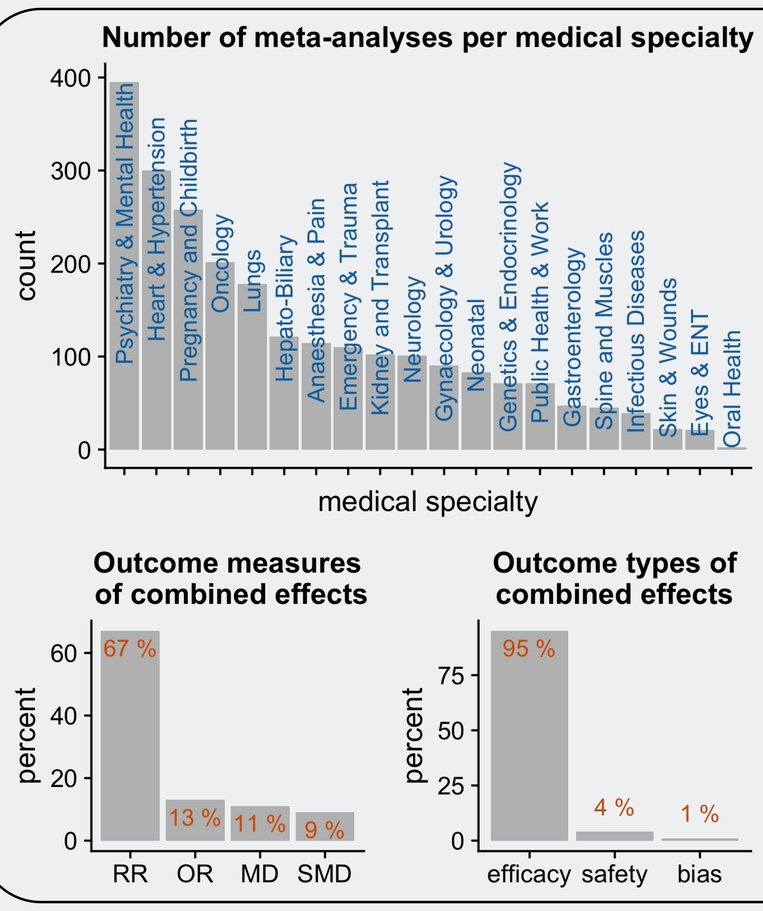
Estimating publication bias in clinical trials across different specialties in medicine

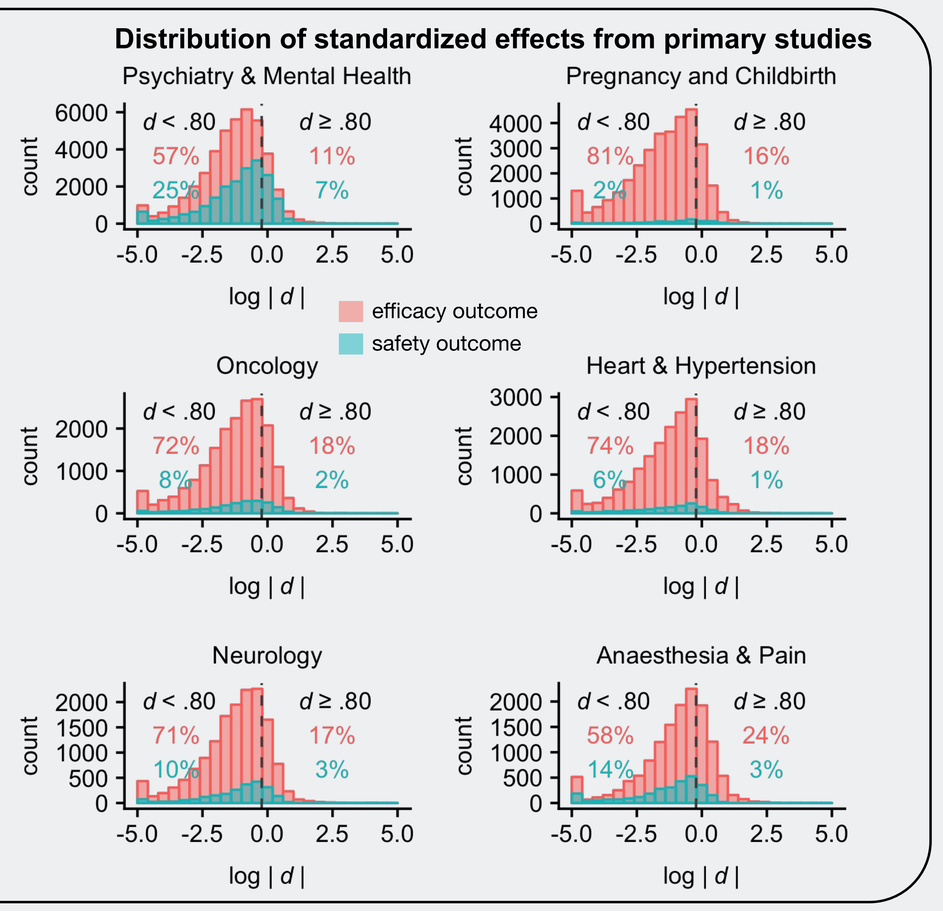
Simon Schwab, Giuachin Kreiliger, and Leonhard Held
Center for Reproducible Science (CRS) & Epidemiology, Biostatistics and Prevention Institute (EBPI)

