

## The R package metafor: Past, present, and future

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## Quick Introduction

- born and raised in Germany
- moved to United States when I was 16
- 1998-2004: PhD at the University of Illinois, Urbana-Champaign
- dissertation research on statistical methods for meta-analysis
- at the time, the meta-analytic landscape in R looked like this ...

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## Meta-Analytic Landscape in R (~1998)

## Early Developments

- 1993: **RevMan** released (not R) [1]
- 1997: **MetaWin** released (also not R) [2]
- 1998: **Comprehensive Meta-Analysis** released (still no R) [3]
- 1999: **rmeta** package, but no 'meta-regression' capabilities
- ~2000: wrote function for fitting random/mixed-effects models
- ~2005: put function on my personal website
- ~2005: **meta** package (still no meta-regression)
- 2006-2009: a few other packages
- 2009: published **metafor** package
- 2009-2019: lots of new packages (current count: 107)  
based on CRAN Task View on Meta-Analysis:  
<https://cran.r-project.org/view=MetaAnalysis>

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## CRAN Task View: Meta-Analysis

### CRAN Task View: Meta-Analysis

**Maintainer:** Michael Dewey  
**Contact:** lists at dewey.myzen.co.uk  
**Version:** 2019-05-06  
**URL:** <https://CRAN.R-project.org/view=MetaAnalysis>

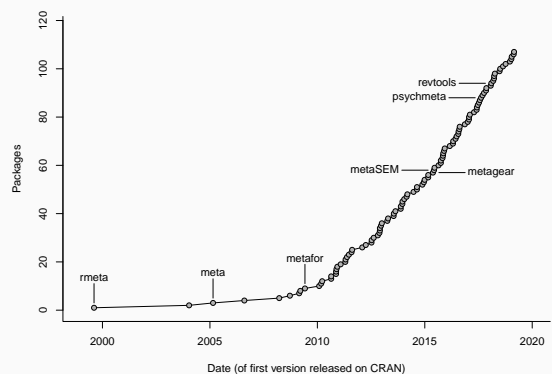
This task view covers packages which include facilities for meta-analysis of summary statistics from primary studies. The task view does not consider the meta-analysis of individual participant data (IPD) which can be handled by any of the standard linear modelling functions but does include some packages which offer special facilities for IPD.

The standard meta-analysis model is a form of weighted least squares and so any of the wide range of R packages providing weighted least squares would in principle be able to fit the model. The advantage of using a specialised package is that (a) it takes care of the small tweaks necessary (b) it provides a range of ancillary functions for displaying and investigating the model. Where the model is referred to below it is this model which is meant.

Where summary statistics are not available a meta-analysis of significance levels is possible. This is not completely unconnected with the problem of adjustment for multiple comparisons but the packages below which offer this, chiefly in the context of genetic data, also offer additional functionality.

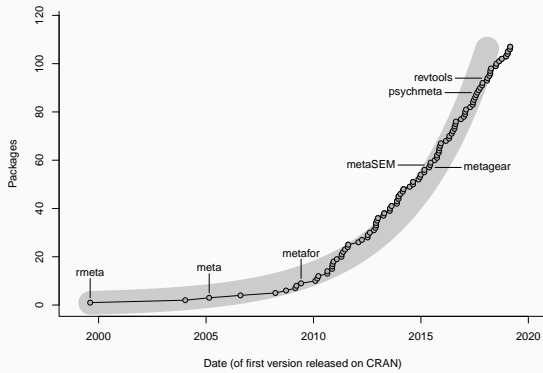
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## First Releases of Meta-Analysis Packages



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## Exponential Growth (sort of)



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## Development of the metafor Package

- first version (0.5-0) released 2009-06-04
- a total of 28 versions released so far
- latest is 2.1-0 released 2019-05-13
- added various illustrative datasets over the years (35 as of now)
- added various outcome measures over the years (60 as of now)
- full changelog: <https://wviechtb.github.io/metafor/news/index.html>

