How trace plots help interpret meta-analysis results

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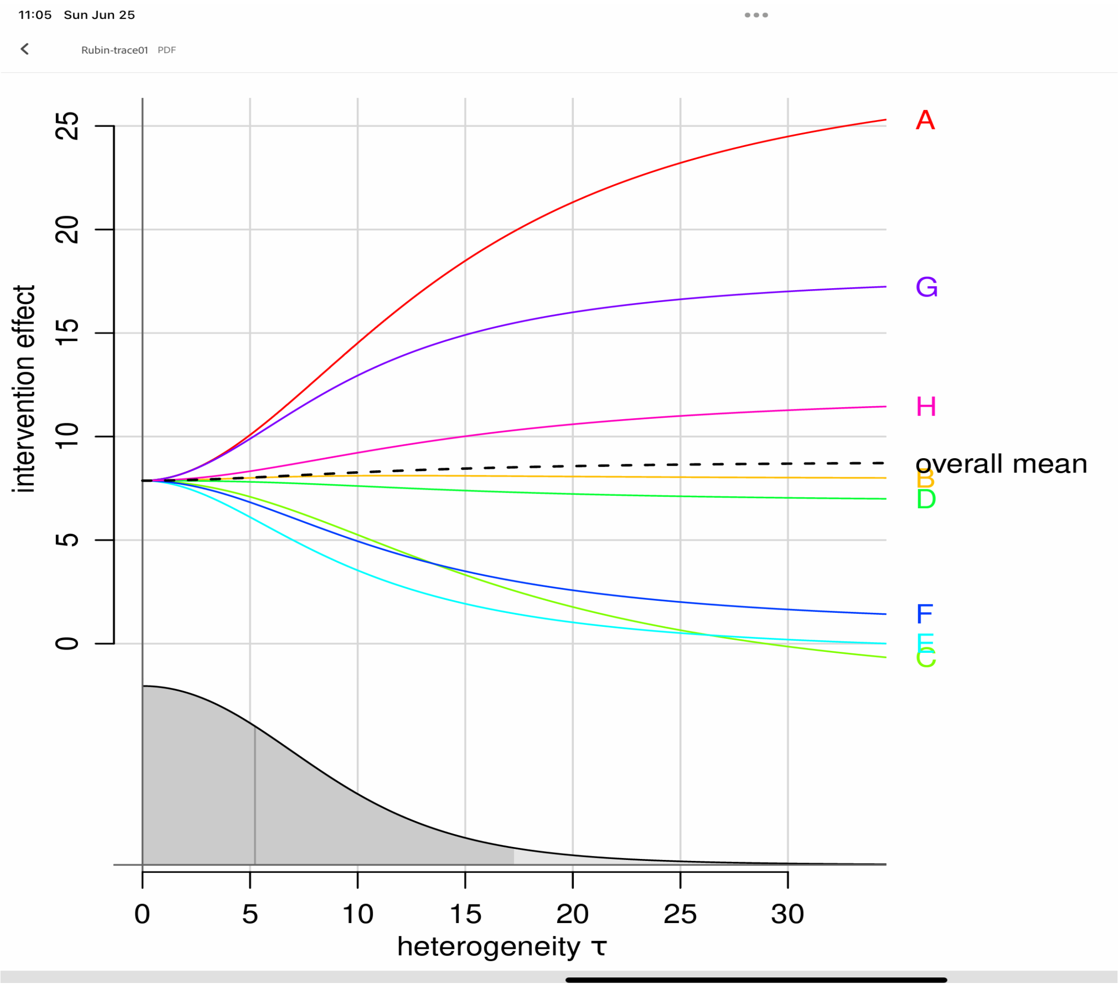
Typical random effects meta-analysis

- Forest plot
- Mean effect size, SE, CI
- Variance or SD of true effect sizes (tau-squared or tau),
- Derived quantities, such as I-squared

What is missing?

