NIPH
Norwegian Institute of Public Health

# Analysing data and conducting a meta-analysis

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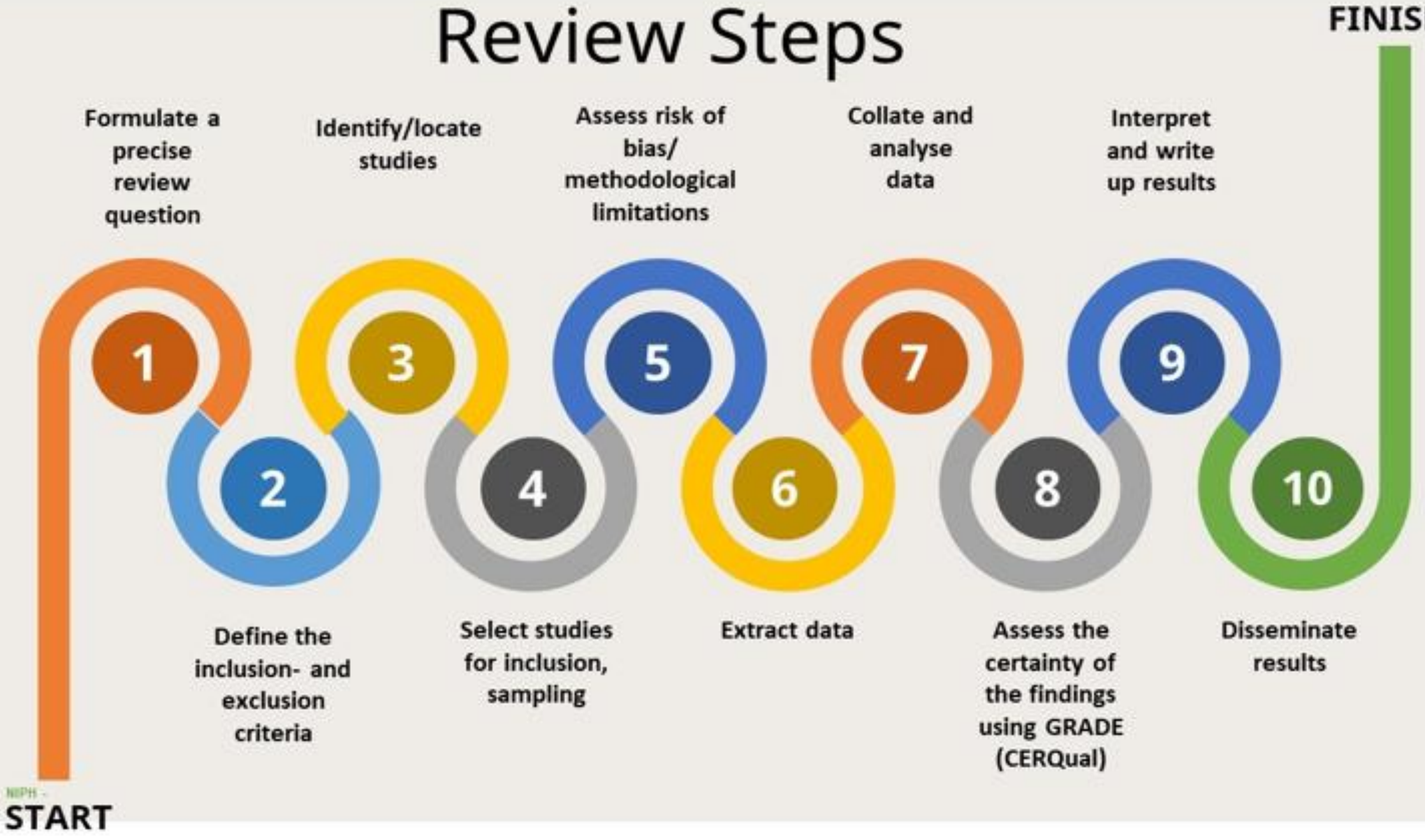
Lillebeth.larun@fhi.no