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## Some Milestones

Version	Date	Notes / Changes
0.5-0	2009-06-04	• first version released on CRAN • <code>rma.uni()</code> , <code>rma.mh()</code> , <code>rma.peto()</code>
0.5-4	2009-09-18	• <code>regtest()</code> and <code>ranktest()</code> functions • <code>anova()</code> function
0.5-5	2009-10-08	• <code>cumul()</code> and <code>leave1out()</code> functions
0.5-7	2009-12-06	• <code>permutest()</code> function
1.0-1	2010-02-02	• version 1 released
1.4-0	2010-07-30	• various improvements for JSS paper
	2010-08-05	• JSS paper published
1.5-0	2010-12-16	• started metafor website • <code>labbe()</code> function

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## Some Milestones

Version	Date	Notes / Changes
1.7-0	2013-02-06	• <code>rma.glmm()</code> function
1.9-0	2013-06-21	• <code>hc()</code> function
1.9-1	2013-07-20	• <code>baujat()</code> function
1.9-2	2013-10-07	• <code>rma.mv()</code> and <code>profile()</code> functions
1.9-3	2014-05-05	• models with user-defined weights • sparse matrices for <code>rma.mv()</code> • autoregressive structures for <code>rma.mv()</code>
1.9-4	2014-07-30	• generalized Q-statistic estimator of $\tau^2$
1.9-6	2015-05-07	• multiple correlated random effects • parallel processing for <code>profile()</code>

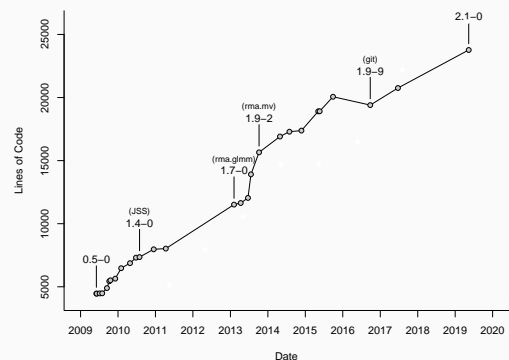
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## Some Milestones

Version	Date	Notes / Changes
1.9-8	2015-09-28	• <code>robust()</code> function • <code>confint()</code> works for <code>rma.mv</code> objects
1.9-9	2016-09-25	• started using git and GitHub • <code>ranef()</code> and <code>gosh()</code> functions • permutation-based CIs of model coefficients
2.1-0	2019-05-13	• <code>vif()</code> and <code>reporter()</code> functions • cluster-level outlier/influence statistics • more parallel processing • continuous time autoregressive structures • spatial correlation structures
2.2-0	devel	• phylogenetic correlation structures

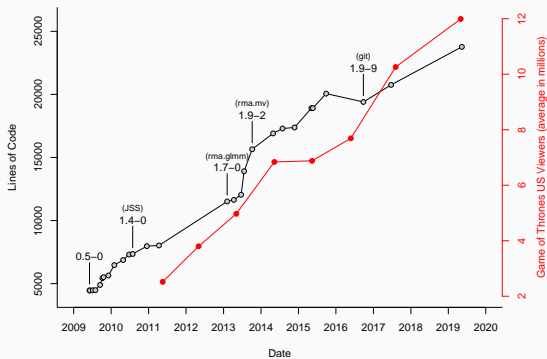
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## Lines of Code



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## Lines of Code vs Game of Thrones Viewers



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## Package Features: Effect Sizes and Outcome Measures

- measures for 2×2 table data (e.g., RD, RR, OR)
- measures for two-group person-time data (e.g., IRR, IRD)
- raw/standardized mean differences and response ratios
- conversions of 2×2 table data / ORs to SMDs and vice-versa
- raw and Fisher's r-to-z transformed correlation coefficients
- (semi)partial correlations and biserial/tetrachoric correlations
- proportions and transformations thereof
- incidence rates and transformations thereof
- raw/standardized mean change measures
- measures of change in 2×2 table data
- reliability measures (Cronbach's alpha and transformations)
- measures that quantify variability (and group differences thereof)

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## Package Features: Models and Analysis Approaches

- fixed-, random-, and mixed-effects (meta-regression) models
- Mantel-Haenszel and Peto's (one-step) method
- generalized linear (mixed-effects) models
- multilevel and multivariate meta-analytic models
- network meta-analysis / mixed treatment comparisons
- phylogenetic meta-analysis
- spatio-temporal meta-analytic models
- models with user-defined weights

