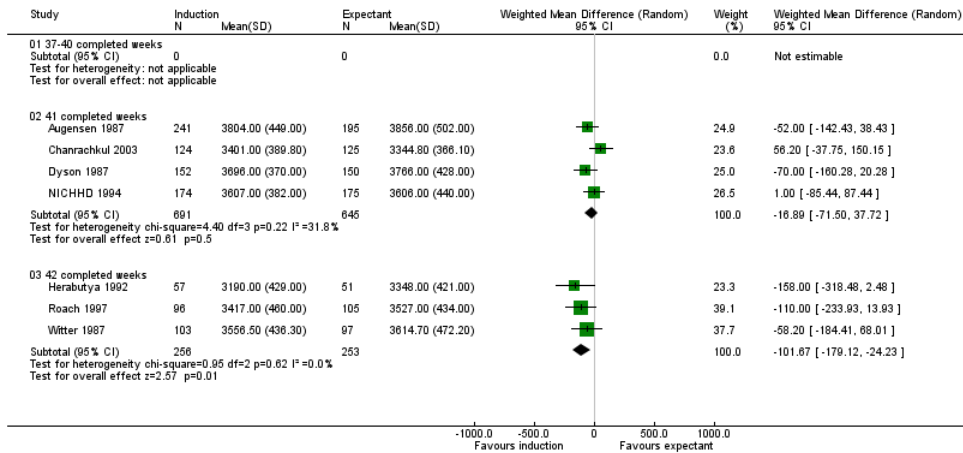


Induction at 42 weeks more beneficial than induction at 41 weeks?  
 Must not be decided by comparing statistical significance

Review: Induction of labour for improving birth outcomes for women at or beyond term  
 Comparison: 01 Labour induction versus expectant management by gestational age (all trials)  
 Outcome: 01 Perinatal death



Review: Induction of labour for improving birth outcomes for women at or beyond term  
 Comparison: 01 Labour induction versus expectant management by gestational age (all trials)  
 Outcome: 10 Birthweight (gm)



Test for difference:  $X = \text{chi-square}(\text{total}) - \text{chi-square}(1) - \text{chi-square}(2)$

$$= 8.76 - 4.40 - 0.95 = 3.41$$

compare with chi-squared with 1 d.f.

Gives  $P = 0.06$

## Test for difference between subgroups

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|-----------|-------|-----------------|------------------|-----------------|------------------|
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| O-E and V | Y     | n/a             | n/a              | n/a             | n/a              |

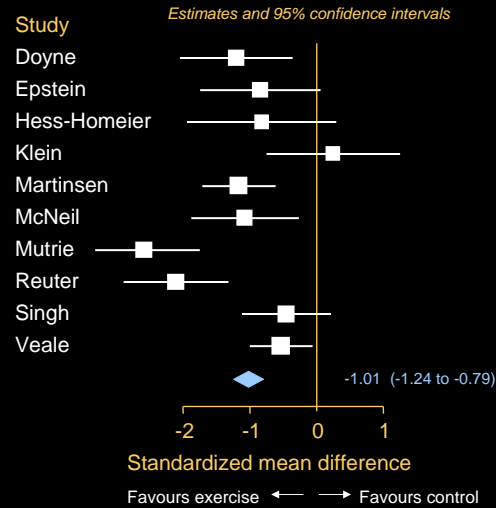
Possible, but conflicts with random-effects model, so has been suppressed. An alternative is available and should be implemented (to be discussed at Freiburg).

$$\tau^2$$

- Random-effects analyses now present the among-study variance

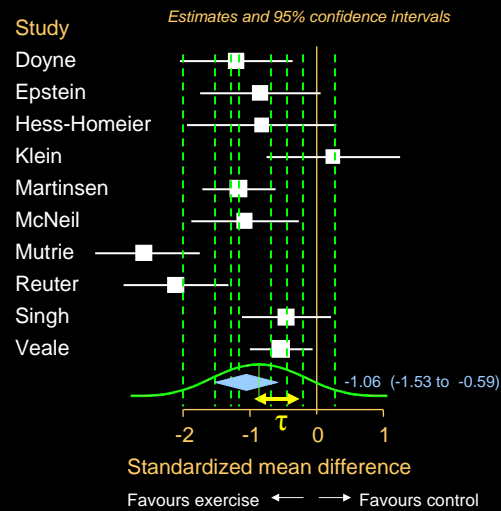
## Review: fixed-effect meta-analysis

- Assume common effect in every study
- No heterogeneity
- (same SMD underlying every study)



## Review: random-effects meta-analysis

- Allow for heterogeneity...
- ... **assuming** it has a particular nature



## Other statistics an author needs to understand to report a meta-analysis

- Forest plot
- Types of data and different effect measures
- Confidence intervals and P values
- Difference between fixed-effect and random-effects models
- Measuring heterogeneity: Q, df, P value and  $I^2$
- Identifying situations where special considerations apply (see later)

### And ideally...

- Sensitivity analyses
- Implications of missing data

## PART 3: Special topics

The image shows two overlapping screenshots of the Cochrane Handbook's Table of Contents. The top screenshot is a browser window showing the 'Part 3: Special topics' section, which includes chapters 13 through 22. The bottom screenshot is a PDF viewer showing the same section, with a detailed list of chapters and their sub-topics.