Thanks to Eva Denison for inspiration and Cochrane Handbook

# Review Steps



# Approaches to data synthesis in quantitative systematic reviews

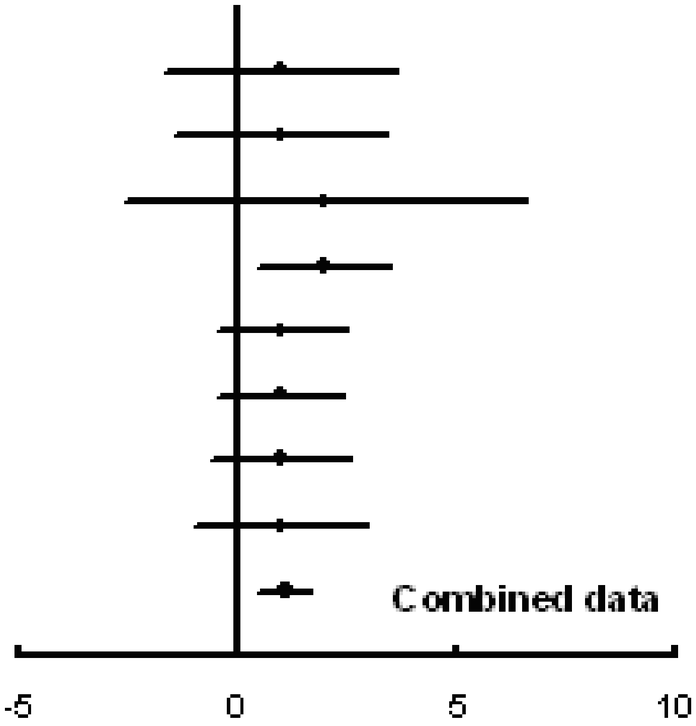
- Narrative
- Quantitative

# Two approaches

## Narrative

**Results** 22 studies met the inclusion criteria. We found some evidence that targeted behaviour change programmes can change the behaviour of motivated subgroups, resulting (in the largest study) in a shift of around 5% of all trips at a population level. Single studies of commuter subsidies and a new railway station also showed positive effects. The balance of best available evidence about publicity campaigns, engineering measures, and other interventions suggests that they have not been effective. Participants in trials of active commuting experienced short term improvements in certain measures of health and fitness, but we found no good evidence on effects on health of any effective intervention at population level.
**Conclusions** The best available evidence of effectiveness in promoting a modal shift is for targeted behaviour change programmes, but the social distribution of their effects is unclear and some other types of intervention have yet to be rigorously evaluated.

## Quantitative – meta-analysis




In between: Forest plot without combining data

# Two approaches

## Narrative

- When quantitative analysis is not deemed appropriate
  - «Clinical heterogeneity», e.g.
    - Complex interventions
    - Different settings
    - Different measurement methods and length of follow-up
- Studies with qualitative data

## Quantitative

- Statistical synthesis of quantitative data
  - Improved power
    - Increased N due to pooling of studies
  - Improved precision
    - Narrower confidence intervals around the population estimate
  - Beware
    - Methodological bias, heterogeneity, publication bias

# Choosing a synthesis method

## Aim to draw conclusions from a body of evidence

- Bringing together data from a set of included studies
- Summary of characteristics of each study in a PICO format (dependent on your type of question) + other relevant information
- State the comparisons planned (dependent on your questions)
- Chose statistical methods dependent on your outcomes, for example if the are reported as dichotomous or continuous
- Check for heterogeneity across the included studies
- This list is not exhaustive – you need to do everything with your research question in mind

For more informatin: Cochrane Handbook. Chapter 9: Summarizing study characteristics and preparing for synthesis https://training.cochrane.org/handbook/current/chapter-09

# Student work

## Protocol stage

- Describe how your effect estimates will be measured, for example dichotomous og continous
- Describe which measurement instruments you think will be used
- State your comparisons

Open access Protocol

BMJ Open

**Predictors of chronic pain and level of physical function in total knee arthroplasty: a protocol for a systematic review and meta-analysis**

Unni Olsen [1,2] Maren Falch Lindberg [1,2] Eva Marie-Louise Denison,[3] Christopher James Rose,[3] Caryl Lynn Gay [4,5] Arild Aamodt,[2] Jens Ivar Brox [6,7] Øystein Skare,[2] Ove Furnes,[8,9] Kathryn A Lee,[4] Anners Lerdal [5,10]

BMJ Open: first published as 10.1136/bmjopen-2020-0

## Data synthesis - example protocol

- A narrative analysis of the results will be conducted for all included studies for the two co-primary outcomes at 12 months. Meta-analyses will be performed for the two co-primary outcomes of chronic pain and impaired physical function assessed 3 months and 6 months after the surgery, if possible.
- Where possible, we will perform quantitative data synthesis following the guidance of the most recent version of the Cochrane Handbook available at the time of the analysis.[36] If meta-analysis cannot be performed, we will conduct a narrative analysis.