University of Zurich[UZH]

Conclusions

Our results demonstrated that 1% out of 2,345 meta-analysis in 591 Cochrane systematic reviews show strong evidence for publication bias, and 21% showed weak evidence. Publication bias ranged from 10% to 35% depending on medical specialty. After adjusting for publication bias we found that treatment effects were reduced in size, with less evidence for efficacy.
Looking at effect sizes from primary studies, their magnitude and type (efficacy vs. safety) demonstrates differences in reporting among the medical specialties.



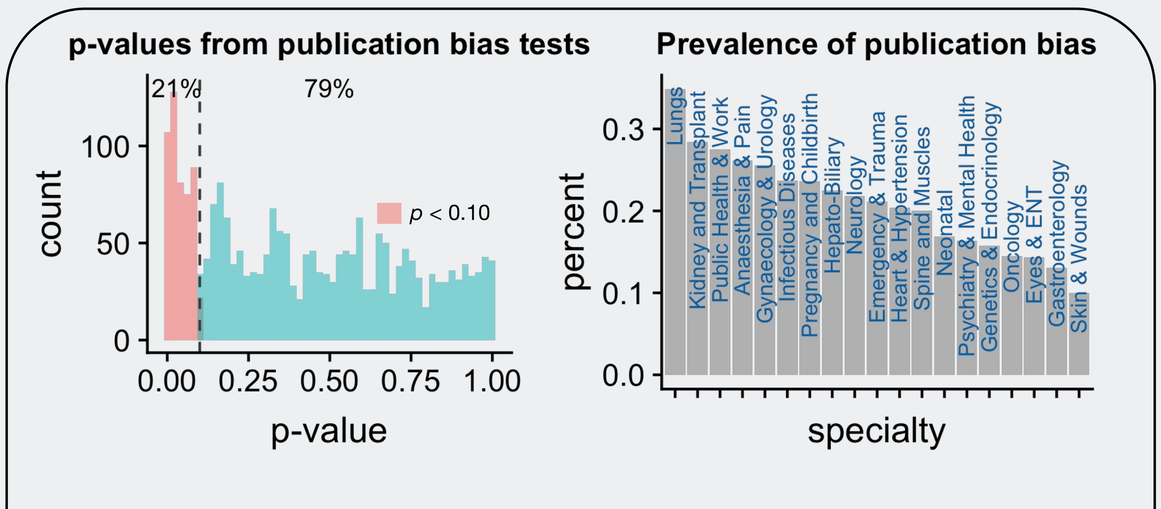


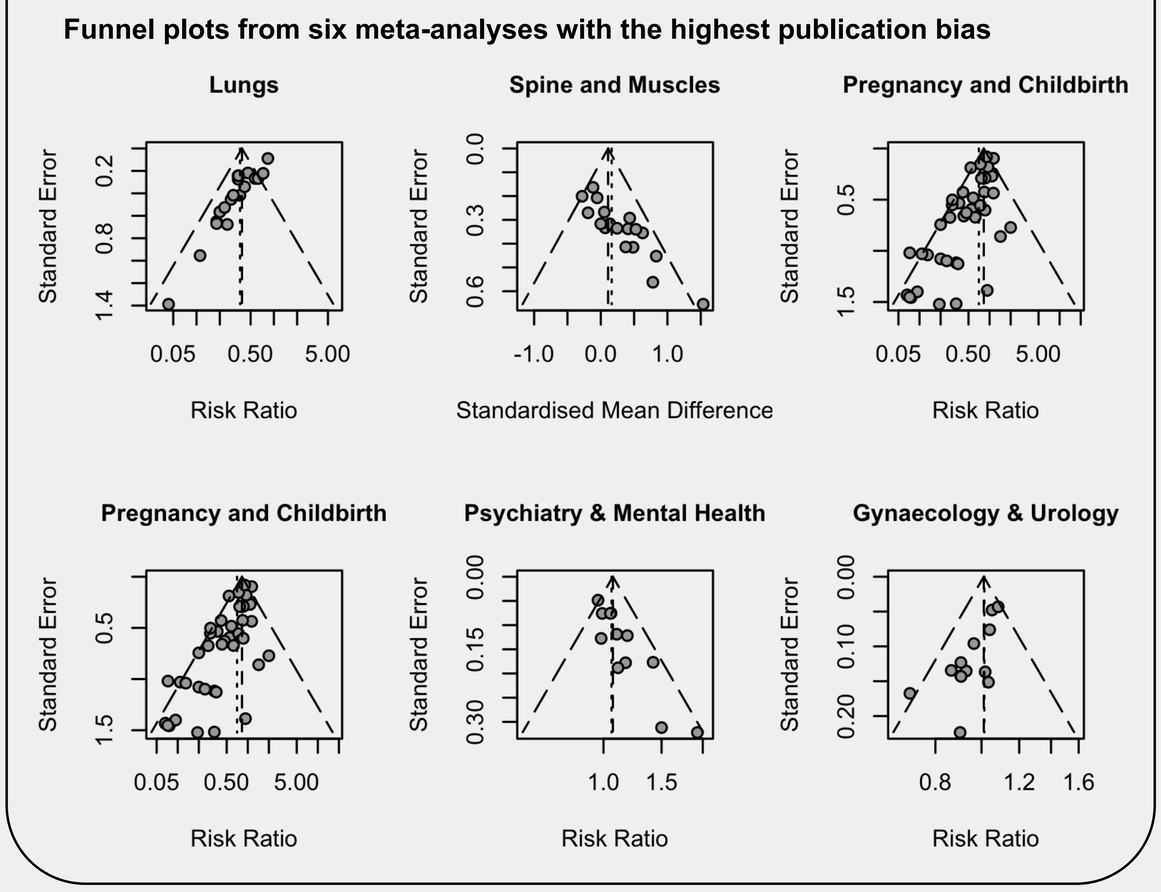