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## Package Features: Plots and Figures

- forest plots
- funnel plots
- Baujat plots
- L'Abbé plots
- radial (Galbraith) plots
- GOSH plots
- profile likelihood plots
- normal quantile-quantile plots

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## Package Features: Publication Bias

- rank correlation test
- Egger's regression test
- trim and fill method
- Henmi and Copas approach
- file drawer analysis

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## Package Features: Inference Methods

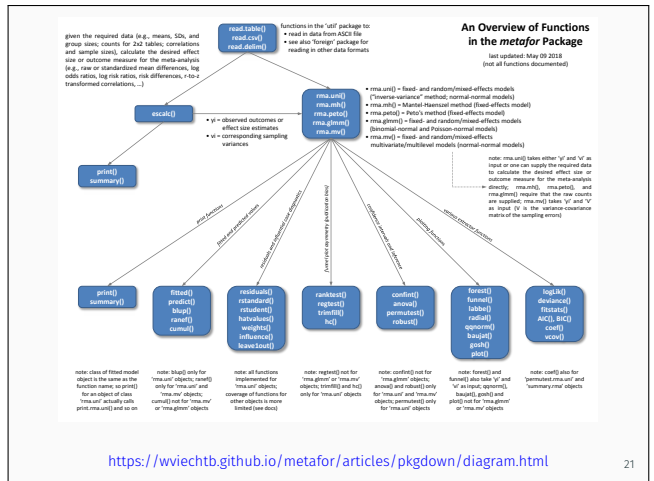
- likelihood ratio and Wald-type tests
- Knapp and Hartung method
- confidence intervals for heterogeneity statistics
- permutation tests / confidence intervals
- (cluster) robust tests and confidence intervals
- cumulative meta-analysis
- best linear unbiased predictions
- model fit / information criteria criteria
- bootstrapping (via `boot` package)
- multimodel inference (via `glmulti` and `MuMIn` packages)
- multiple imputation (via `mice` package)

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## Package Features: Outlier and Influence Diagnostics

- raw, standardized, and studentized residuals
- DFFITS, DFBETAS values, Cook's distances, covariance ratios
- cluster-level outlier/influence statistics
- model weights and hat values
- leave-one-out analyses

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## Demo: Random-Effects Model

```
### load metafor package
library(metafor)

### look at BCG dataset
dat.bcg

## trial      author year tpos tneg cpos cneg ablat alloc
## 1          Aronson 1948  4  119  11  128  44  random
## 2          Ferguson & Simes 1949  6  300  29  274  55  random
## 3          Rosenthal et al 1960  3  228  11  209  42  random
## 4          Hart & Sutherland 1977  62 13536 248 12619 52  random
## 5          Frimodt-Moller et al 1973  33 5036  47 5761  13  alternate
## 6          Stein & Aronson 1953  180 1361  372 1079  44  alternate
## 7          Vandiviere et al 1973  8  2537  10  619  19  random
## 8          TPT Madras 1980  505 87886 499 87892  13  random
## 9          Coetzee & Berjak 1968  29 7470  45 7232  27  random
## 10         Rosenthal et al 1961  17 1699  65 1600  42  systematic
## 11         Comstock et al 1974  186 50448 141 27197  18  systematic
## 12         Comstock & Webster 1969  5 2493  3 2338  33  systematic
## 13         Comstock et al 1976  27 16886  29 17825  33  systematic
```

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## Demo: Random-Effects Model

```
### calculate log risk ratios and corresponding sampling variances
dat <- escalc(measure="RR", ai=tpos, bi=tneg, ci=cpos, di=cneg, data=dat.bcg)
dat

## trial      author year ... yi vi
## 1          Aronson 1948 ... -0.8893 0.3256
## 2          Ferguson & Simes 1949 ... -1.5854 0.1946
## 3          Rosenthal et al 1960 ... -1.3481 0.4154
## 4          Hart & Sutherland 1977 ... -1.4416 0.0200
## 5          Frimodt-Moller et al 1973 ... -0.2175 0.0512
## 6          Stein & Aronson 1953 ... -0.7861 0.0069
## 7          Vandiviere et al 1973 ... -1.6209 0.2230
## 8          TPT Madras 1980 ... 0.0120 0.0040
## 9          Coetzee & Berjak 1968 ... -0.4694 0.0564
## 10         Rosenthal et al 1961 ... -1.3713 0.0730
## 11         Comstock et al 1974 ... -0.3394 0.0124
## 12         Comstock & Webster 1969 ... 0.4459 0.5325
## 13         Comstock et al 1976 ... -0.0173 0.0714
```