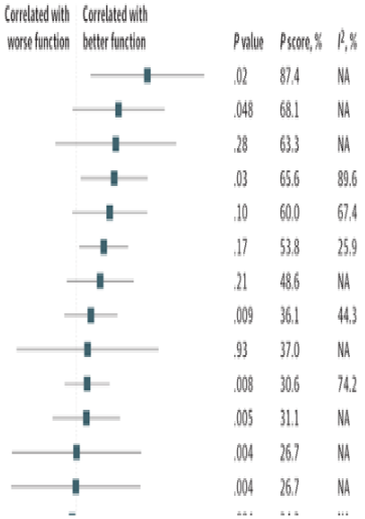
Olsen U, Lindberg MF, Denison EM*, et al* Predictors of chronic pain and level of physical function in total knee arthroplasty: a protocol for a systematic review and meta-analysis *BMJ Open* 2020;**10:**e037674. doi: 10.1136/bmjopen-2020-037674

# Factors Correlated With Physical Function 1 Year After Total Knee Arthroplasty in Patients With Knee Osteoarthritis

## Result (example)

Figure 2. Forest Plot of Factors Associated With Physical Function at 12 mo

| Factor | Studies, No. | Correlation (95% CI) | *P* value | *P* score, % | $I^2$, % |
|---|---|---|---|---|---|
| Mobility[24] | 1 | 0.25 (0.05 to 0.44) | .02 | 87.4 | NA |
| Pain self-efficacy[28] | 1 | 0.15 (-0.01 to 0.31) | .048 | 68.1 | NA |
| Knee status[37] | 1 | 0.14 (-0.08 to 0.35) | .28 | 63.3 | NA |
| Preoperative function[22,24-26,28,37] | 6 | 0.14 (0.02 to 0.26) | .03 | 65.6 | 89.6 |
| Mental health[22,23,25,26,28] | 5 | 0.12 (-0.01 to 0.25) | .10 | 60.0 | 67.4 |
| K-L grade[22,27] | 2 | 0.10 (0.01 to 0.19) | .17 | 53.8 | 25.9 |
| Cruciate retaining[22] | 1 | 0.09 (-0.03 to 0.21) | .21 | 48.6 | NA |
| Male sex[22,25,28,38] | 4 | 0.05 (-0.04 to 0.15) | .009 | 36.1 | 44.3 |
| Outcome expected[26] | 1 | 0.04 (-0.21 to 0.29) | .93 | 37.0 | NA |
| Preoperative pain[22,25,27,38] | 4 | 0.04 (-0.04 to 0.12) | .008 | 30.6 | 74.2 |
| Patella resurfaced[22] | 1 | 0.04 (-0.09 to 0.16) | .005 | 31.1 | NA |
| Surgery duration[25] | 1 | 0 (-0.23 to 0.23) | .004 | 26.7 | NA |
| Kinesophobia[25] | 1 | 0 (-0.23 to 0.23) | .004 | 26.7 | NA |



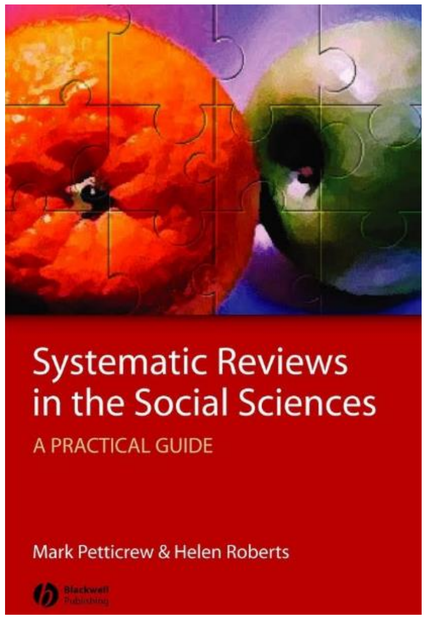

## Statistical analysis (part)

- Findings for all included studies were synthesized by outcomes at 3, 6, or 12 months after TKA as described in the protocol.[14] We were unable to complete planned multivariate random-effects meta-analysis because extracted data were too sparse (with a large number of factors reported by relatively few studies). Accordingly, we used a frequentist version of the bayesian multivariate model.[15] Additional protocol deviations are explained in eMethods in the Supplement.

