# Package 'meta'

July 11, 2022

```
Title General Package for Meta-Analysis
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URL https://github.com/guido-s/meta/
      https://link.springer.com/book/10.1007/978-3-319-21416-0
Description User-friendly general package providing standard methods for meta-
      analysis and supporting Schwarzer, Carpenter, and Rücker < DOI:10.1007/978-3-319-21416-
      0>, ``Meta-Analysis with R'' (2015):
      - common effect and random effects meta-analysis;
      - several plots (forest, funnel, Galbraith / radial, L'Abbe, Baujat, bubble);
      - statistical tests and trim-and-fill method to evaluate bias in meta-analysis;
      - import data from 'RevMan 5';
      - prediction interval, Hartung-Knapp method for random effects model;
      - cumulative meta-analysis and leave-one-out meta-analysis;
      - meta-regression;
      - generalised linear mixed models;
      - produce forest plot summarising several (subgroup) meta-analyses.
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```

# R topics documented:

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### Description

R package **meta** is a user-friendly general package providing standard methods for meta-analysis and supporting Schwarzer et al. (2015), https://link.springer.com/book/10.1007/978-3-319-21416-0.

#### **Details**

R package **meta** (Schwarzer, 2007; Balduzzi et al., 2019) provides the following statistical methods for meta-analysis.

- 1. Common effect (also called fixed effect) and random effects model:
  - Meta-analysis of continuous outcome data (metacont)
  - Meta-analysis of binary outcome data (metabin)
  - Meta-analysis of incidence rates (metainc)
  - Generic inverse variance meta-analysis (metagen)
  - Meta-analysis of single correlations (metacor)
  - Meta-analysis of single means (metamean)
  - Meta-analysis of single proportions (metaprop)
  - Meta-analysis of single incidence rates (metarate)
- 2. Several plots for meta-analysis:
  - Forest plot (forest.meta, forest.metabind)
  - Funnel plot (funnel.meta)
  - Galbraith plot / radial plot (radial.meta)
  - L'Abbe plot for meta-analysis with binary outcome data (labbe.metabin, labbe.default)
  - Baujat plot to explore heterogeneity in meta-analysis (baujat.meta)
  - Bubble plot to display the result of a meta-regression (bubble.metareg)
- 3. Statistical tests for funnel plot asymmetry (metabias.meta, metabias.rm5) and trim-and-fill method (trimfill.meta, trimfill.default) to evaluate bias in meta-analysis
- 4. Cumulative meta-analysis (metacum) and leave-one-out meta-analysis (metainf)
- 5. Meta-regression (metareg)

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6. Import data from Review Manager 5 (read.rm5); see also metacr to conduct meta-analysis for a single comparison and outcome from a Cochrane review

- 7. Prediction interval for the treatment effect of a new study (Higgins et al., 2009); see argument prediction in meta-analysis functions, e.g., metagen
- 8. Hartung-Knapp method for random effects meta-analysis (Hartung & Knapp, 2001a,b); see argument hakn in meta-analysis functions, e.g., metagen
- 9. Various estimators for the between-study variance  $\tau^2$  in a random effects model (Veroniki et al., 2016); see argument method. tau in meta-analysis functions, e.g., metagen
- 10. Generalised linear mixed models (metabin, metainc, metaprop, and metarate)

The following more advanced statistical methods are provided by add-on R packages:

- Frequentist methods for network meta-analysis (R package **netmeta**)
- Advanced methods to model and adjust for bias in meta-analysis (R package **metasens**)

Results of several meta-analyses can be combined with metabind. This is, for example, useful to generate a forest plot with results of subgroup analyses.

See settings.meta to learn how to print and specify default meta-analysis methods used during your R session. For example, the function can be used to specify general settings:

- settings.meta("revman5")
- settings.meta("jama")
- settings.meta("iqwig5")
- settings.meta("iqwig6")
- settings.meta("geneexpr")

The first command can be used to reproduce meta-analyses from Cochrane reviews conducted with *Review Manager 5* (RevMan 5, https://training.cochrane.org/online-learning/core-software-cochrane-reviewmen) and specifies to use a RevMan 5 layout in forest plots.

