University of Zurich[UZH]

Biostatistics

Publication Bias in the Cochrane Library of Systematic Reviews

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## Error in UseMethod("mutate_"):  no applicable
method for 'mutate_' applied to an object of class
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Cochrane Library

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

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

Reviews are peer-reviewed and prepared after guidelines.

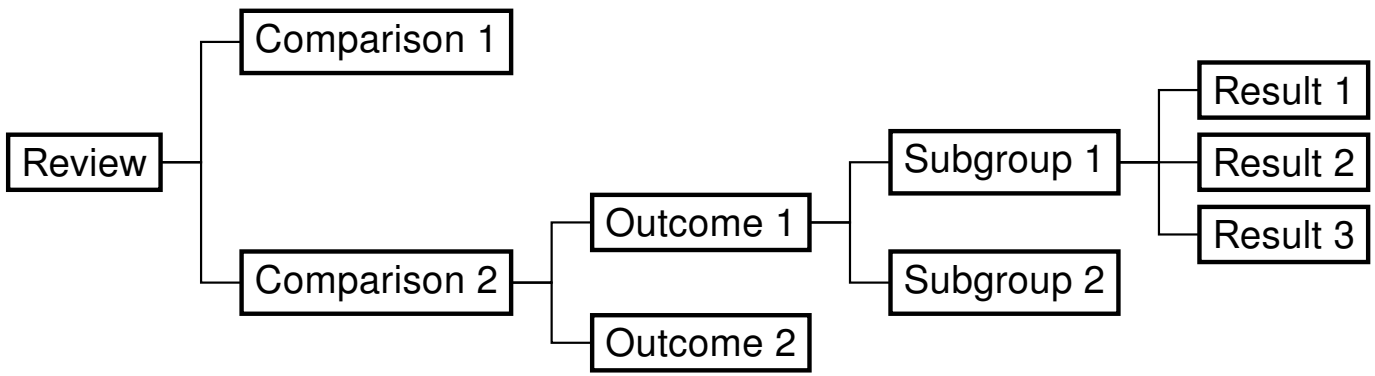
Cochrane Library Dataset

5016 systematic reviews with studies published until 2018.

52995 studies.

463820 study results.

Dataset structure



Review Example

Study	Comparison	Outcome
Bohn 1989	Barbiturate vs no barbiturate	Death at the end of follow-up
Bohn 1989	Barbiturate vs no barbiturate	Death or severe disability at the end of follow-up
Eisenberg 1988	Barbiturate vs no barbiturate	Uncontrolled ICP during treatment
Eisenberg 1988	Barbiturate vs no barbiturate	Hypotension during treatment
Perez-Barcena 2008	Pentobarbital vs Thiopental	Death at the end of follow-up (6 months)
Perez-Barcena 2008	Pentobarbital vs Thiopental	Death or severe disability at the end of follow-up (6 months)
Perez-Barcena 2008	Pentobarbital vs Thiopental	Uncontrolled ICP during treatment
Perez-Barcena 2008	Pentobarbital vs Thiopental	Hypotension during treatment
Schwartz 1984	Barbiturate vs Mannitol	Death at the end of follow-up (1 year)
Schwartz 1984	Barbiturate vs Mannitol	Uncontrolled ICP during treatment
Ward 1985	Barbiturate vs no barbiturate	Mean ICP during treatment
Ward 1985	Barbiturate vs no barbiturate	Mean arterial pressure during treatment
Ward 1985	Barbiturate vs no barbiturate	Mean body temperature during treatment

Study	Comparison	Outcome	Events	Total	Events_c	Total_c
Bohn 1989	Barbiturate vs ..	Death at ..	11	41	11	41
Ward 1985	Barbiturate vs ..	Death at ..	14	27	13	26

Pooling studies - Meta-analysis

Possible if results have same outcome, comparison and subgroup.

Evidence synthesis - more reliable results.

Different methods - f.ex. random or fixed effects meta-analysis.

