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Biostatistics

Publication Bias in the Cochrane Library of Systematic Reviews

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Cochrane Library

Database of high-quality, systematic reviews in clinical science.

Currently $\sim$ 8,000 reviews, prepared by independent groups.

Reviews are peer-reviewed and prepared after guidelines.

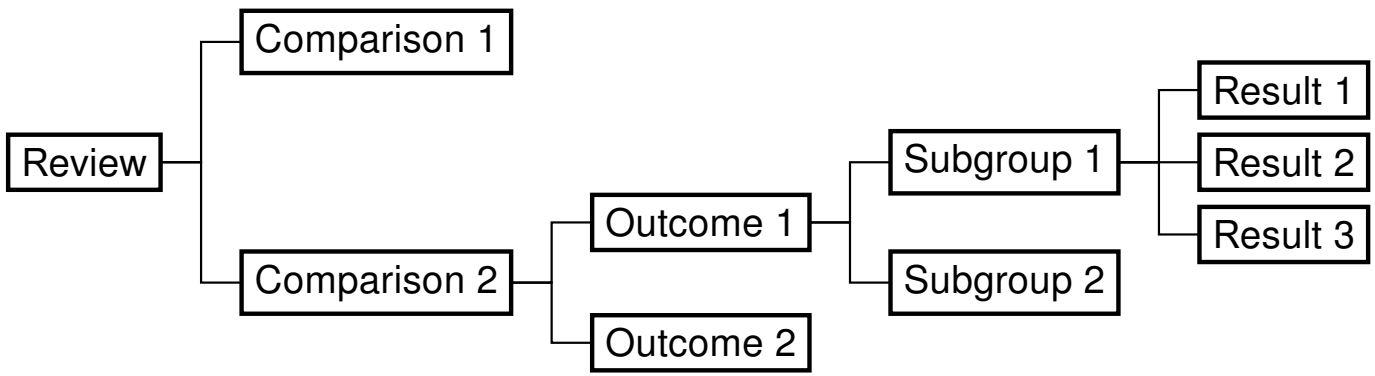
Cochrane Library Dataset

5,016 systematic reviews with studies published until 2018.

52,995 studies.

463,820 study results.

Dataset Structure



Dataset Structure

- Comparison: What is compared, e.g. treatment vs. control
- Outcome: How it is compared
- Subgroup: Subgroup affiliation
- Meta-Analysis Group: Results from same comparison, outcome and subgroup

Review Example: binary outcome

Barbiturate efficacy in head injury

Study	Comparison	Outcome	Events	Total	Events_c	Total_c
Bohn 1989	Barbiturate vs no b	Death at the end of	11	41	11	41
Bohn 1989	Barbiturate vs no b	Death or severe dis	18	41	13	41
Eisenberg 1988	Barbiturate vs no b	Uncontrolled ICP du	25	37	30	36
Eisenberg 1988	Barbiturate vs no b	Hypotension during	23	37	18	36
Perez-Barcena 2008	Pentobarbital vs Th	Death at the end of	16	21	9	21
Perez-Barcena 2008	Pentobarbital vs Th	Death or severe dis	17	21	13	21
Perez-Barcena 2008	Pentobarbital vs Th	Uncontrolled ICP du	18	22	11	22
Perez-Barcena 2008	Pentobarbital vs Th	Hypotension during	20	22	21	22
Schwartz 1984	Barbiturate vs Mann	Death at the end of	6	15	7	14
Schwartz 1984	Barbiturate vs Mann	Uncontrolled ICP du	19	28	12	31
Ward 1985	Barbiturate vs no b	Mean ICP during tre	0	27	0	26
Ward 1985	Barbiturate vs no b	Mean arterial press	0	27	0	26
Ward 1985	Barbiturate vs no b	Mean body temperatu	0	27	0	26

Dataset Properties

Missing data:

Missing mean values and mean differences	984
Missing standard deviations and standard errors	1300
Missing sample sizes	12173
Missing study year	44649

Dataset Properties

Review and study properties:

	5% quantile	median	mean	95% quantile
Study number	1	7	12	40
Comparison number	1	2	4	12
Group number	2	19	37	132
Study years	1981	2002	2000	2013
Study sample size	13	78	750	890

Pooling Studies - Meta-Analysis

Multiple results in a meta-analysis group can be pooled:

n	Number of groups	Cumulative sum of groups
1	102344	188079
2	31686	85735
3	16072	54049
4	9628	37977
5	6444	28349
6	4230	21905
7	2961	17675
8	2114	14714
9	1592	12600
10	11008	11008

Meta-analysis

Benefits:

- Summary of evidence (e.g. of a treatment)
- More reliable evidence (?)