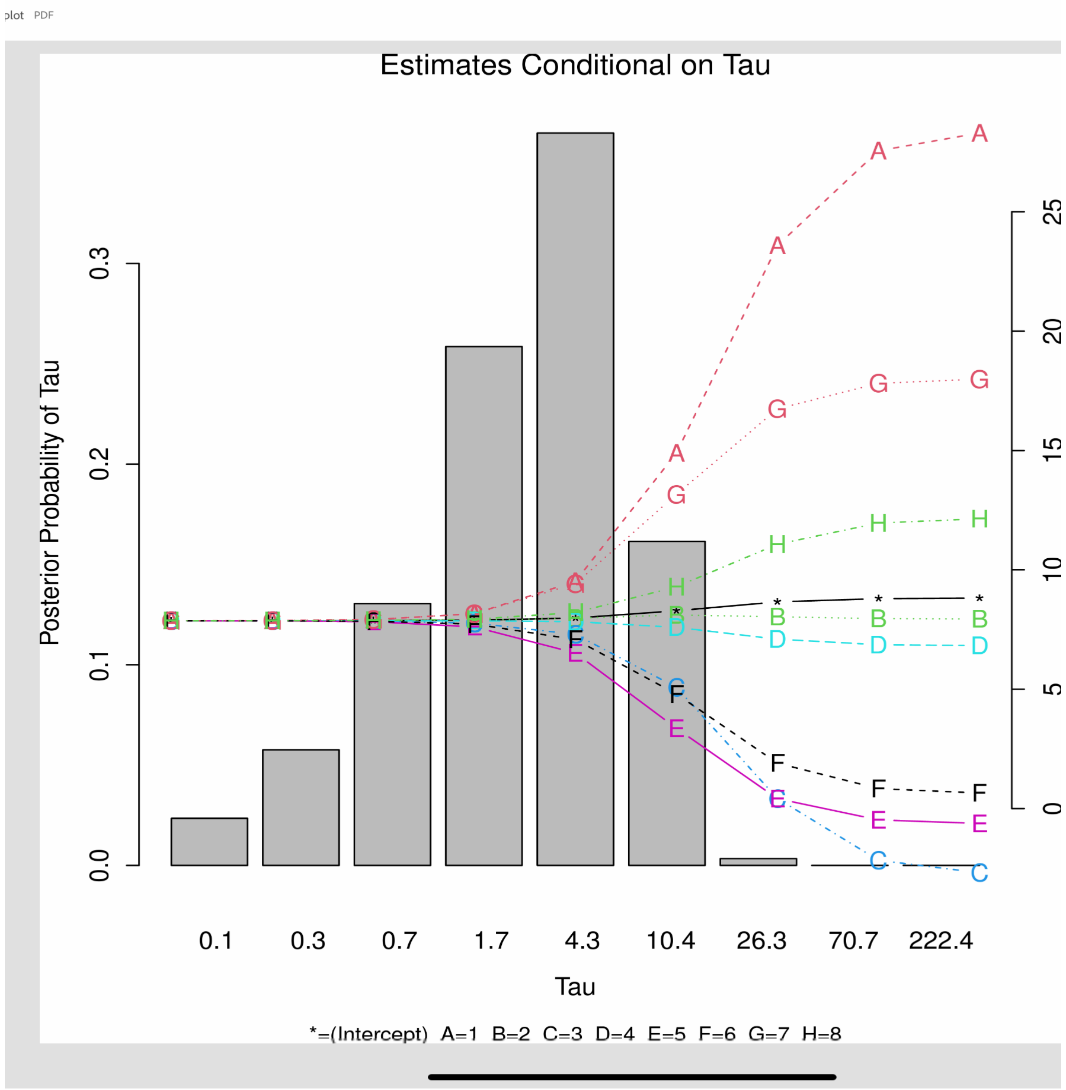
- Uncertainty in estimate of tau
- Sensitivity to tau of:
  - Parameter estimates
  - Shrunken estimates
  - Standard errors of all quantities
- Usually of concern only when number of studies is small to moderate