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## Demo: Random-Effects Model

```
### random-effects model (using log risk ratios and variances as input)
res <- rma(yi, vi, data=dat)
res

## Random-Effects Model (k = 13; tau^2 estimator: REML)
##
## tau^2 (estimated amount of total heterogeneity): 0.3132 (SE = 0.1664)
## tau (square root of estimated tau^2 value): 0.5597
## I^2 (total heterogeneity / total variability): 92.22%
## H^2 (total variability / sampling variability): 12.86
##
## Test for Heterogeneity:
## Q(df = 12) = 152.2330, p-val < .0001
##
## Model Results:
##
## estimate se zval pval ci.lb ci.ub
## -0.7145 0.1798 -3.9744 <.0001 -1.0669 -0.3622
```

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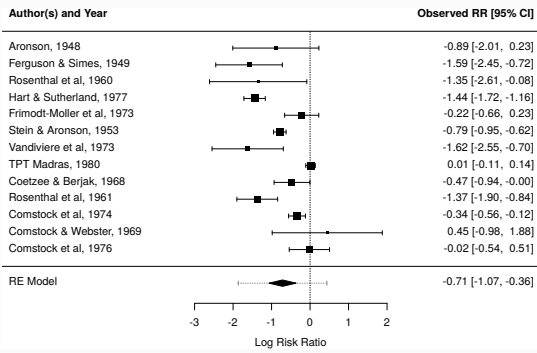
## Demo: Random-Effects Model

```
### then do lots more stuff ...
forest(res)
funnel(res)
influence(res)
plot(influence(res))
leaveout(res)
baujat(res)
ranktest(res)
regtest(res)
trimfill(res)
funnel(trimfill(res))
cumul(res)
forest(cumul(res))
radial(res)
labbe(res)
plot(gosh(res))

# note: the following plots are based on various datasets
```

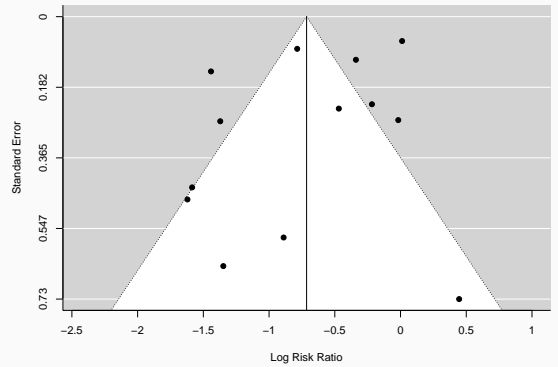
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### Demo: Forest Plot



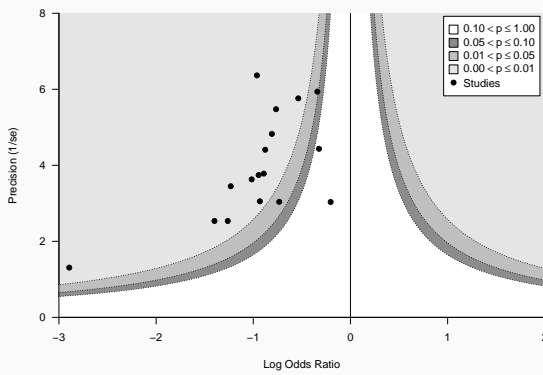
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### Demo: Funnel Plot



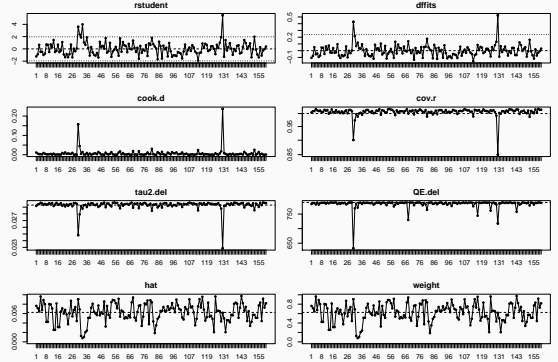
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### Demo: Contour-Enhanced Funnel Plot