Publication bias

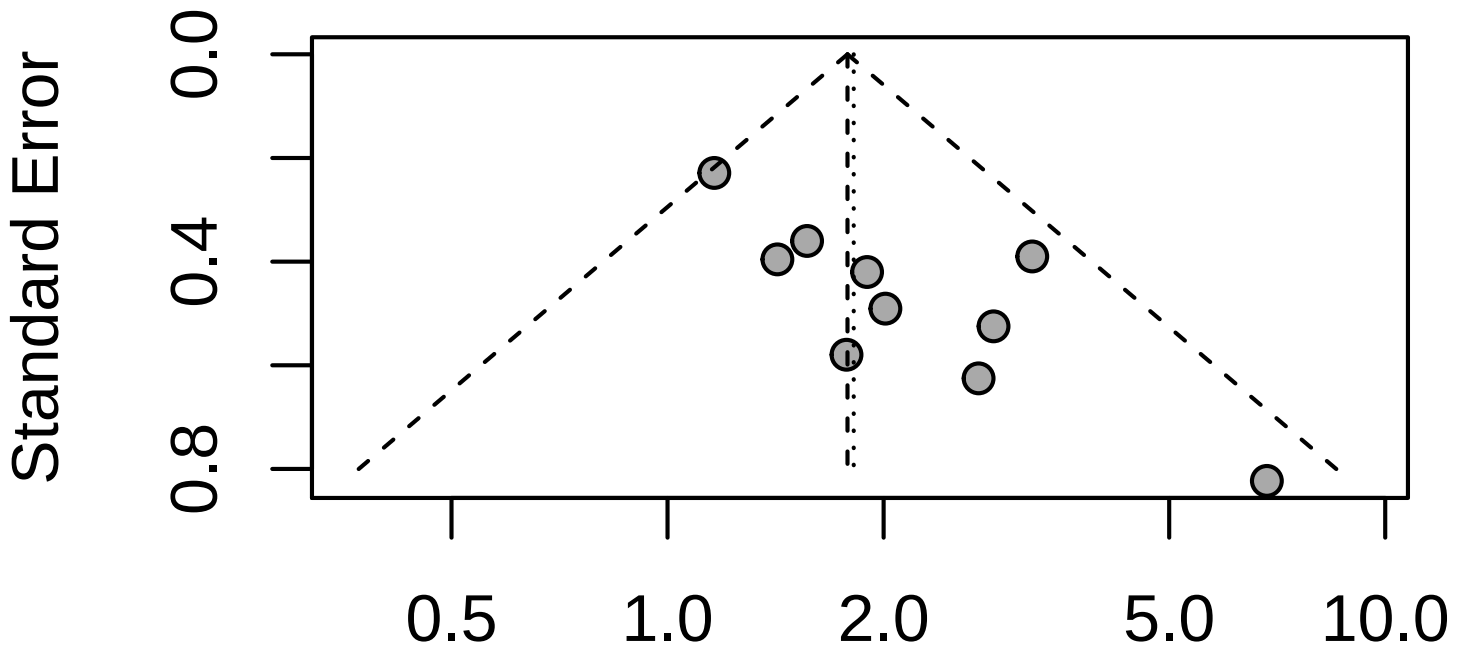
Selection of studies with treatment effects.

Stronger selection for smaller studies - small study effect.

Leads to biased results of meta-analysis.

Publication Bias Tests

Test for funnel plot asymmetry:



Publication Bias Tests

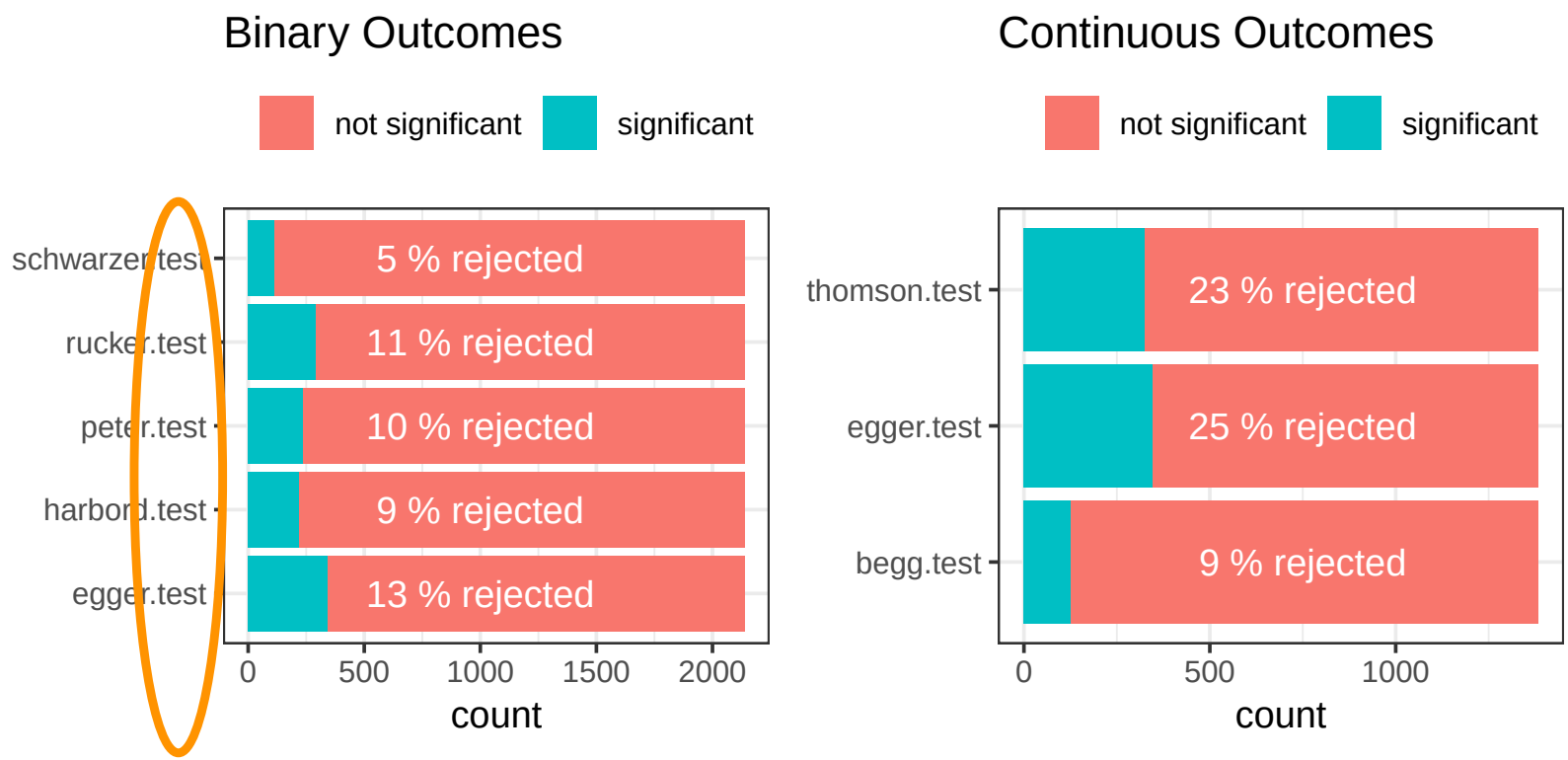
Critical: Number of studies in meta-analysis must be large (>10).