**Part 3: Special topics**

- [Chapter 13: Including non-randomized studies](#)
- [Chapter 14: Adverse effects](#)
- [Chapter 15: Incorporating economics evidence](#)
- [Chapter 16: Special topics in statistics](#)
- [Chapter 17: Patient-reported outcomes](#)
- [Chapter 18: Reviews of individual patient data](#)
- [Chapter 19: Prospective meta-analysis](#)
- [Chapter 20: Qualitative research and Cochrane](#)
- [Chapter 21: Reviews in health promotion and public health](#)
- [Chapter 22: Overviews of reviews](#)

**Part 3: Special topics**

- 13 Including non-randomized studies
- 14 Adverse effects
- 15 Incorporating economics evidence
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- 18 Reviews of individual patient data
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- 20 Qualitative research and Cochrane
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## Special types of study

- Randomized trials
  - cluster-randomized trials §16.3
  - cross-over trials §16.4
  - multi-arm trials §16.5
  - factorial trials §16.5
- Non-randomized studies 13
  - quasi-randomized trials
  - other experimental studies
  - observational studies
- Economics studies 15
- Studies collecting qualitative data 20

## Special types of outcome

- Time-to-event outcome §9.2 §9.4
- Ordinal outcomes §9.2 §9.4
- Rates §9.2 §9.4
- Adverse outcome 14
- Economic outcome 15
- Patient-reported outcome 17
- Qualitative data 20
- Rare event §16.5

## Special types of review

- Intervention review
  - Adverse effects review  14
  - Economics review  15
  - Individual patient data review  18
  - Prospective meta-analysis  19
- Diagnostic accuracy review 
- Overview  22
- Methodology review  A  
 5
- Qualitative review  20

## Non-randomized studies

- For some Cochrane reviews, the question of interest cannot be answered by randomized trials, and review authors may be justified in including non-randomized studies.
- Potential biases are likely to be greater for non-randomized studies compared with randomized trials, so results should always be interpreted. Particular concerns arise with respect to selection bias and reporting bias.
- We recommend that eligibility criteria, data collection and critical assessment of included studies place an emphasis on specific features of study design (e.g. which parts of the study were prospectively designed) rather than 'labels' for study designs (such as case-control versus cohort).
- Risk of bias in non-randomized studies can be assessed in a similar manner to that used for randomized trials, although more attention must be paid to the possibility of selection bias.
- Meta-analyses of non-randomized studies must consider how potential confounders are addressed, and consider the likelihood of increased heterogeneity resulting from residual confounding and from other biases that vary across studies.

## Adverse effects

- To achieve a balanced perspective, all reviews should try to consider the adverse aspects of the interventions.
- Interventions may have many different adverse effects, and reviews may need to focus on a few important ones in detail, together with a broader, more general summary of other potential adverse effects.
- Different **eligibility criteria** may be necessary for adverse effects.
- Sometimes a separate **review** might be appropriate for adverse effects.
- Data on adverse effects are often sparse, but the absence of information does not mean that the intervention is safe.

## Economics

- Economics is the study of the optimal allocation of limited resources for the production of benefit to society and is therefore relevant to any healthcare decision.
- This chapter describes methods for incorporating economics perspectives and evidence into Cochrane reviews, with a focus on critical review of health economics studies.
- Incorporating economics perspectives and evidence into Cochrane reviews can enhance their usefulness and applicability for healthcare decision-making and new economic analyses.

## Qualitative research

- Qualitative research can contribute to Cochrane Intervention reviews in four ways:
  - *informing* reviews by using evidence from qualitative research to help define and refine the question, and to ensure the review includes appropriate studies and addresses important outcomes;
  - *enhancing* reviews by synthesizing evidence from qualitative research identified whilst looking for evidence of effectiveness;
  - *extending* reviews by undertaking a search to specifically seek out evidence from qualitative studies to address questions directly related to the effectiveness review;
  - *supplementing* reviews by synthesizing qualitative evidence within a stand-alone, but complementary, qualitative review to address questions on aspects other than effectiveness.

## Qualitative research

- Studies included in Cochrane reviews may have qualitative research embedded within, or associated with, them.
- There are many methods of qualitative evidence synthesis that are appropriate to the aims and scope of Cochrane Intervention reviews.
- The synthesis of qualitative research is an area of debate and evolution. The Cochrane Qualitative Methods Group provides a forum for discussion and further development of methodology in this area.

## Discussion

### What statistics do review authors need to know?

- Data collection
  - understand types of data
  - understand statistics likely to be reported
  - mean, SD, SE, risk, confidence interval, sample sizes
- Data analysis
  - understand manipulations to obtain useful data from reported statistics
  - understand effect sizes (OR, RR, RD, MD, SMD etc)
  - understand principles of meta-analysis
  - understand what is heterogeneity and how to measure it
  - choose meta-analysis model
  - identify issues where expert input needed

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