The R package metafor:
Past, present, and future
Research Synthesis 2019
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Maastricht University
2019-05-31

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 ...

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: published 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

CRAN Task View: Meta-Analysis

Maintainer: Michael Dewey
Contact: lisa@lisa.mynren.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.

First Releases of Meta-Analysis Packages

<table>
<thead>
<tr>
<th>Package</th>
<th>Date (of first version released on CRAN)</th>
</tr>
</thead>
<tbody>
<tr>
<td>meta</td>
<td>2000</td>
</tr>
<tr>
<td>metafor</td>
<td>2009</td>
</tr>
<tr>
<td>metaSEM</td>
<td>2010</td>
</tr>
<tr>
<td>metafor</td>
<td>2015</td>
</tr>
<tr>
<td>metaSEM</td>
<td>2017</td>
</tr>
<tr>
<td>metafor</td>
<td>2019</td>
</tr>
<tr>
<td>metafor</td>
<td>2020</td>
</tr>
</tbody>
</table>

The CRAN Task View on Meta-Analysis is available at:
https://cran.r-project.org/view=MetaAnalysis

This also applies to Illinois in general ...

Meta-Analytic Landscape in R (~1998)
Exponential Growth (sort of)

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:

Some Milestones

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

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<tbody>
<tr>
<td>1.7-0</td>
<td>2013-02-06</td>
<td>- rma.glmm() function</td>
</tr>
<tr>
<td>1.9-0</td>
<td>2013-06-21</td>
<td>- hc() function</td>
</tr>
<tr>
<td>1.9-1</td>
<td>2013-07-20</td>
<td>- baujat() function</td>
</tr>
<tr>
<td>1.9-2</td>
<td>2013-10-07</td>
<td>- rma.mv() and profile() functions</td>
</tr>
<tr>
<td>1.9-3</td>
<td>2014-05-05</td>
<td>- models with user-defined weights</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- sparse matrices for rma.mv()</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- autoregressive structures for rma.mv()</td>
</tr>
<tr>
<td>1.9-4</td>
<td>2014-07-30</td>
<td>- generalized Q-statistic estimator of ( \tau^2 )</td>
</tr>
<tr>
<td>1.9-6</td>
<td>2015-05-07</td>
<td>- multiple correlated random effects</td>
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<tr>
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<td>- parallel processing for profile()</td>
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</tbody>
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</tr>
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<tbody>
<tr>
<td>1.9-8</td>
<td>2015-09-28</td>
<td>- robust() function</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- confint() works for rma.mv objects</td>
</tr>
<tr>
<td>1.9-9</td>
<td>2016-09-25</td>
<td>- started using git and GitHub</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- ranef() and gosh() functions</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- permutation-based CIs of model coefficients</td>
</tr>
<tr>
<td>21-0</td>
<td>2019-05-13</td>
<td>- vif() and reporter() functions</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- cluster-level outlier/influence statistics</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- more parallel processing</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- continuous time autoregressive structures</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- spatial correlation structures</td>
</tr>
<tr>
<td>22-0</td>
<td>devel</td>
<td>- phylogenetic correlation structures</td>
</tr>
</tbody>
</table>

Lines of Code

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1.9-2 2013-10-07 rma.mv() and profile() functions
1.9-3 2014-05-05 models with user-defined weights
  sparse matrices for rma.mv()
  autoregressive structures for rma.mv()
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 profile()
Lines of Code vs Game of Thrones Viewers

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)

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

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

Package Features: Publication Bias
- rank correlation test
- Egger’s regression test
- trim and fill method
- Henmi and Copas approach
- file drawer analysis

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)
transformed correlations, and sample sizes), calculate the desired effect size or outcome measure for the meta-analysis using either log risk ratios, log risk ratios, risk differences, r-to-z transformations of correlations, or other effects. The demo code for a random-effects model follows:

```r
### load metafor package
library(metafor)
### look at BCG dataset
dat.bcg
## trial author year tpos tspo cpos cneg ablat alloc
## 1 1 Aronson 1948 4 119 11 128 44 random
## 2 2 Ferguson & Simes 1949 6 300 29 274 55 random
## 3 3 Rosenthal et al. 1960 3 228 11 209 42 random
## 4 4 Hart & Sutherland 1977 62 13536 248 12619 52 random
## 5 5 Frimodt-Moller et al. 1973 33 5036 47 5761 13 alternate
## 6 6 Stein & Aronson 1953 180 1361 372 1079 44 alternate
## 7 7 Vandiviere et al. 1973 8 2537 10 619 19 alternate
## 8 8 TPT Madras 1980 505 87886 499 87892 13 random
## 9 9 Coetzee & Berjak 1968 29 7470 45 7232 27 random
## 10 10 Rosenthal et al. 1961 17 1699 65 1600 42 systematic
## 11 11 Comstock & Webster 1969 26 2691 11 2570 38 systematic
## 12 12 Comstock et al. 1974 27 16886 29 17825 33 systematic
## 13 13 Comstock et al. 1976 24 341 12 128 35 systematic
```

Next, calculate log risk ratios and corresponding sampling variances using the `escalc()` function:

```r
res <- escalc(measure = "RR", ai = tpos, bi = tspo, ci = cpos, di = cneg, data = dat.bcg)
```

Finally, fit a random-effects model using the `rma.uni()` function:

```r
res <- rma(yi, vi, data = res)
```