Trace plot SAT coaching from Rubin 1981



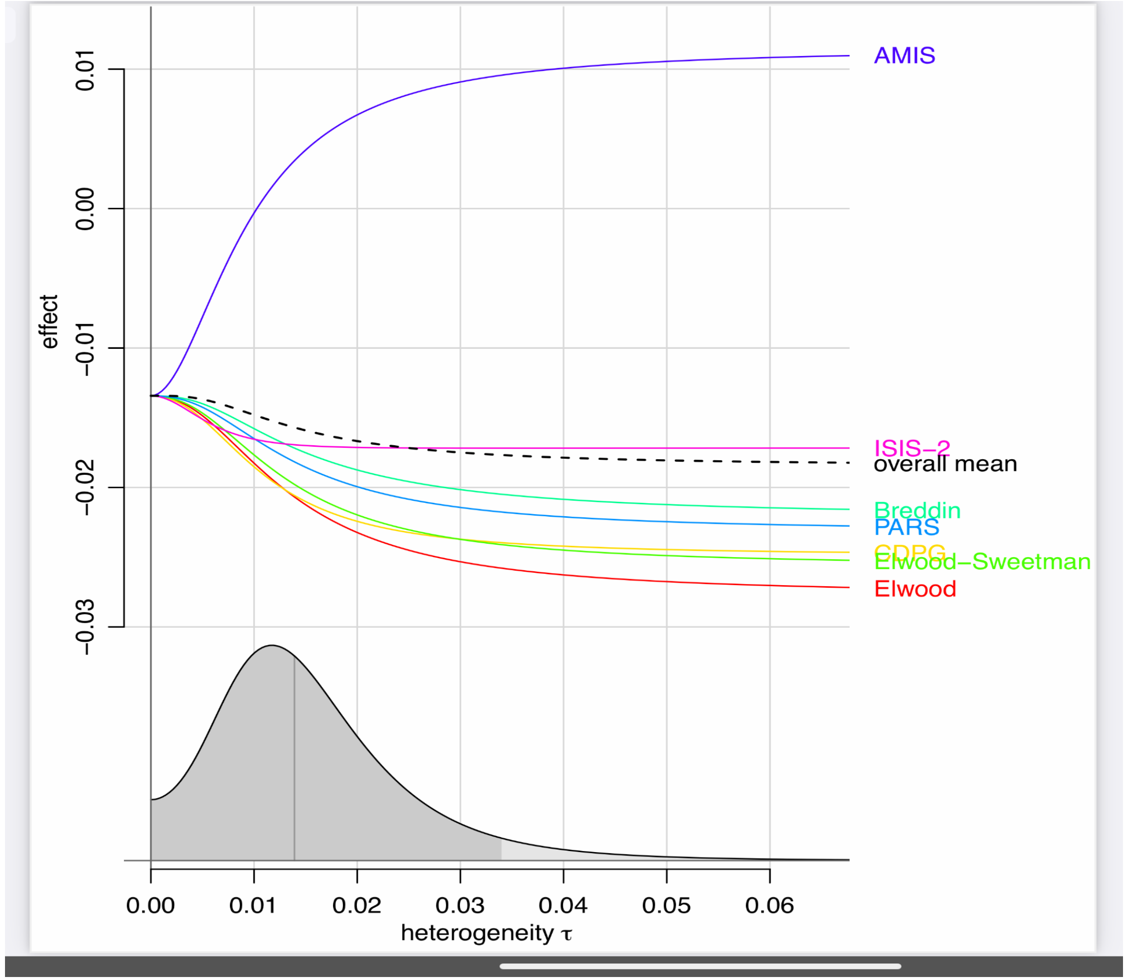
- 8 parallel experiments
- Left side: Fixed Effects
- Right side: Independent studies
- Bottom: Posterior (or likelihood) of tau
  - Note zero is most likely, but wide range is possible
- Lines: Shrunken estimates of study effects, for each possible value of tau
  - Shrinkage changes a lot over plausible values of tau