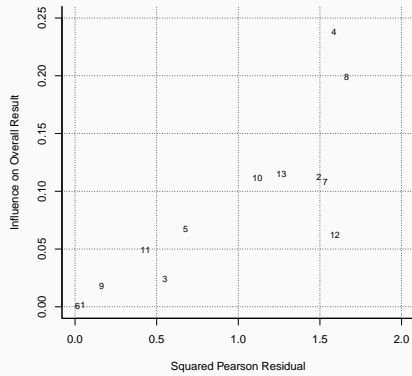
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### Demo: Outlier / Influence Diagnostics



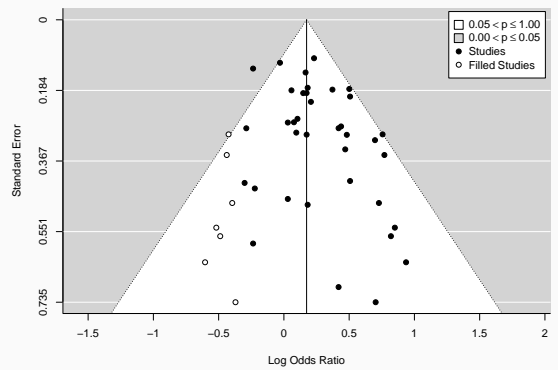
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### Demo: Baujat Plot



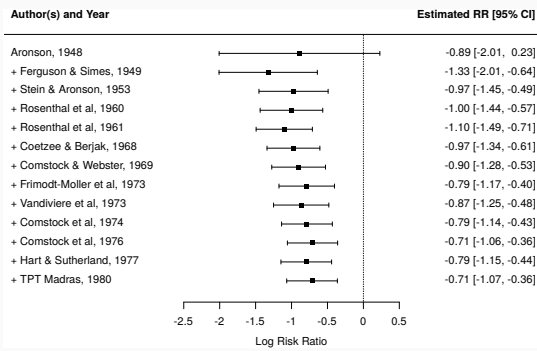
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### Demo: Trim-and-Fill



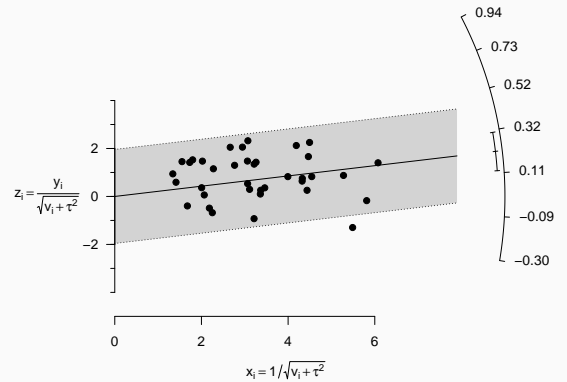
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## Demo: Cumulative Meta-Analysis



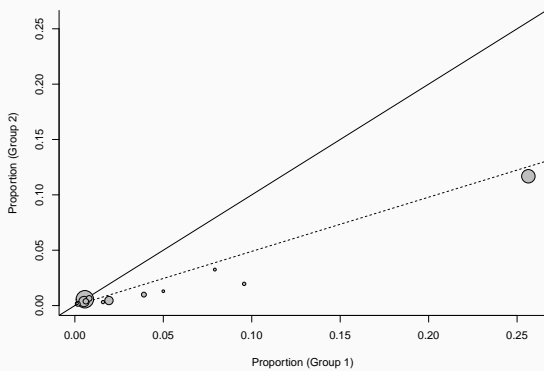
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## Demo: Radial (Galbraith) Plot