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

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

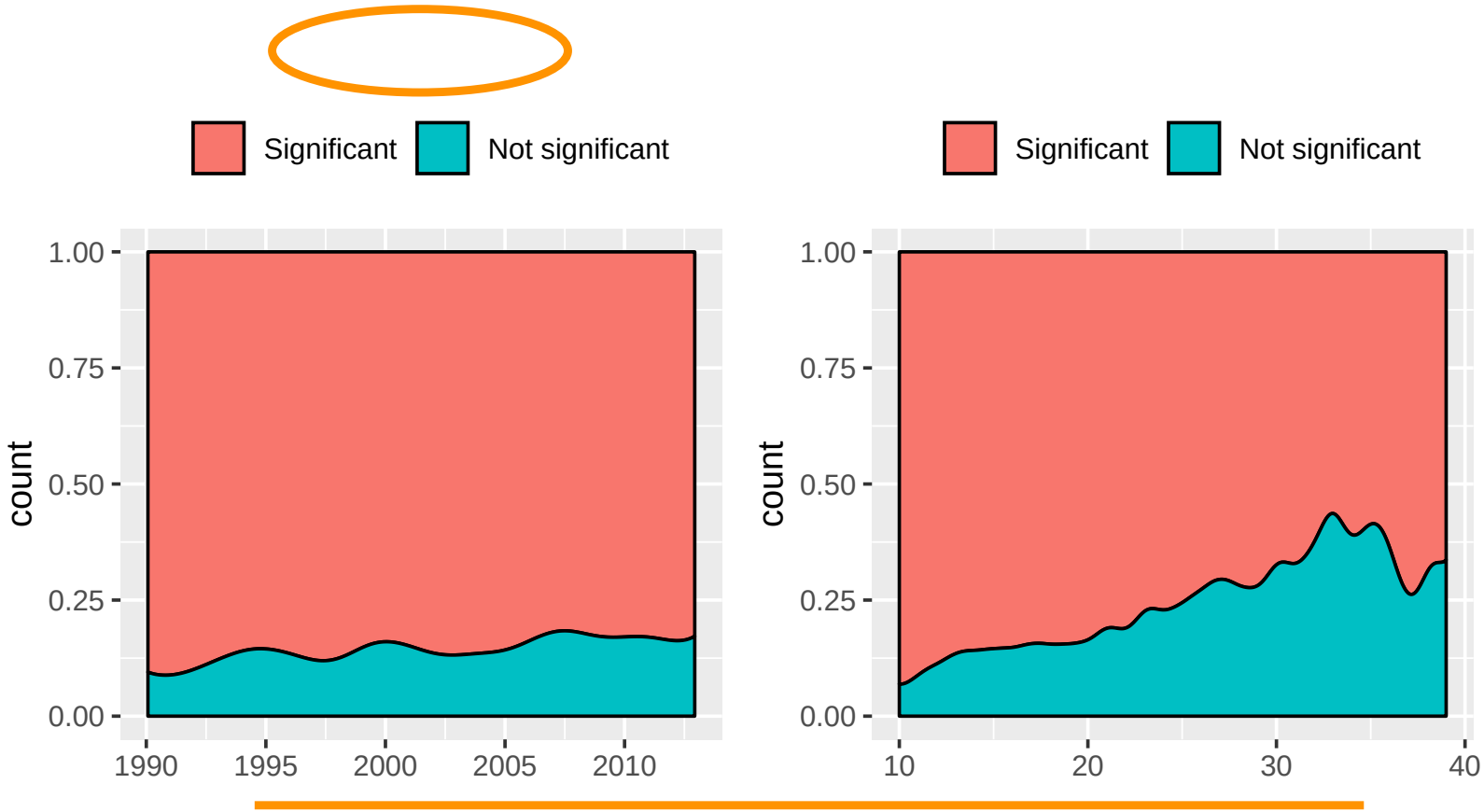
Rank based: Begg and Mazumdar's Test

Publication Bias in Cochrane Library



Publication Bias

