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Meta-analysis

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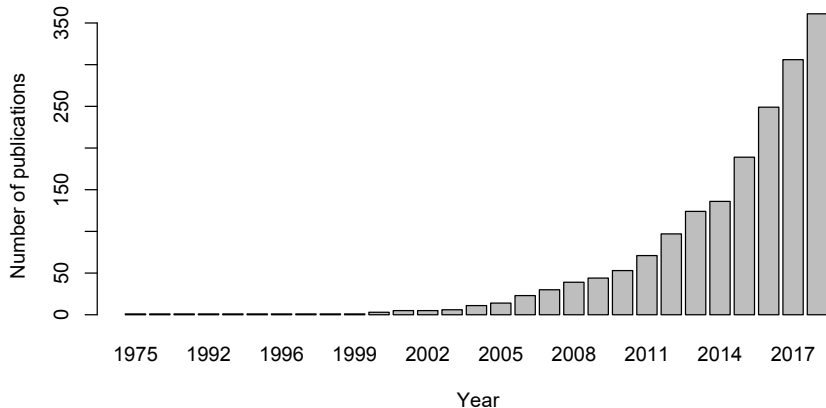
# Content

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(see full schedule online)

# Motivation

Results from a PubMed search for papers with "meta-analysis" or "meta analysis" or "systematic review" in the title:



# What is a systematic review?

## Systematic review

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## Systematic review

- Collection and description of empirical evidence to a specific research question, with specified criteria.
- Yields a systematic list of the entire published literature for a research question, in contrary to a simple review, which is often based on an arbitrary selection of studies.
- Can always be done.

—→ qualitative description of all relevant studies and results.

# What is a meta-analysis?

## Meta-analysis

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## Meta-analysis

- Statistical analysis and "pooling" of the collected results of a systematic review.
- Should be based on a systematic review.
- Is not always possible - only if the studies can be meaningfully aggregated.

→ quantitative summary of the studies (if meaningful).

# Steps of a systematic review/meta-analysis

- 1 Specify research question, search strategy, filtering steps.

Prospectively register the protocol.

- 2 Search articles.

- 3 Filter articles.

- 4 Extract information from the selected articles  
(and present in table).

- 5 Judge the quality of the extracted studies.

- 6 Judge the heterogeneity of the articles.

- 7 Estimate pooled total effect.

- 8 Determine publication bias.

- 9 Analyze subgroups.

Publish results after completion.



## Overview of ressources in R

- Overview of R packages for meta-analysis: <https://cran.r-project.org/web/views/MetaAnalysis.html>
- R package for helping with systematic review, extracting information, and e.g. creating PRISMA plots: <https://cran.r-project.org/web/packages/metagear/>
- Different functions for meta-analysis: <https://cran.r-project.org/web/views/MetaAnalysis.html>

## Doing a meta-analysis in R

Use metafor R package, see `R_12b_meta_analysis.Rmd`.

## Step 6: estimate the heterogeneity of the articles

### Reminder

- Studies are too different  
→ no meta-analysis, only systematic review.
- All studies are collected and their results homogeneous  
→ fixed-effect meta-analysis.
- Studies are not complete/only a sample  
→ random-effect meta-analysis.

## Step 6: estimate the heterogeneity of the articles

### Measures of heterogeneity

- $\tau^2$  = heterogeneity  
= variance of the effect estimates (e.g. log relative risk) between studies
- $I^2$  = heterogeneity / total variance  
= heterogeneity / (variance between + within studies)  
Possible orientation: small 25% / moderate 50% / large 75%
- $H^2$  = heterogeneity / variance within studies
- Cochran's heterogeneity statistic  $Q$  = weighted quadratic difference between study effects and summary effect
- $Q$  can be used to test heterogeneity ( $\chi^2$ -distribution with  $K - 1$  degrees of freedom,  $K$  = number of studies).
- all directly computed in `rma()` function in `metafor` package.

## Step 7: estimate pooled total effect

- Estimate the total effect as weighted mean of the study effects ...
- ... in a statistical model, in which the studies are the observations and their effect measures are the outcome ( $y$ ), through the intercept of the model, which only contains the intercept as fixed effect and potentially also a random intercept.
- Default weights in `rma()` function:  $1/\text{variance}$
- Analogously: estimate the variance of the total effect estimate.

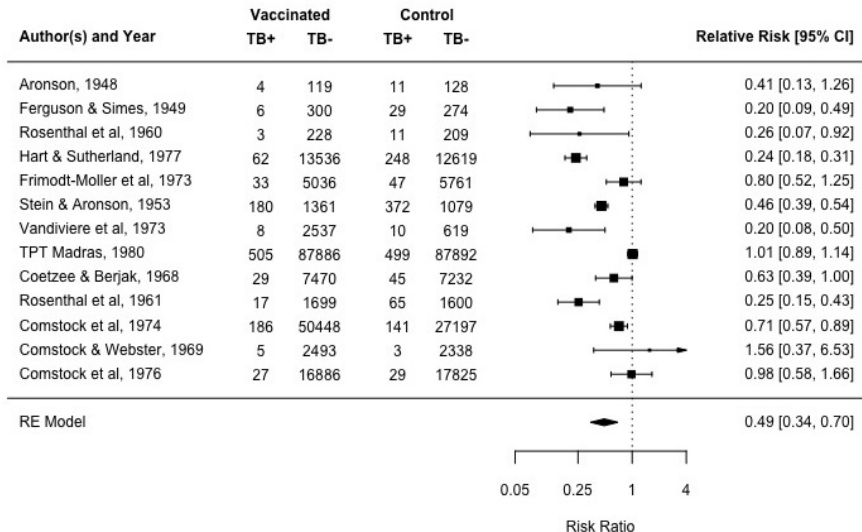
## Step 7: estimate pooled total effect

### Implemented in `metafor`:

- Relative risk, odds ratio, risk difference, ...
- Mean difference, standardized mean difference
- Different transformations of correlation coefficients
- Different transformations of proportions
- Extract the effect measures with the `escalc()` function, pool with the `rma()` function
- ...

For further measures, see `meta` package and the overview in `help(meta)`.

## Step 7: visualize the results: forest plot



In the `metafor` package with the `forest()` function.

## Exercises

- 1 Do a meta-analysis with the `dat.bcg` dataset with all steps as in `R_12b_meta_analysis.Rmd`, but with the risk difference as effect measure.
- 2 Do a meta-analysis with the dataset `dat.begg1989` in the `metafor` package.
- 3 Do a meta-analysis with the dataset `dat.bourassa1996` in the `metafor` package.
- 4 For help with the last two exercises, see the vignette <https://cran.r-project.org/web/packages/metafor/metafor.pdf>



Questions?

# References

- `www.ccace.ed.ac.uk/research/software-resources/systematic-reviews-and-meta-analyses`.
- Handbuch für Cochrane Handbook for Systematic Reviews of Interventions: <https://training.cochrane.org/handbook>
- Pigott (2012). Advances in Meta-Analysis. Springer.
- Chen & Peace (2013). Applied Meta-Analysis with R. CRC Press.