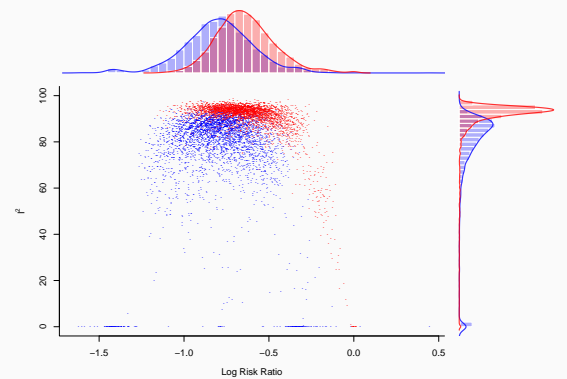
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## Demo: L'Abbé Plot



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## Demo: GOSH Plot



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## Demo: Meta-Regression

```

### mixed-effects meta-regression model
res <- rma(yi, vi, mods = ~ ablat + alloc, data=dat)
res

## Mixed-Effects Model (k = 13; tau^2 estimator: REML)
##
## tau^2 (estimated amount of residual heterogeneity): 0.1446 (SE = 0.1124)
## tau (square root of estimated tau^2 value): 0.3803
## I^2 (residual heterogeneity / unaccounted variability): 70.11%
## H^2 (unaccounted variability / sampling variability): 3.35
## R^2 (amount of heterogeneity accounted for): 53.84%
##
## Test for Residual Heterogeneity:
## QE(df = 9) = 26.2034, p-val = 0.0019
##
## ...

```

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## Demo: Meta-Regression

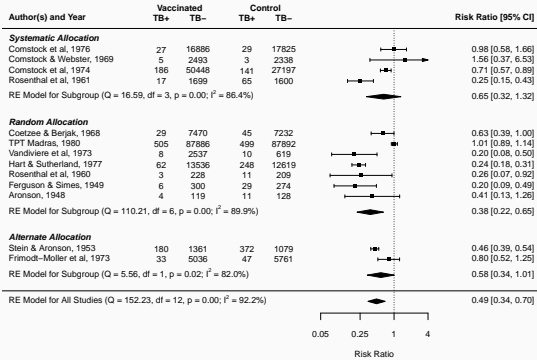
```

## ...
##
## Test of Moderators (coefficients 2:4):
## QM(df = 3) = 11.0605, p-val = 0.0114
##
## Model Results:
##
##          estimate    se    zval    pval    ci.lb    ci.ub
## intrcpt      0.2932  0.4050   0.7239  0.4691  -0.5006  1.0870
## ablat       -0.0273  0.0092  -2.9650  0.0030  -0.0453  -0.0092
## allocrandom -0.2675  0.3504  -0.7633  0.4453  -0.9543  0.4193
## allocsystematic 0.0585  0.3795   0.1540  0.8776  -0.6854  0.8023

```

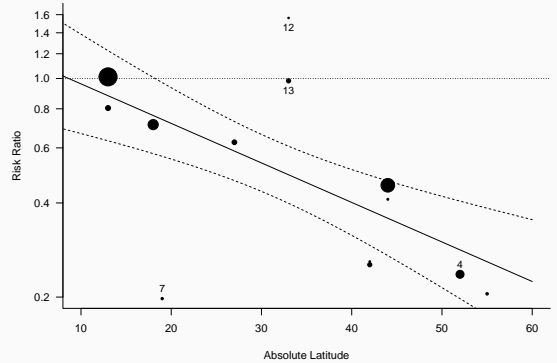
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## Demo: Forest Plot with Subgroups



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## Demo: Meta-Analytic Scatterplot



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## The reporter() Function

- automatically generates a report based on `rma.uni` objects
- describes the statistical methods used
- gives a natural language summary of the results
- includes a forest and a funnel plot
- gives references for all methods used
- output can be html, pdf, or docx

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## Quick Demo: Using reporter()

```
dat <- escalc(measure="RR", ai=tpos, bi=tneg, ci=cpos, di=cneg,
             slab=paste(author, " ", year, sep=" "),
             data=dat.bcg)
res <- rma(yi, vi, data=dat)
reporter(res)
```

Directory for generating the report is: /tmp/RtmpfH6xxC

```
Copying references.bib and apa.csl to report directory ...
Saving model object to report_res.rdata ...
Creating report_res.rmd file ...
Rendering report_res.rmd file ...
Generated /tmp/RtmpfH6xxC/report_res.html ...
Opening report ...
```