Trace Plot from DuMouchel's hblm program



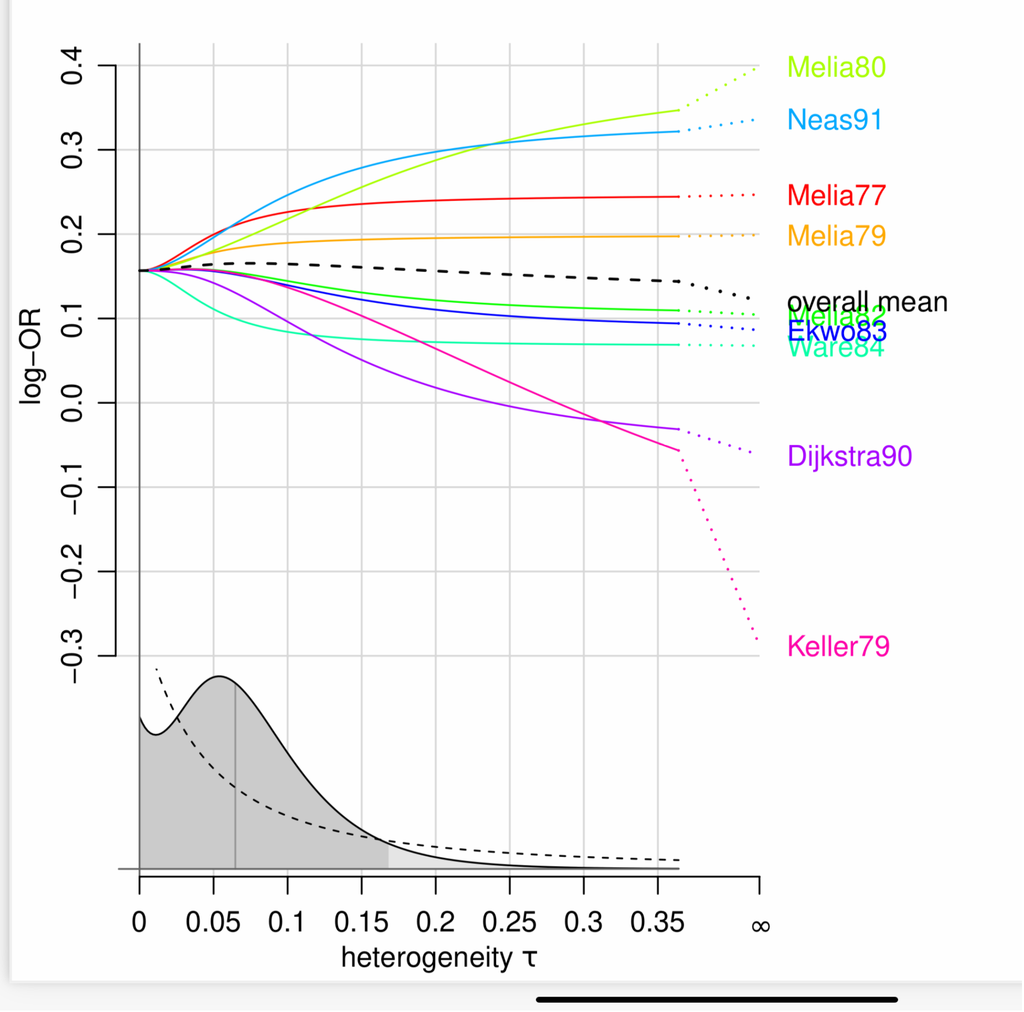
- For decades, the only program to product trace plots
- Discrete version of tau (for numerical integration)
- Note spacing looks approximately exponential, not linear
  - Gives misleading view of posterior distribution of tau

Aspirin Effect on Future Heart Attack



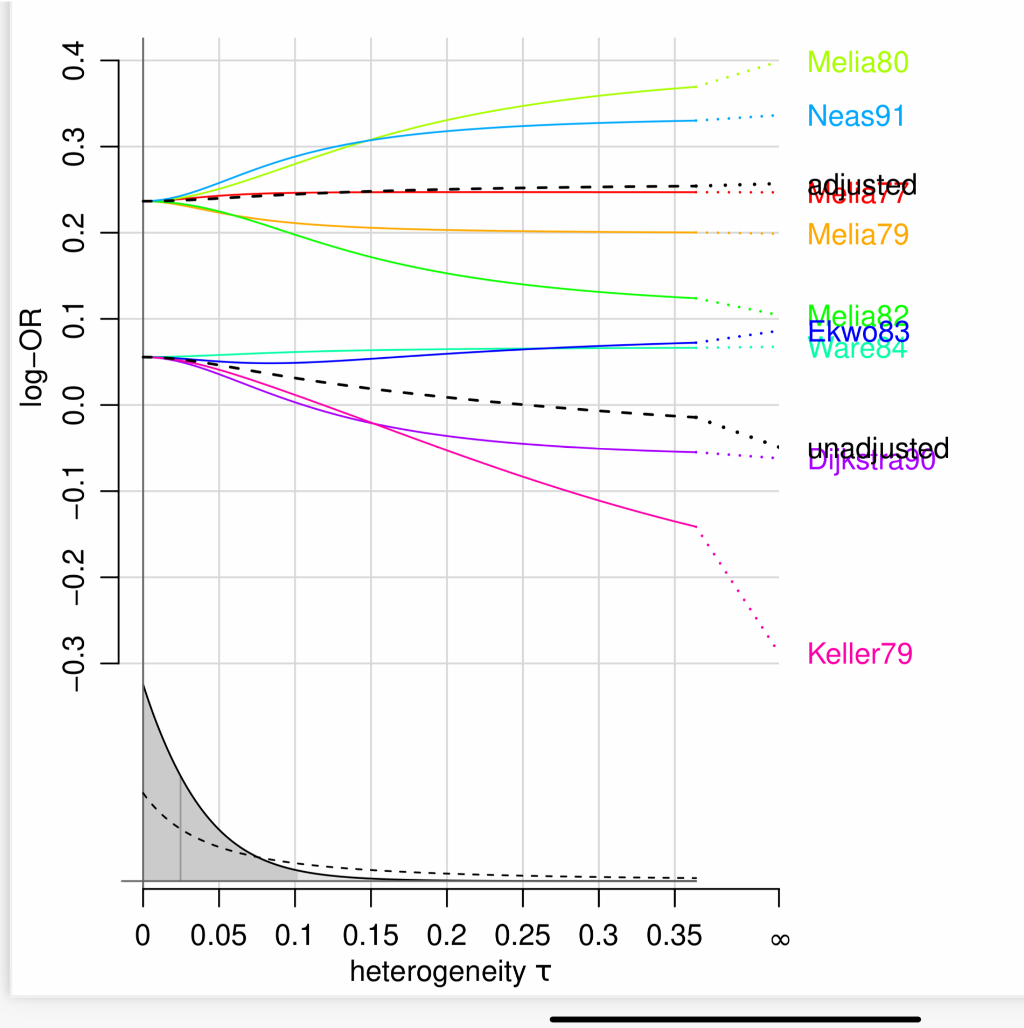
- Clearly AMIS is an outlier
- Other studies are similar, even if tau were relatively large
  - (But size of tau is affected by the AMIS study, and is much lower without it.)
- For most reasonable values of tau, other studies are remarkably consistent