Olsen U, Lindberg MF, Rose C, et al. Factors Correlated With Physical Function 1 Year After Total Knee Arthroplasty in Patients With Knee Osteoarthritis: A Systematic Review and Meta-analysis. *JAMA Netw Open.* 2022;5(7):e2219636. doi:10.1001/jamanetworkopen.2022.19636

# Narrative synthesis in three steps

1. Organize the description of the studies in logical categories
2. Analyse the findings within each category
3. Summarize the findings across all categories



# Narrative synthesis

- All data are summarized in tables
  - PIO/PICO/PEO/PECO
  - Methodological quality
  - Findings
  - Context
  - Other information of interest
- The tables themselves are not the synthesis but the basis for the synthesis

# «Vote counting»

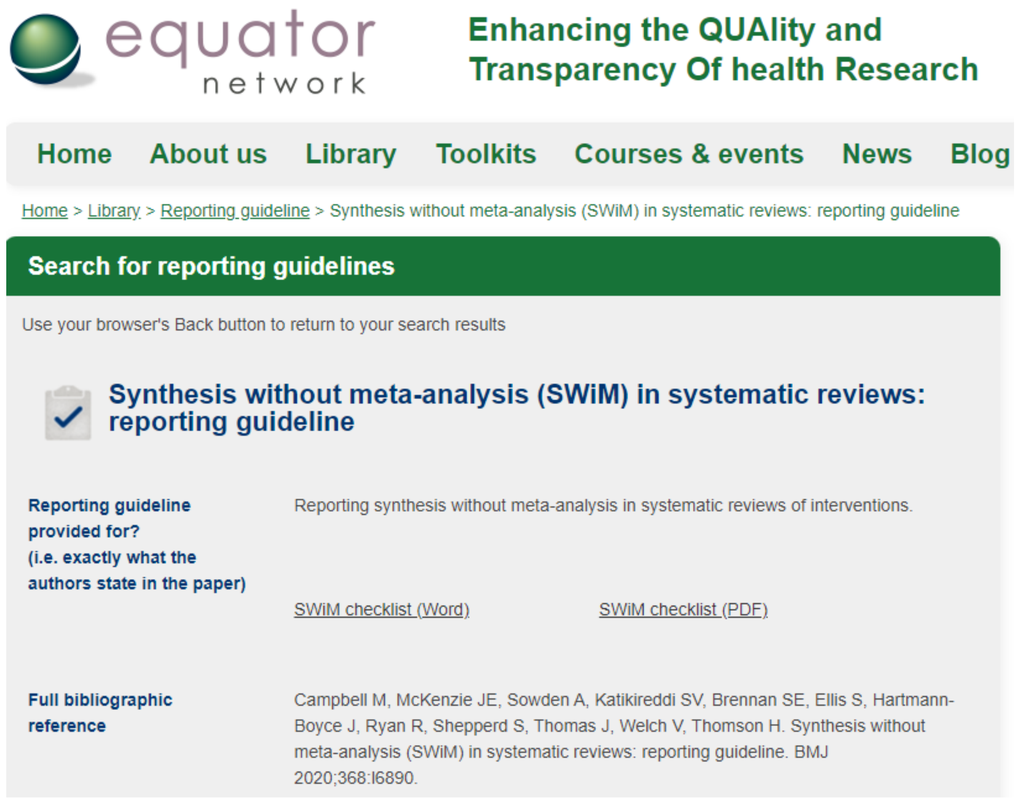
- How many studies have positive or negative results?
- NOT recommended – does not account for
  - The size of the sample
  - Study methods and quality
  - Qualitative differences between the studies
  - Interactions between the variables in the studies

# SWiM

## Synthesis Without Meta-analysis - guideline

- Nine-item checklist to promote transparent reporting for reviews of interventions that use alternative synthesis methods