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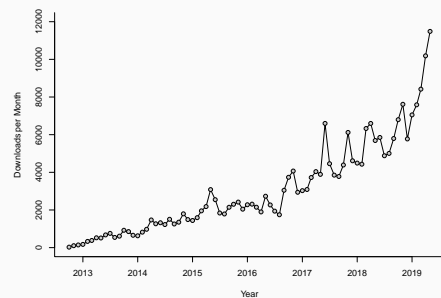
## To-Do for reporter()

- make `reporter()` work with meta-regression models
- other ideas:
  - option to suppress/customize forest/funnel plots
  - allow transformation of results (e.g., log risk ratio to risk ratio)
  - add explanatory footnotes
  - more customization (group names, outcome name, ...)
  - extend to `rma.mh`, `rma.peto`, and `rma.glmm` objects
  - ...

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## Impact: Downloads

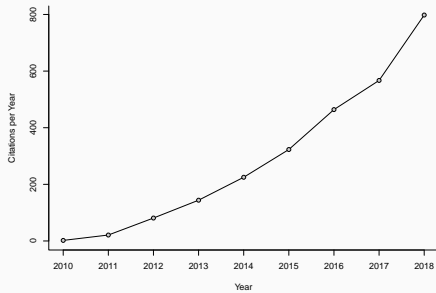
- not possible to track total downloads across all CRAN mirrors
- can get counts for the RStudio CRAN mirror (Oct 2012 - now)
- roughly 244k downloads in total



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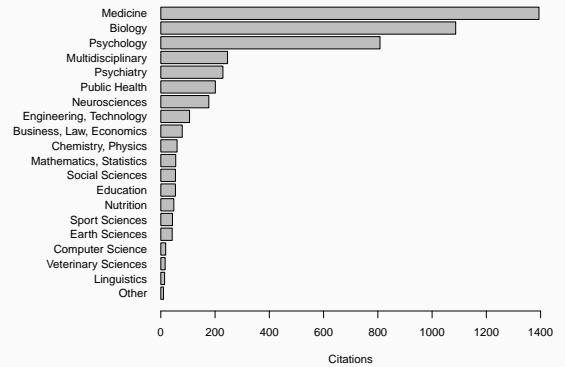
## Impact: Citations

- Viechtbauer, W. (2010). Conducting meta-analyses in R with the metafor package. *Journal of Statistical Software*, 36(3), 1-48.
- Citations: WoS Core Collection: 2968 / Google Scholar: 4282



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## Impact: Disciplines



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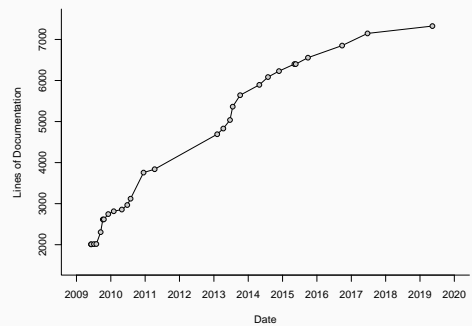
## Impact: Tools that makes use of metafor

- CRAN packages: bayesmeta, hetmeta, metaforest, metawho, SAMURAI, catmap, concurve, ConfoundedMeta, eefAnalytics, EValue, fmri, getmstatistic, ggstatsplot, KenSyn, mc.heterogeneity, meta, metagear, metagen, metamedian, metamisc, metaplus, MetaUtility, metaviz, NSM3, psychmeta, PublicationBias, puniform, RcmdrPlugin.MA, Replicate, reproducer, rma.exact, SimTimeVar, SSDforR, xmeta, ...
- [OpenMeta](#) & [OpenMEE](#) (Center for Evidence Synthesis in Health)
- [metaforGUI](#)
- [jamovi](#) + [MAJOR](#) and [JASP](#)
- [metaBUS](#) and [MetaLab](#)
- ...