Ex with covariates: DuMouchel reanalysis of NO2 data



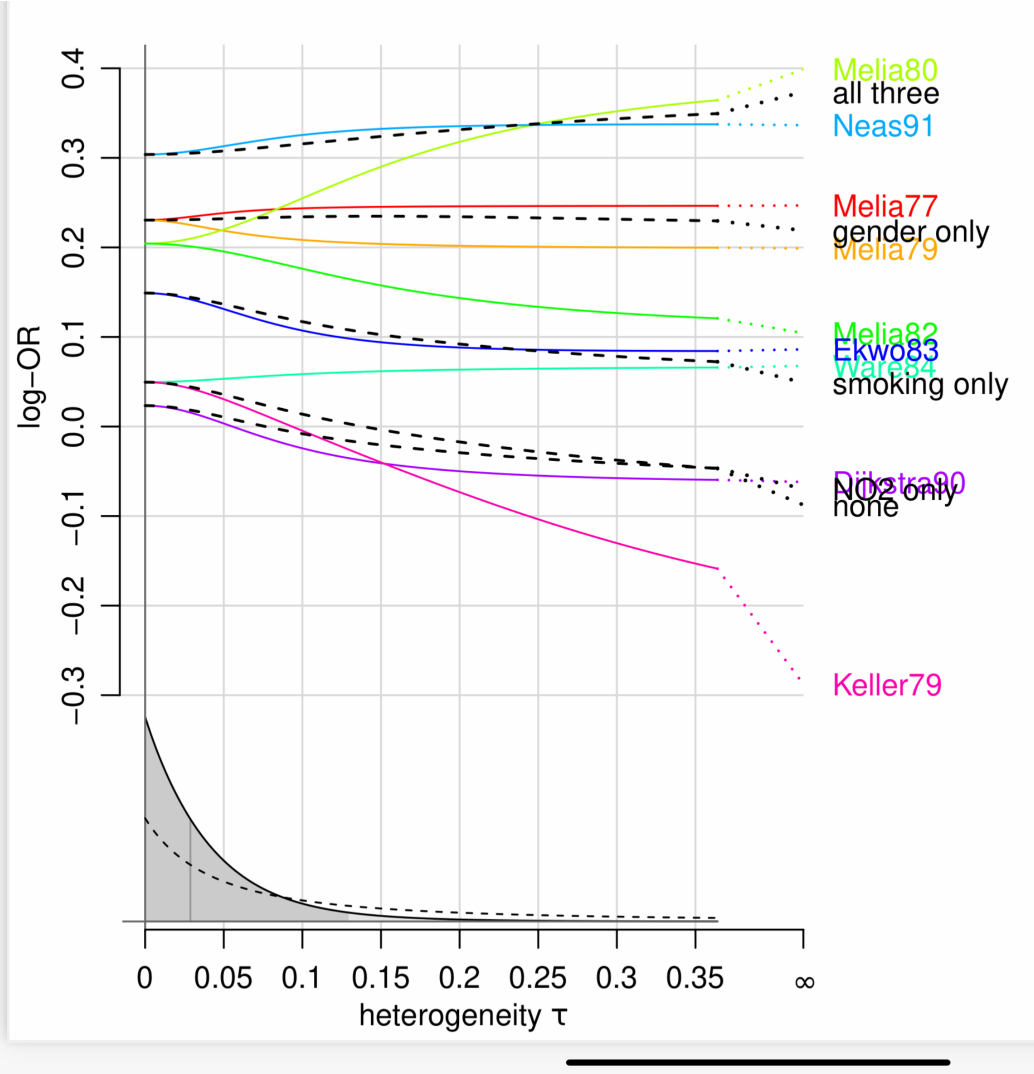
- Effect of NO2 on breathing
- Range of conclusions depending on value of tau, which is uncertain
- If tau=0, small effect
- If tau=.15, effects range from about .05 to .28
- Studies varied in how well they controlled for various sources of bias