The second command can be used to generate forest plots following instructions for authors of the *Journal of the American Medical Association* (https://jamanetwork.com/journals/jama/pages/instructions-for-authors/). Study labels according to JAMA guidelines can be generated using labels.meta.

The next two commands implement the recommendations of the Institute for Quality and Efficiency in Health Care (IQWiG), Germany accordinging to General Methods 5 and 6, respectively (https://www.iqwig.de/en/about-us/methods/methods-paper/).

The last setting can be used to print p-values in scientific notation and to suppress the calculation of confidence intervals for the between-study variance.

In addition, settings.meta can be used to change individual settings. For example, the following R command specifies the use of the Hartung-Knapp and Paule-Mandel methods, and the printing of prediction intervals in the current R session for any meta-analysis generated after execution of this command:

• settings.meta(hakn=TRUE, method.tau="PM", prediction=TRUE)

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Type help(package = "meta") for a listing of R functions and datasets available in meta.

Balduzzi et al. (2019) is the preferred citation in publications for **meta**. Type citation("meta") for a BibTeX entry of this publication.

To report problems and bugs

- type bug.report(package = "meta") if you do not use RStudio,
- send an email to Guido Schwarzer <sc@imbi.uni-freiburg.de> if you use RStudio.

The development version of **meta** is available on GitHub https://github.com/guido-s/meta/.

#### Note

R package meta imports R functions from metafor (Viechtbauer, 2010) to

- estimate the between-study variance  $\tau^2$ ,
- · conduct meta-regression,
- estimate three-level models (Van den Noortgate et al., 2013),
- estimate generalised linear mixed models (Stijnen et al., 2010).

#### Author(s)

Guido Schwarzer <sc@imbi.uni-freiburg.de>

### References

Balduzzi S, Rücker G, Schwarzer G (2019): How to perform a meta-analysis with R: a practical tutorial. *Evidence-Based Mental Health*, **22**, 153–160

Hartung J, Knapp G (2001a): On tests of the overall treatment effect in meta-analysis with normally distributed responses. *Statistics in Medicine*, **20**, 1771–82

Hartung J, Knapp G (2001b): A refined method for the meta-analysis of controlled clinical trials with binary outcome. *Statistics in Medicine*, **20**, 3875–89

Higgins JPT, Thompson SG, Spiegelhalter DJ (2009): A re-evaluation of random-effects metaanalysis. *Journal of the Royal Statistical Society: Series A*, **172**, 137–59

Schwarzer G (2007): meta: An R package for meta-analysis. R News, 7, 40–5

Schwarzer G, Carpenter JR and Rücker G (2015): *Meta-Analysis with R (Use-R!)*. Springer International Publishing, Switzerland

Stijnen T, Hamza TH, Ozdemir P (2010): Random effects meta-analysis of event outcome in the framework of the generalized linear mixed model with applications in sparse data. *Statistics in Medicine*, **29**, 3046–67

Veroniki AA, Jackson D, Viechtbauer W, Bender R, Bowden J, Knapp G, et al. (2016): Methods to estimate the between-study variance and its uncertainty in meta-analysis. *Research Synthesis Methods*, **7**, 55–79

Van den Noortgate W, López-López JA, Marín-Martínez F, Sánchez-Meca J (2013): Three-level meta-analysis of dependent effect sizes. *Behavior Research Methods*, **45**, 576–94

Viechtbauer W (2010): Conducting Meta-Analyses in R with the metafor Package. *Journal of Statistical Software*, **36**, 1–48

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amlodipine

Amlodipine for Work Capacity

### Description

Meta-analysis on the effect of amlodipine on work capacity.

This meta-analysis is used as a data example in Hartung and Knapp (2001).

#### **Format**

A data frame with the following columns:

study
 n.amlo
 mean.amlo
 var.amlo
 n.plac
 mean.plac
 var.plac
 var.plac
 var.plac
 mean.plac
 placebo group
 var.plac
 var.plac

#### **Source**

Hartung J & Knapp G (2001): On tests of the overall treatment effect in meta-analysis with normally distributed responses. *Statistics in Medicine*, **20**, 1771–82

### See Also

metacont

### **Examples**