Publication bias variation for time and sample size



Publication Bias Adjustment

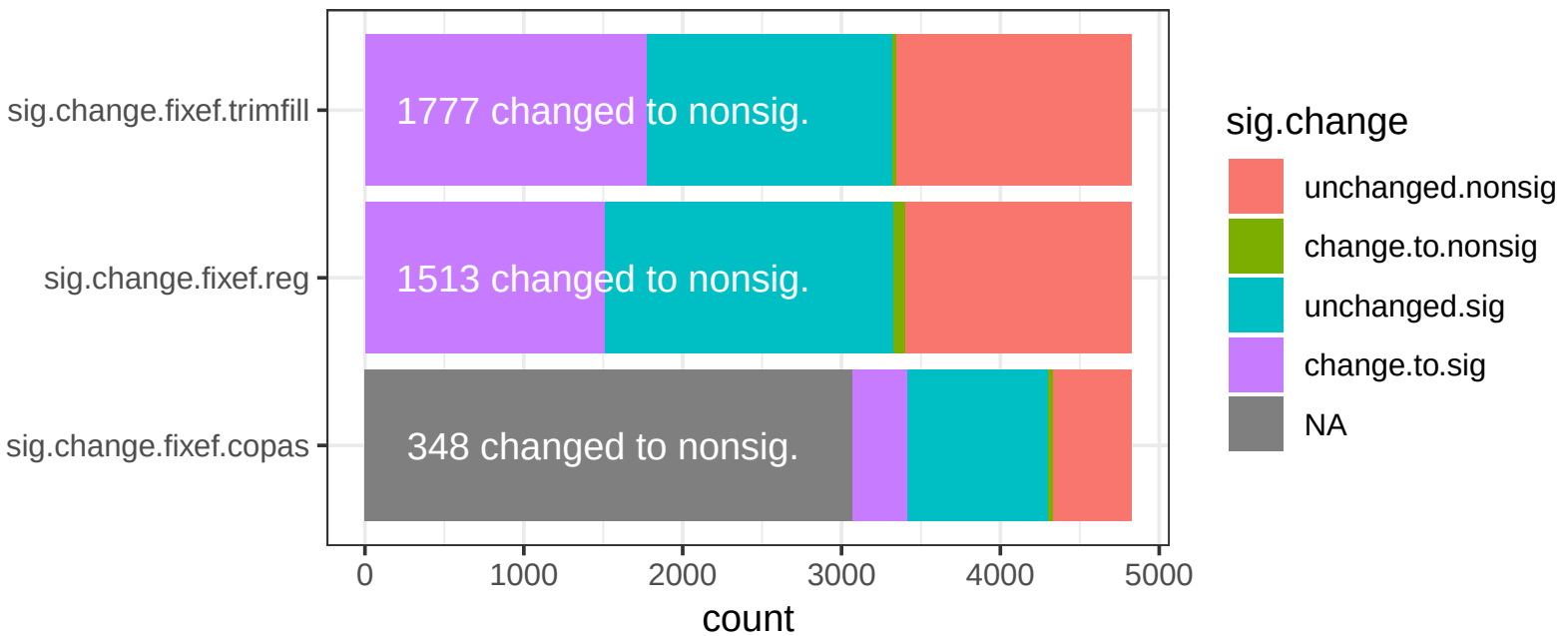
Three approaches:

Trim-and-fill: Non-parametric

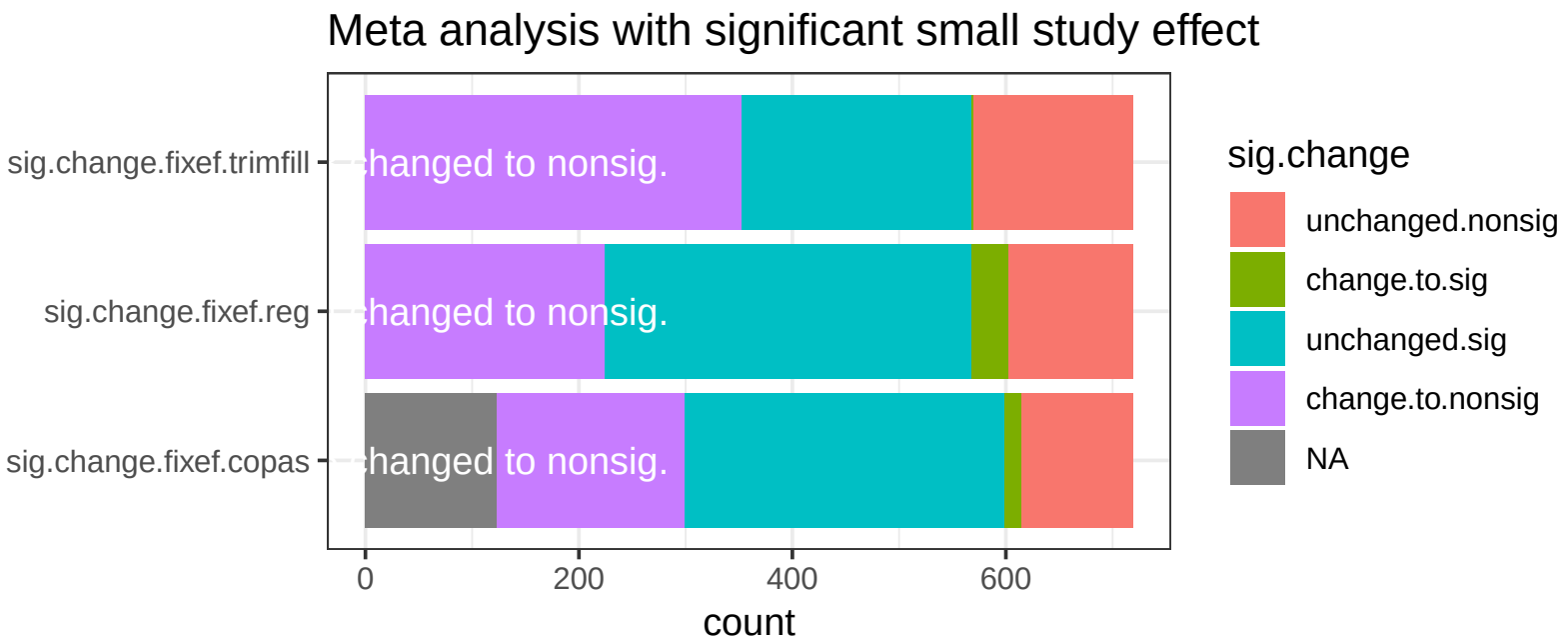
Copas: Selection modelling, estimation by sensitivity analysis