- The SWiM items prompt users to report how studies are grouped, the standardised metric used for the synthesis, the synthesis method, how data are presented, a summary of the synthesis findings, and limitations of the synthesis



# Meta-analysis

- The statistical combination of results from two or more studies
  - Potential advantages of meta-analyses
    - increase in power
    - improvement in precision
    - ability to answer questions not posed by individual studies
    - opportunity to settle controversies arising from conflicting claims
  - Potential to mislead seriously
    - specific study designs
    - within-study biases
    - variation across studies
    - reporting biases

# Steps in performing a meta-analysis

- Define a clear and focused topic for the review
- Establish inclusion- and exclusion criteria
- Locate all studies relevant to the topic
- Abstract information from the publications
- Assess risk of bias
- Carry out a descriptive analysis
- Carry out a statistical analysis
- Interprete the results

# Effect estimates

- Dichotomous outcomes
  - Relative risk (RR)
  - Odds ratio (OR)
  - Hazard ratio (HR)

- Continuous outcomes
  - Mean difference (MD)
  - Standardized mean difference (SMD)
    - Only shows direction and magnitude of effects
    - 0.2 small effect; 0.5 medium effect; 0.8 large effect

# Also consider

## If you have another core question than effect

- Measures of incidence
- Measures of disease risk
- Measures of association
- Measures of impact

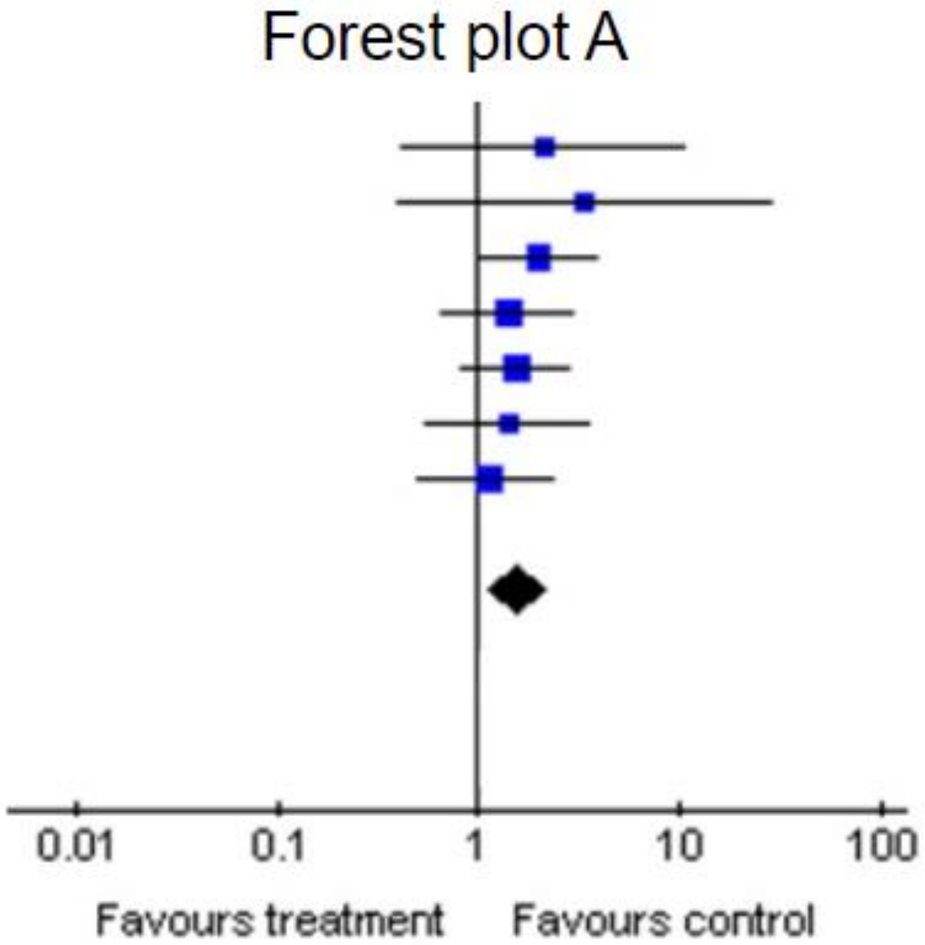
- …and consider consulting a statistician!