Introduction

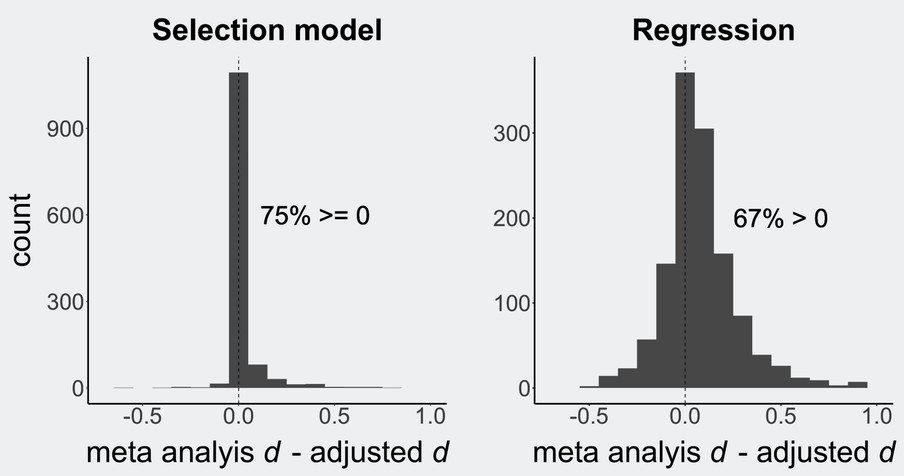
- Publication bias is a major concern in research (Bishop, 2019). In medical research the bias can mislead clinical practice and harm patients as well.
- Previous research has estimated the prevalence of publication bias in meta-analyses of Cochrane systematic reviews to be 7%–18% (Ioannidis & Trikalinos; 2007) or even as large as 50% (Sutton et al.; 2000).
- **The aim of our study was a large-scale empirical assessment publication bias in meta-analyses of clinical trials across different specialties in medicine. We also examined the reported effect sizes of primary studies.**