Regression: Estimation of a treatment effect with infinite sample size

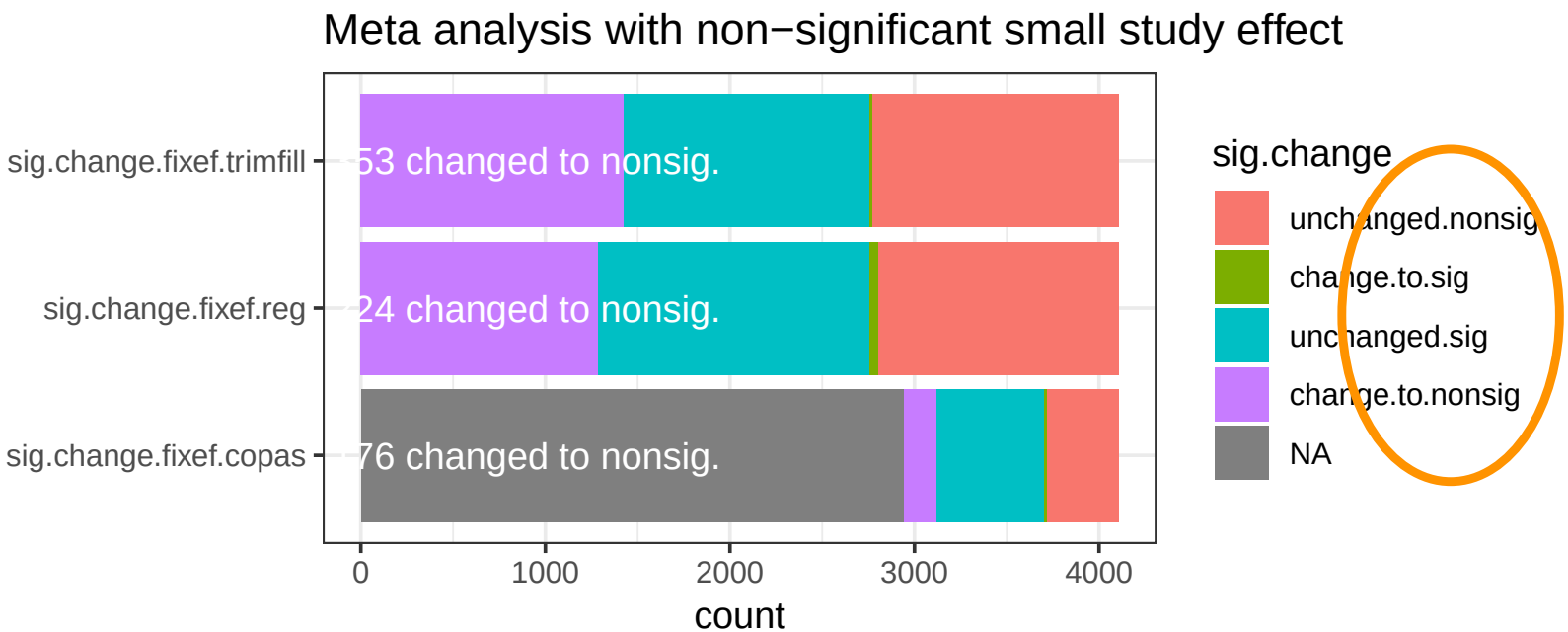
Correction of significance