```
data(amlodipine)

m <- metacont(n.amlo, mean.amlo, sqrt(var.amlo),
    n.plac, mean.plac, sqrt(var.plac),
    data = amlodipine, studlab = study,
    method.tau = "DL")
m.hakn <- update(m, hakn = TRUE)

# Same results for mean difference as in Table III in Hartung and
# Knapp (2001)
#
vars.common <- c("TE.common", "lower.common", "upper.common")
vars.random <- c("TE.random", "lower.random", "upper.random")
#
res.common <- as.data.frame(m[vars.common])
names(res.common) <- vars.random
#</pre>
```

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```
res.md <- rbind(res.common,
   as.data.frame(m[vars.random]),
   as.data.frame(m.hakn[vars.random]))
#
res.md <- round(res.md, 5)
#
row.names(res.md) <- c("CE", "RE", "RE (HaKn)")
names(res.md) <- c("Absolute difference", "CI lower", "CI upper")
#
res.md</pre>
```

as.data.frame.meta

Additional functions for objects of class meta

### Description

The as.data.frame method returns a data frame containing information on individual studies, e.g., estimated treatment effect and its standard error.

### Usage

```
## S3 method for class 'meta'
as.data.frame(x, row.names = NULL, optional = FALSE, ...)
```

### Arguments

x An object of class meta.

row.names NULL or a character vector giving the row names for the data frame.

optional logical. If TRUE, setting row names and converting column names (to syntactic

names) is optional.

... other arguments

### Value

A data frame is returned by the function as.data.frame.

### Author(s)

```
Guido Schwarzer <sc@imbi.uni-freiburg.de>
```

#### See Also

```
metabin, metacont, metagen, forest.meta
```

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### **Examples**

```
data(Fleiss1993cont)
# Generate additional variable with grouping information
Fleiss1993cont$group <- c(1, 2, 1, 1, 2)$
# Do meta-analysis without grouping information
m1 <- metacont(n.psyc, mean.psyc, sd.psyc, n.cont, mean.cont, sd.cont,</pre>
  data = Fleiss1993cont, sm = "SMD", studlab = paste(study, year))
# Update meta-analysis object and do subgroup analyses
update(m1, subgroup = group)
# Same result using metacont function directly
m2 <- metacont(n.psyc, mean.psyc, sd.psyc, n.cont, mean.cont, sd.cont,</pre>
  data = Fleiss1993cont, sm = "SMD", studlab = paste(study, year),
  subgroup = group)
m2
# Compare printout of the following two commands
as.data.frame(m1)
m1$data
```

baujat.meta

Baujat plot to explore heterogeneity in meta-analysis

### Description

Draw a Baujat plot to explore heterogeneity in meta-analysis.

### Usage

```
## S3 method for class 'meta'
baujat(
    x,
    yscale = 1,
    xlim,
    ylim,
    xlab = "Contribution to overall heterogeneity",
    ylab = "Influence on overall result",
    pch = 21,
    cex = 1,
    col = "black",
```

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```
bg = "darkgray",
studlab = TRUE,
cex.studlab = 0.8,
pos.studlab,
offset = 0.5,
xmin = 0,
ymin = 0,
grid = TRUE,
col.grid = "lightgray",
lty.grid = "dotted",
lwd.grid = par("lwd"),
pty = "s",
....
)
```

### Arguments

x	An object of class meta.
yscale	Scaling factor for values on y-axis.
xlim	The x limits (min,max) of the plot.
ylim	The y limits (min,max) of the plot.
xlab	A label for the x-axis.
ylab	A label for the y-axis.
pch	The plotting symbol used for individual studies.
cex	The magnification to be used for plotting symbol.
col	A vector with colour of plotting symbols.
bg	A vector with background colour of plotting symbols (only used if pch in 21:25).
studlab	A logical indicating whether study labels should be printed in the graph. A vector with study labels can also be provided (must be of same length as x\$TE then).
cex.studlab	The magnification for study labels.
pos.studlab	Position of study labels, see argument pos in text.
	resition of study labels, see argument pos in text.
offset	Offset for study labels (see text).
offset xmin	•
	Offset for study labels (see text).
xmin	Offset for study labels (see text).  A numeric specifying minimal value to print study labels (on x-axis).
xmin ymin	Offset for study labels (see text).  A numeric specifying minimal value to print study labels (on x-axis).  A numeric specifying minimal value to print study labels (on y-axis).
xmin ymin grid	Offset for study labels (see text).  A numeric specifying minimal value to print study labels (on x-axis).  A numeric specifying minimal value to print study labels (on y-axis).  A logical indicating whether a grid is printed in the plot.
xmin ymin grid col.grid	Offset for study labels (see text).  A numeric specifying minimal value to print study labels (on x-axis).  A numeric specifying minimal value to print study labels (on y-axis).  A logical indicating whether a grid is printed in the plot.  Colour for grid lines.
xmin ymin grid col.grid lty.grid	Offset for study labels (see text).  A numeric specifying minimal value to print study labels (on x-axis).  A numeric specifying minimal value to print study labels (on y-axis).  A logical indicating whether a grid is printed in the plot.  Colour for grid lines.  The line type for grid lines.

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#### **Details**

Baujat et al. (2002) introduced a scatter plot to explore heterogeneity in meta-analysis. On the x-axis the contribution of each study to the overall heterogeneity statistic (see list object Q of the meta-analysis object x) is plotted. On the y-axis the standardised difference of the overall treatment effect with and without each study is plotted; this quantity describes the influence of each study on the overall treatment effect.

Internally, the metainf function is used to calculate the values on the y-axis.

#### Value

A data.frame with the following variables:

x Coordinate on x-axis (contribution to heterogeneity statistic)

y Coordinate on y-axis (influence on overall treatment effect)

### Author(s)

Guido Schwarzer <sc@imbi.uni-freiburg.de>

#### References

Baujat B, Mahé C, Pignon JP, Hill C (2002): A graphical method for exploring heterogeneity in meta-analyses: Application to a meta-analysis of 65 trials. *Statistics in Medicine*, **30**, 2641–52

### See Also