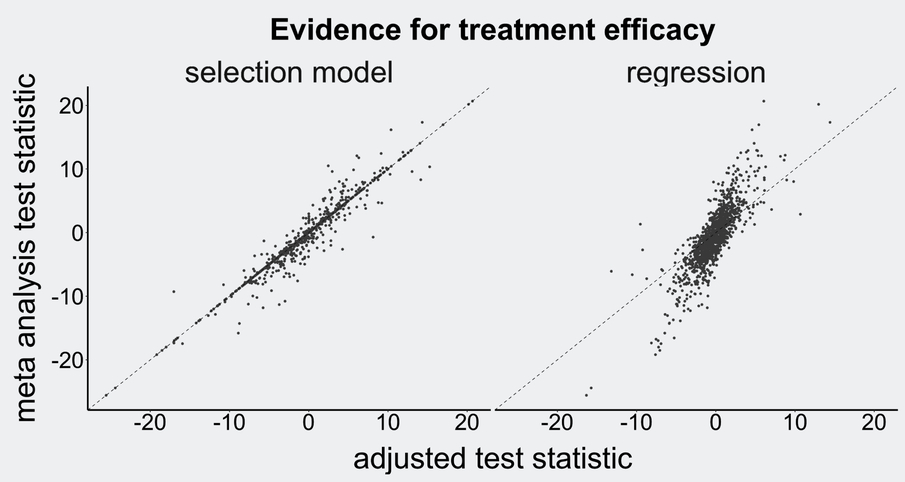
Methods

- We considered 7,778 Cochrane systematic reviews of the category “intervention” covering 23 years of clinical research from 1996 to 2019.
- Meta-analyses with efficacy outcomes and meeting the criteria for appropriateness to evaluate publication bias were included, i.e., a minimal number of 10 studies in meta-analysis, heterogeneity I^2 < 50% (Ioannidis & Trikalinos; 2007).
- There are methods to assess publication bias; we followed guidelines by Sterne et al. (2011) and used Egger’s test for continuous, and Harbord’s test for dichotomous data. We evaluated combined effects of the type mean difference (MD), std. mean difference (SMD), risk ratio (RR) and odds ratio (OR) which covered 91% of all outcome measures. It is common practice to test for publication bias using $p < 0.10$; however, this reflects weak evidence, therefore, we also used $p < 0.001$, i.e., strong evidence against the null (no publication bias).
- The 20 medical specialties were derived from the Cochrane review groups and merged if appropriate, e.g., all cancer groups into “Oncology”.
- For adjustment of combined effects from meta-analyses we used a regression based method and the Copas selection model (Schwarzer et al.; 2015).
- The study protocol has been registered at OSF and developed R software to analyse data from the Cochrane Library will be made available at https://osf.io/uv397/.









Simon Schwab
Center for Reproducible Science (CRS) &
Epidemiology, Biostatistics and Prevention Institute
Hirschengraben 84
8001 Zurich
Switzerland
simon.schwab@uzh.ch

UZH Center for Reproducible Science
www.crs.uzh.ch

METASCIENCE 2019 SYMPOSIUM The Emerging Field of Research on the Scientific Process.

References

- Bishop, D. (2019). Rein in the four horsemen of irreproducibility. *Nature*, 568(7753), 435. https://doi.org/10.1038/d41586-019-01307-2
- Ioannidis, J. P. A., & Trikalinos, T. A. (2007). The appropriateness of asymmetry tests for publication bias in meta-analyses: a large survey. *CMAJ*, 176(8), 1091–1096. https://doi.org/10.1503/cmaj.060410
- Schwarzer, G., Carpenter, J. R., & Rücker, G. (2015). *Meta-Analysis with R*. Springer. https://doi.org/10.1007/978-3-319-21416-0
- Sterne, J. A. C. et al. (2011). Recommendations for examining and interpreting funnel plot asymmetry in meta-analyses of randomised controlled trials. BMJ , 343, d4002. https://doi.org/10.1136/bmj.d4002