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## Support

- documentation, documentation, documentation



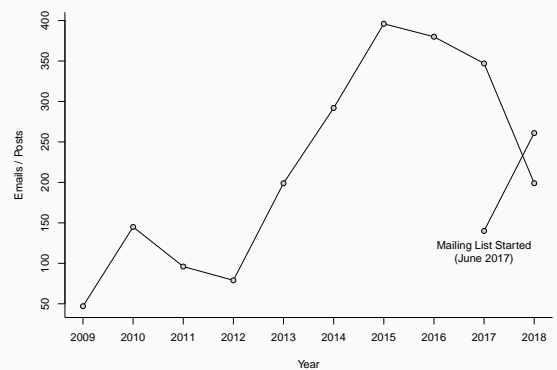
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## Support

- documentation, documentation, documentation
- documentation on GitHub: <https://wviechtb.github.io/metafor/>
- website: <http://www.metafor-project.org/>
- R-sig-meta-analysis mailing list: <https://stat.ethz.ch/mailman/listinfo/r-sig-meta-analysis>
- CrossValidated: <https://stats.stackexchange.com/search?tab=newest&q=metafor>
- StackOverflow: <https://stackoverflow.com/search?tab=newest&q=metafor>
- via email

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## Email Support → Mailing List



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## Validation / Testing

- extensive comparisons with other R/software packages
- comparison with published results (e.g., [analysis examples](#))
- testing via simulation studies
- appreciable user base
- automated testing + code coverage (~70%)

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## Philosophy

- build a toolbox, not individuals tools
- try to avoid special cases
- coherent and general modeling framework; e.g., `rma.mv()` for:
  - multilevel meta-analysis (e.g., [4], [website](#))
  - multivariate meta-analysis (e.g., [5], [website](#))
  - network meta-analysis (e.g., [example 1](#), [example 2](#))
  - phylogenetic meta-analysis (e.g., [6], [7])
  - spatio-temporal models (e.g., [8])
- figure out logical generalizations
- listen to users

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## The Future

- keep expanding on the capabilities
  - add location-scale models to `rma.uni()`
  - add selection models to `rma.uni()` (and `rma.mv()`?)
  - allow fitting `rma.uni()` models using fully Bayesian methods
  - make `reporter()` work with meta-regression models
  - ...
- a meta-analysis data package (`metadat`) – in progress!

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  - make `reporter()` work with meta-regression models
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- ...

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  - add location-scale models to `rma.uni()`
  - add selection models to `rma.uni()` (and `rma.mv()`?)
  - allow fitting `rma.uni()` models using fully Bayesian methods
  - make `reporter()` work with meta-regression models
  - ...
- a meta-analysis data package (`metadat`) – in progress!
- ...
- rewrite everything from scratch!

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## References i

1. Starr, M., Chalmers, I., Clarke, M., & Oxman, A. D. (2009). The origins, evolution, and future of The Cochrane Database of Systematic Reviews. *International Journal of Technology Assessment in Health Care*, 25(51), 182–195.
2. Rosenberg, M. S., Adams, D. C., & Gurevitch, J. (1997). *MetaWin: Statistical software for meta-analysis with resampling tests*. Sunderland, MA: Sinauer Associates.
3. Borenstein, M., & Rothstein, H. (1998). *Comprehensive Meta-Analysis: A computer program for research synthesis*. Englewood, NJ: Biostat Inc.
4. Konstantopoulos, S. (2011). Fixed effects and variance components estimation in three-level meta-analysis. *Research Synthesis Methods*, 2(1), 61–76.
5. Berkey, C. S., Hoaglin, D. C., Antczak-Bouckoms, A., Mosteller, F., & Colditz, G. A. (1998). Meta-analysis of multiple outcomes by regression with random effects. *Statistics in Medicine*, 17(22), 2537–2550.

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6. Nakagawa, S., & Santos, E. S. A. (2012). Methodological issues and advances in biological meta-analysis. *Evolutionary Ecology*, 26(5), 1253–1274.
7. Hoeksema, J. D., Bever, J. D., Chakraborty, S., Chaudhary, V. B., Gardes, M., Gehring, C. A., ... Zee, P. C. (2018). Evolutionary history of plant hosts and fungal symbionts predicts the strength of mycorrhizal mutualism. *Communications Biology*, 1(1), 116.
8. Maire, A., Thierry, E., Viechtbauer, W., & Daufresne, M. (2019). Poleward shift in large-river fish communities detected with a novel meta-analysis framework. *Freshwater Biology*, 64(6), 1143–1156.

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Thank You!

Questions, Comments, Suggestions?

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