Corrected Significance for Biased Meta-Analyses

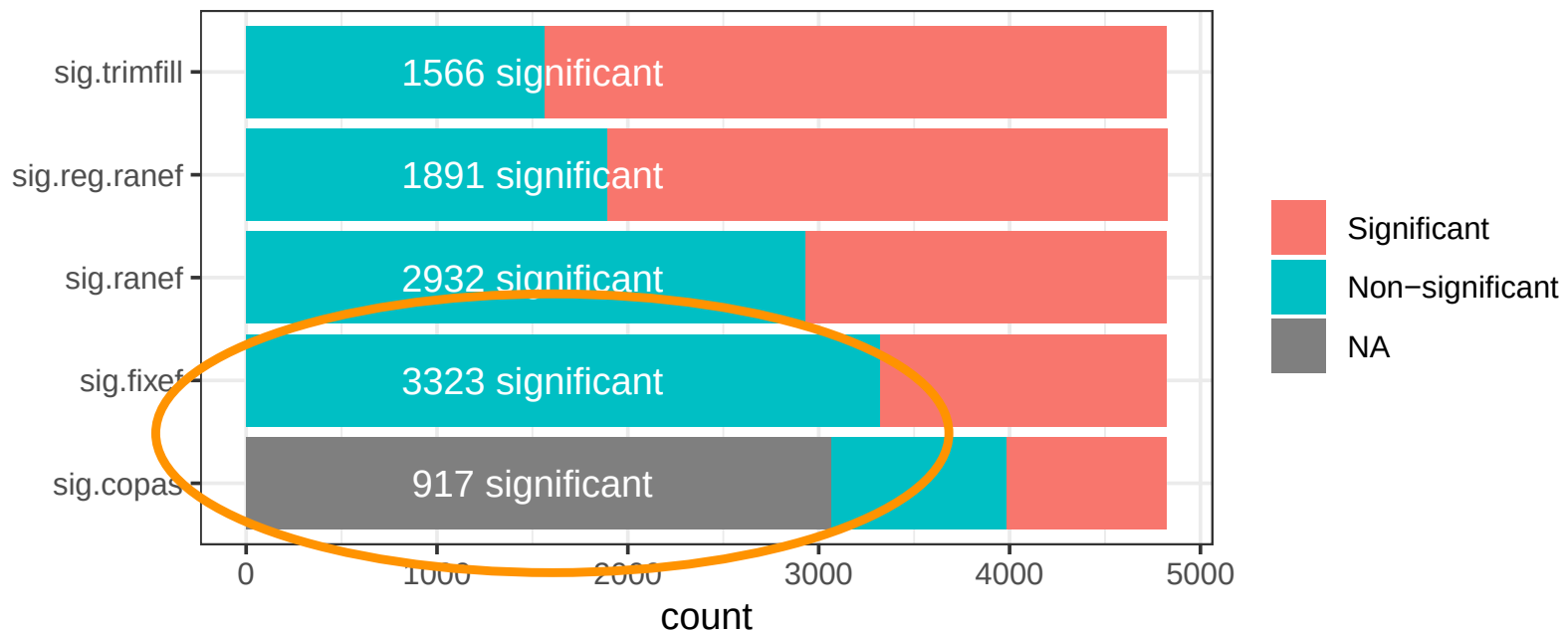


Corrected Significance for Unbiased Meta-Analyses

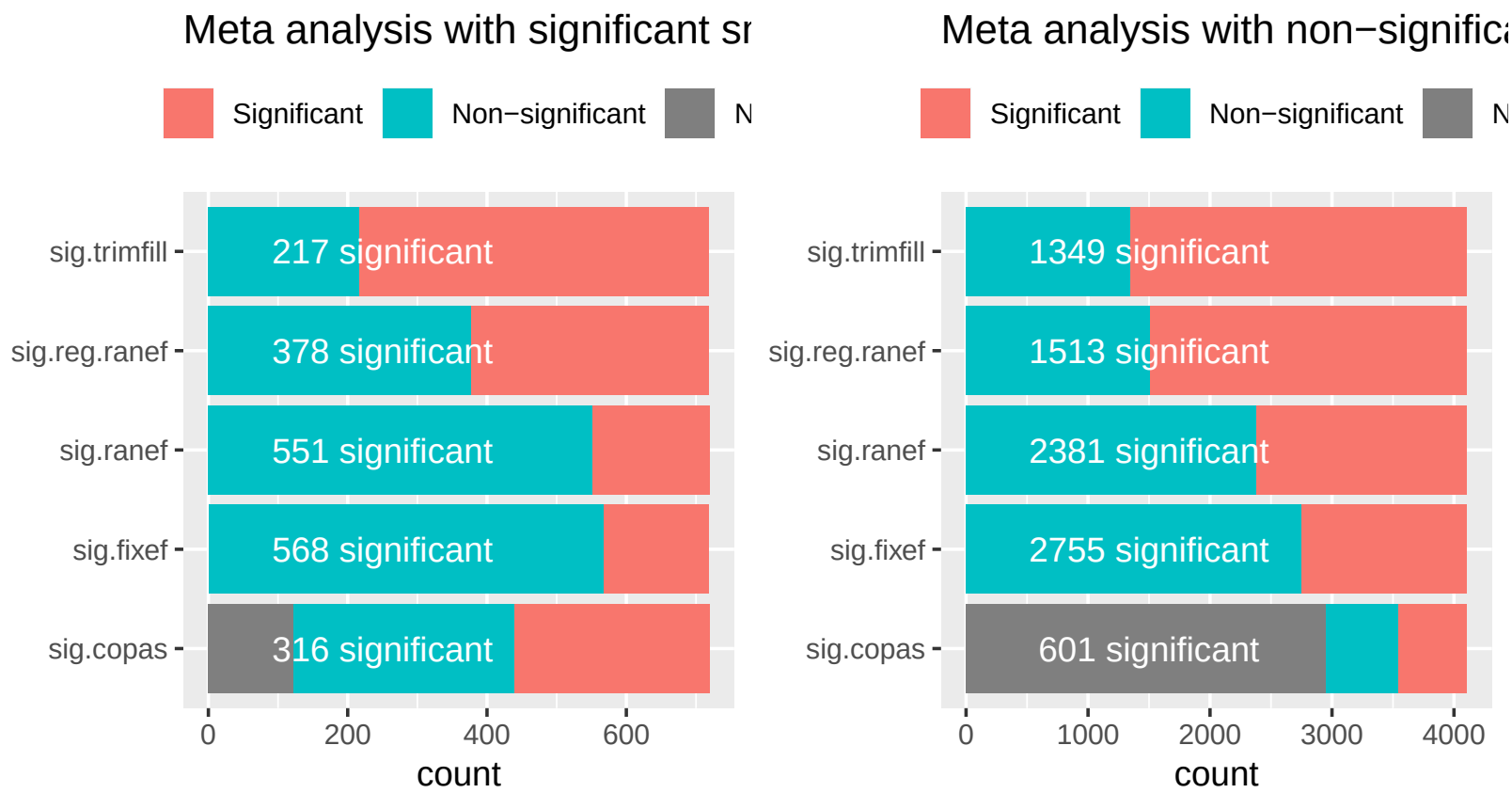