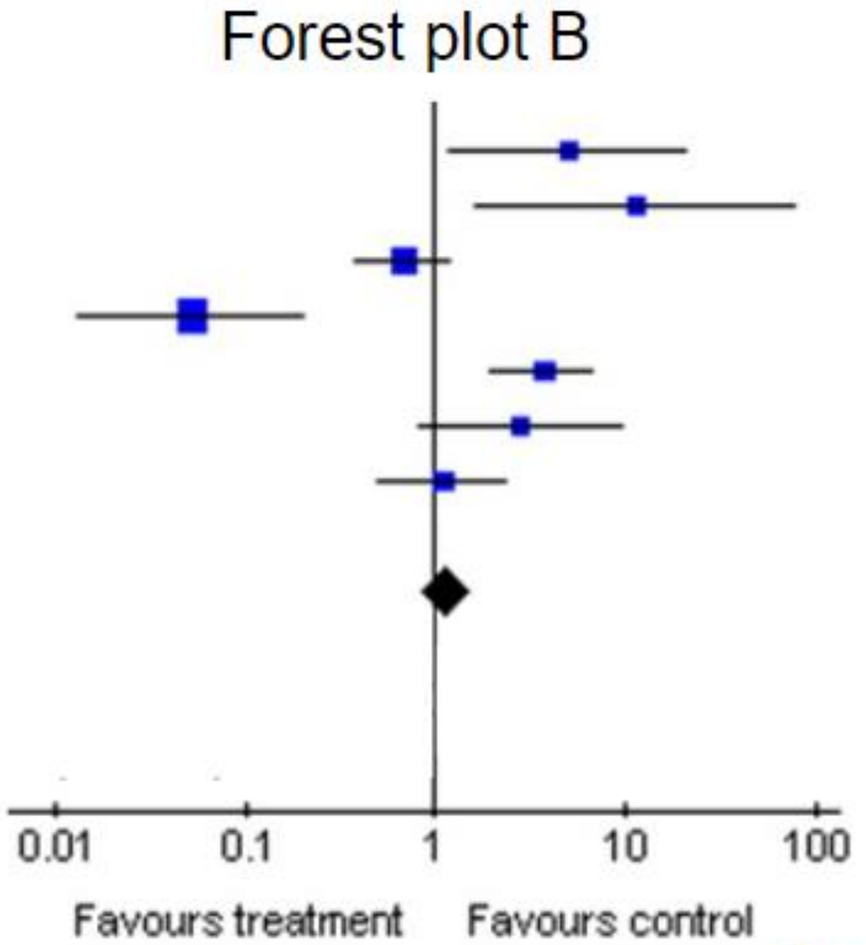
# Statistical models

- Fixed effect – we assume that
  - All studies estimate the same intervention effect
  - All variation in observed effects are due to sampling error
- Random effect – we assume that
  - Intervention effects may vary across studies, e.g. due to different mix of participants and implementation of interventions
  - Distribution of effects across studies

# Heterogeneity

- «Clinical»
  - Comparing apples and oranges
  - PICO, broad inclusion criteria
  - Splitting/lumping
  - Is it appropriate to conduct meta-analysis?
- Statistical – what proportion of the variation that cannot be explained by random variation
  - Calculated in the meta-analysis
  - **I-square, Chi-square ($p < 0.10$ indicates statistical significance)**
- Statistical - the extent of variation among the effects observed in different studies
  - Calculated in the meta-analysis
  - **Tau square**



# Interpretation of heterogeneity

| $I^2$ | Interpretation |
|---|---|
| 0 – 40 % | Might not be important |
| 30 – 60 % | May represent moderate heterogeneity |
| 50 – 90 % | May represent substantial heterogeneity |
| 75 – 100 % | Considerable heterogeneity |

Importance

- Size and direction of observed effects
- Strength of evidence (p-value from Chi-square test)

# Strategies for dealing with heterogeneity

| Strategy | Possible solution |
|---|---|
| Check data | Correct extraction errors or choice of unit |
| Evade | Try other effect measures |
| Ignore | Don't! |
| Give up | Drop meta-analysis |
| Explore | Does the heterogeneity disappear in subgroup- and sensitivity analyses? |
| Embrace | Use a statistical model that opens for variation between primary studies |