Adjust for one possible source of bias



- Gender is either adjusted for in the study, or not
- Shrinkage is toward mean of subgroups
- If not adjusted for, effect sizes (for plausible ranges of tau) are small
- If adjusted for, effect sizes are large (about 25-30 percent increase in breathing issues for high NO2)
- Within each, residual variation is relatively small (over plausible range of tau values, but not outside that range)

Covariates for all three potential bias sources



- When studies have none of the three potential flaws, effect size is estimated to be about .30 to .33 (for plausible values of tau)
- When studies have all three flaws, effect size is estimated to be about 0 to .05
- By using linear combinations of parameter estimates, we can estimate effect size for any study design

Implementation in R::bayesmeta

- All but one slide in this presentation was produced by bayesmeta
- Includes basic trace plot, but many additional options
  - Confidence intervals
  - Plots for frequentist models using metafor
  - Q statistic rather than posterior if desired
  - Control of translucency of lines (make some lighter to highlight others)

Summary

- Trace plots are a rich source of information for meta-analysts
- Easy to see whether/how estimates depend on plausible values of tau
- (And what values of tau are plausible)
- Can illustrate outlying studies, and other abnormalities (literally)
  - Vital because we usually assume normal distribution, even though this is not scientifically necessary
- Can illustrate effects of covariates, and dependence on tau

References: Theory and use of trace plots

- Rubin DB. Estimation in parallel randomized experiments. Journal of Educational Statistics 1981; 6(4): 377401.
- Rubin DB. Meta-analysis: literature synthesis or effectsize surface estimation?. Journal of Educational Statistics 1992; 17(4): 363-374. doi: 10.2307/1165129

- DuMouchel W. Hierarchical Bayes linear models meta-analysis. Techical report 27, National Institute of Statistical Sciences (NISS); Research Triangle Park, NC, USA: 1994.
- Gaver DP, Draper D, Goel PK, et al. Combining information: Statistical issues and opportunities for research. Washington, D.C., USA: National Research Council, The National Academies Press . 1992. URL: https://nap. nationalacademies.org/20865
- Raudenbush SW, Bryk AS. Empirical Bayes meta-analysis. Journal of Educational Behavioural Statistics 1985; 10(2): 75-98.
- Zucker DR, Schmid CH, McIntosh MW, D'Agustino RB, Selker HP, Lau J. Combining single patient (N-of-1) trials to estimate population treatment efects and to evaluate individual patient responses to treatment. Journal of Clinical Epidemiology 1997; 50(4): 401-410.

References: Software

- Röver C. bayesmeta: Bayesian random-effects meta analysis. R package. URL: http://cran.r-project.org/package= bayesmeta; 2015.
- Röver C. Bayesian random-effects meta-analysis using the bayesmeta R package. Journal of Statistical Software 2020; 93(6): 1-51. doi: 10.18637/jss.v093.i06 17.
- Röver C, Friede T. Using the bayesmeta R package for Bayesian random-effects meta-regression. Computer Methods and Programs in Biomedicine 2023; 229: 107303. doi: 10.1016/j.cmpb.2022.107303
- Viechtbauer W. Conducting meta-analyses in R with the metafor package. Journal of Statistical Software 2010; 36(3). doi: 10.18637/jss.v036.i03