Significance of different Estimates

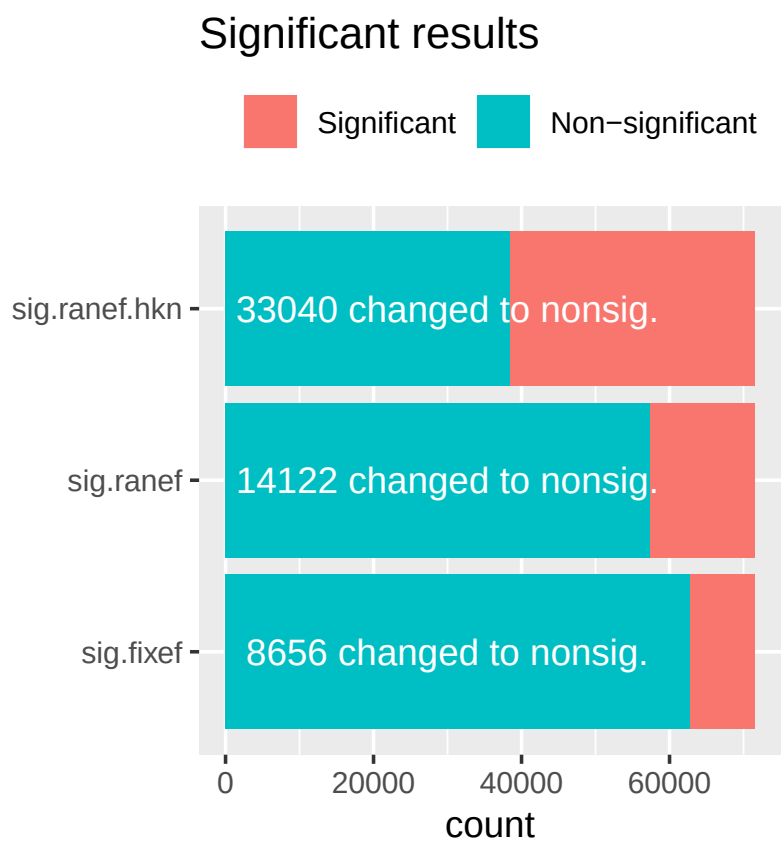
Significance of random, fixed effects and adjusted meta-analyses:

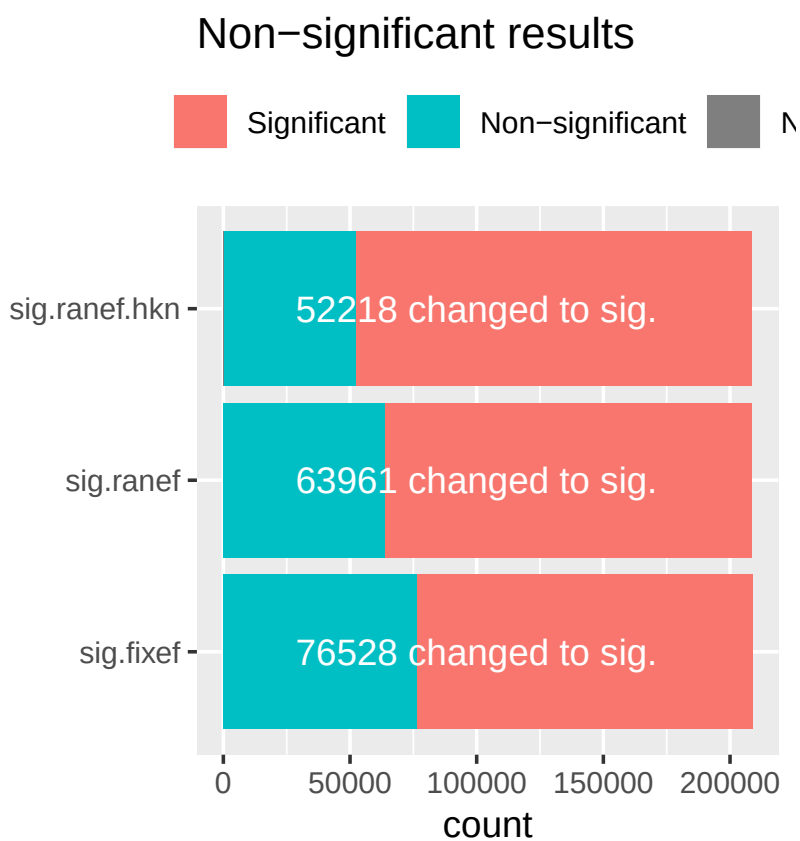


Significance separated for biased and unbiased meta-analyses

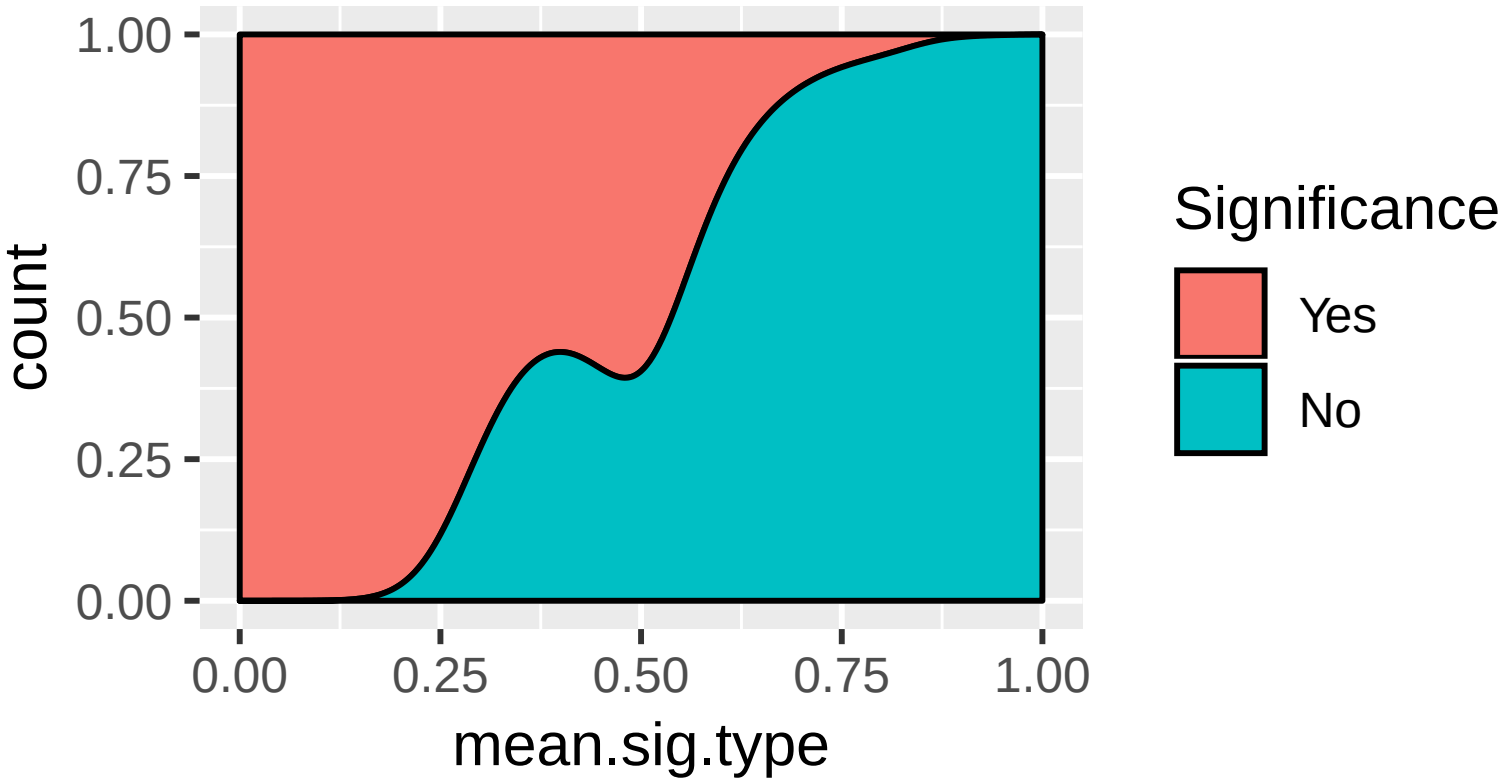


Significance after meta-analysis





Significance after meta-analysis



References

Harris, G., Thompson, W. D., Fitzgerald, E., and Wartenberg, D. (2014). The association of pm2.5 with full term low birth weight at different spatial scales. *Environmental Research*, 134:427 – 434. Linking Exposure and Health in Environmental Public Health Tracking.