### Demo: Random-Effects Model

#### Demo: Random-Effects Model

### load metafor package
library(metafor)

### look at BCG dataset
dat.bcg

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

### Random-Effects Model (k = 13; tau^2 estimator: REML)
### then do lots more stuff ...
forest(res)
funnel(res)
earheid(res)
plot(influence(res))
leavesout(res)
betafit(res)
ranktest(res)
regtest(res)
trimfill(res)
funnel(trimfill(res))
cumul(res)
forest(cumul(res))
radial(res)
labbe(res)
plot(galbraith(res))

# note: the following plots are based on various datasets
Demo: Cumulative Meta-Analysis

<table>
<thead>
<tr>
<th>Author(s) and Year</th>
<th>Estimated RR [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aronson, 1948</td>
<td>0.09 [0.01, 0.22]</td>
</tr>
<tr>
<td>Ferguson &amp; Simes, 1949</td>
<td>-1.33 [-2.01, -0.64]</td>
</tr>
<tr>
<td>Stein &amp; Aronson, 1953</td>
<td>-0.97 [-1.45, -0.49]</td>
</tr>
<tr>
<td>Rosenthal et al. 1960</td>
<td>-1.00 [-1.44, -0.57]</td>
</tr>
<tr>
<td>Rosenthal et al. 1981</td>
<td>-1.10 [-1.43, -0.77]</td>
</tr>
<tr>
<td>Coote &amp; Benjak, 1968</td>
<td>-0.97 [-1.34, -0.61]</td>
</tr>
<tr>
<td>Comstock &amp; Webster, 1963</td>
<td>-0.90 [-1.28, -0.53]</td>
</tr>
<tr>
<td>Friesdod-Moller et al. 1973</td>
<td>-0.79 [-1.17, -0.40]</td>
</tr>
<tr>
<td>Vanderveen et al. 1973</td>
<td>-0.87 [-1.25, -0.48]</td>
</tr>
<tr>
<td>Comstock et al. 1974</td>
<td>-0.74 [-1.14, -0.34]</td>
</tr>
<tr>
<td>Comstock et al. 1976</td>
<td>-0.71 [-1.06, -0.36]</td>
</tr>
<tr>
<td>Hart &amp; Sutherland, 1977</td>
<td>-0.79 [-1.19, -0.44]</td>
</tr>
<tr>
<td>TPT Madras, 1990</td>
<td>-0.71 [-1.07, -0.36]</td>
</tr>
</tbody>
</table>

Demo: Radial (Galbraith) Plot

Demo: L’Abbé Plot

Demo: GOSH Plot

Demo: Meta-Regression

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

# Mixed-Effects Model (k = 13; tau2 estimator: REML)

# tau2 (estimated amount of residual heterogeneity): 0.1446 (SE = 0.1124)
# tau (square root of estimated tau2 values): 0.3803
# I^2 (residual heterogeneity / unaccounted variability): 70.1%
# H^2 (unaccounted variability / sampling variability): 3.36
# R^2 (amount of heterogeneity accounted for): 53.84%

# Test for Residual Heterogeneity:
# QE(df = 9) = 26.2034, p-val = 0.0019
#
# ...
Demo: Forest Plot with Subgroups

Author(s) and Year | Vaccinated | TB+ | Control | TB− | Risk Ratio [95% CI] | RE Model for Subgroup (Q = 5.56 , df = 1 , p = 0.02 ; I² = 82.0 %)
--- | --- | --- | --- | --- | --- | ---
Systolic Distribution | Comstock & Webster, 1969 | 1684 | 27 | 9 | 0.66 [0.33, 1.34] | 0.66 [0.33, 1.34]
Comstock et al, 1976 | 3 | 27 | 10 | 0.58 [0.34, 0.99] | 0.58 [0.34, 0.99]
Comstock et al, 1974 | 6 | 6 | 3 | 0.38 [0.22, 0.65] | 0.38 [0.22, 0.65]
Rosenthal et al, 1960 | 11 | 21 | 70 | 0.35 [0.18, 0.66] | 0.35 [0.18, 0.66]
Rosenthal et al, 1961 | 21 | 10 | 127 | 0.40 [0.23, 0.69] | 0.40 [0.23, 0.69]
Rosenthal et al, 1969 | 10 | 13 | 228 | 0.47 [0.31, 0.72] | 0.47 [0.31, 0.72]
Rosenthal et al, 1973 | 4 | 17 | 100 | 0.63 [0.39, 1.00] | 0.63 [0.39, 1.00]
TPT Madras, 1980 | 128 | 11 | 12 | 0.65 [0.33, 1.31] | 0.65 [0.33, 1.31]
Vandiviere et al, 1973 | 4 | 17 | 100 | 0.52 [0.29, 0.92] | 0.52 [0.29, 0.92]

The reporter() Function

- automatically generates a report based on \texttt{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

Quick Demo: Using reporter()

\begin{verbatim}
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.bcg)
reporter(res)
\end{verbatim}

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 ...

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
Impact: Citations

- Citations: WoS Core Collection: 2968 / Google Scholar: 4282

Impact: Disciplines

- Medicine
- Biology
- Psychology
- Multidisciplinary
- Psychiatry
- Public Health
- Neurosciences
- Engineering, Technology
- Business, Law, Economics
- Chemistry, Physics
- Mathematics, Statistics
- Social Sciences
- Education
- Nutrition
- Sport Sciences
- Earth Sciences
- Computer Science
- Veterinary Sciences
- Linguistics
- Others

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
- ...

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

Email Support → Mailing List

- Mailing List Started (June 2017)
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%)

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., [5], 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

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!
  • …
• rewrite everything from scratch!