Assumptions:

- Identical study settings (can be relaxed)
- Random sample of studies

Small Study Effects

"The tendency for the smaller studies to show larger treatment effects" (Sterne et al., 2001)

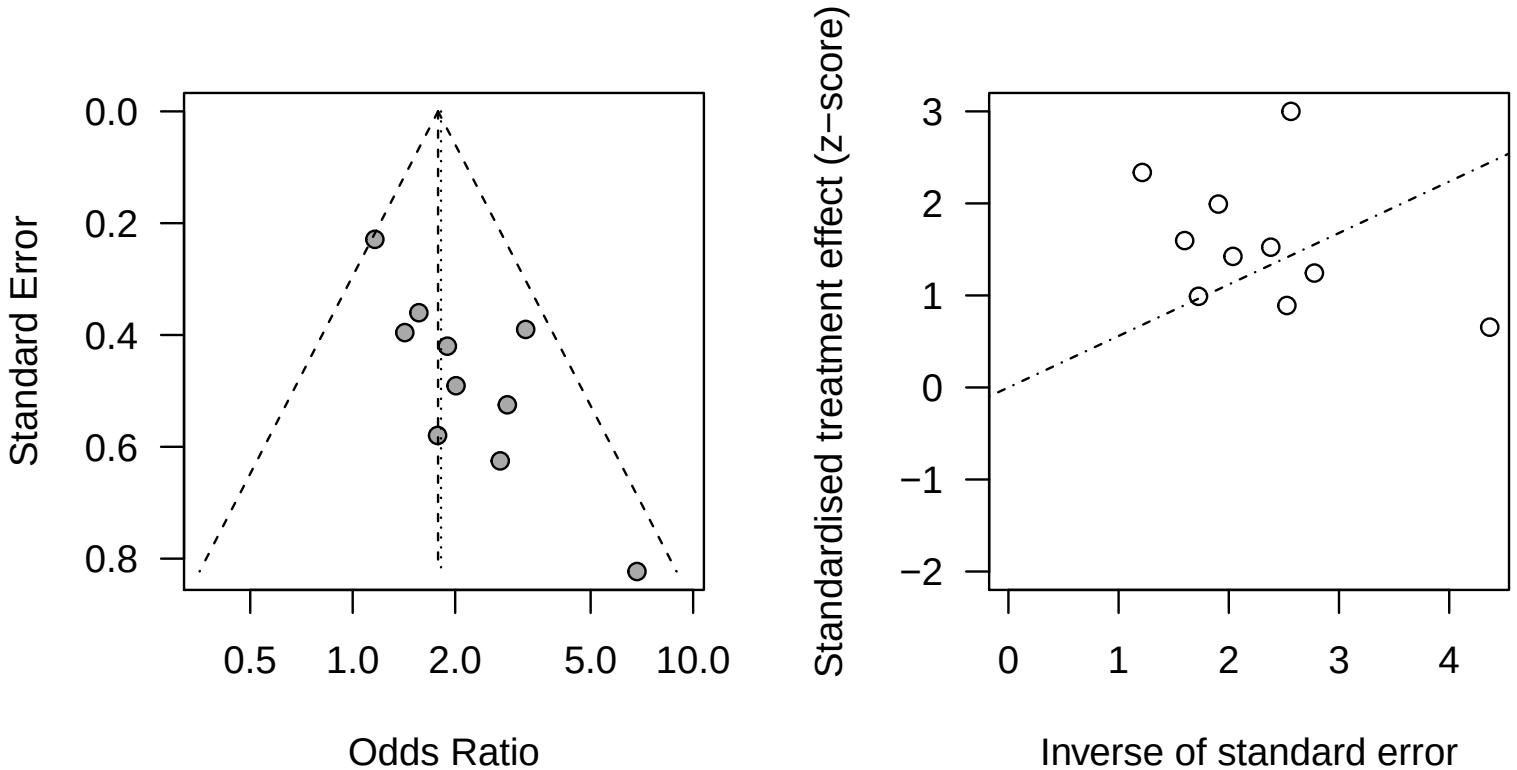
Small Study Effects

Causes:

- Selective publication of studies with large effects
- Bias in smaller studies
- Systematical differences in study settings
- ...

Publication Bias Tests

Test for funnel plot asymmetry:



Publication Bias Tests

Critical: Number of studies in meta-analysis must be large ($\geq$ 10).

Various tests for meta-analyses with continuous and binary outcomes:

Regression based: Egger's, Peter's or Thompson and Sharp's test

Rank based: Begg and Mazumdar's Test

References

Sterne, J. A. C., Egger, M., and Smith, G. D. (2001). Investigating and dealing with publication and other biases in meta-analysis. *BMJ*, 323(7304):101–105.