```
metagen, metainf
```

### **Examples**

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```
# Calculate overall heterogeneity statistic
sum(b1$x)
m1$Q
## End(Not run)
```

bubble.metareg

Bubble plot to display the result of a meta-regression

### **Description**

Draw a bubble plot to display the result of a meta-regression.

### Usage

```
## S3 method for class 'metareg'
bubble(
  х,
  xlim,
 ylim,
  xlab,
 ylab,
  cex,
 min.cex = 0.5,
 max.cex = 5,
 pch = 21,
  col = "black",
  bg = "darkgray",
  lty = 1,
  lwd = 1,
  col.line = "black",
  studlab = FALSE,
  cex.studlab = 0.8,
  pos.studlab = 2,
 offset = 0.5,
  regline = TRUE,
  backtransf = x$.meta$x$backtransf,
  ref,
  col.ref = "lightgray",
  lty.ref = 1,
  lwd.ref = 1,
  axes = TRUE,
 box = TRUE,
)
bubble(x, ...)
```

bubble.metareg

## Arguments

x	An object of class metareg.
xlim	The x limits (min,max) of the plot.
ylim	The y limits (min,max) of the plot.
xlab	A label for the x-axis.
ylab	A label for the y-axis.
cex	The magnification to be used for plotting symbols.
min.cex	Minimal magnification for plotting symbols.
max.cex	Maximal magnification for plotting symbols.
pch	The plotting symbol used for individual studies.
col	A vector with colour of plotting symbols.
bg	A vector with background colour of plotting symbols (only used if pch in 21:25).
lty	The line type for the meta-regression line.
lwd	The line width for the meta-regression line.
col.line	Colour for the meta-regression line.
studlab	A logical indicating whether study labels should be printed in the graph. A vector with study labels can also be provided (must be of same length as the numer of studies in the meta-analysis then).
cex.studlab	The magnification for study labels.
pos.studlab	Position of study labels, see argument pos in text.
offset	Offset for study labels (see text).
regline	A logical indicating whether a regression line should be added to the bubble plot.
backtransf	A logical indicating whether results for relative summary measures (argument sm equal to "OR", "RR", "HR", or "IRR") should be back transformed. If backtransf=TRUE, results for sm="OR" are printed as odds ratios rather than log odds ratios, for example.
ref	A numerical giving the reference value to be plotted as a line in the bubble plot. No reference line is plotted if argument ref is equal to NA.
col.ref	Colour of the reference line.
lty.ref	The line type for the reference line.
lwd.ref	The line width for the reference line.
axes	A logical indicating whether axes should be printed.
box	A logical indicating whether a box should be printed.
	Graphical arguments as in par may also be passed as arguments.

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#### **Details**

A bubble plot can be used to display the result of a meta-regression. It is a scatter plot with the treatment effect for each study on the y-axis and the covariate used in the meta-regression on the x-axis. Typically, the size of the plotting symbol is inversely proportional to the variance of the estimated treatment effect (Thompson & Higgins, 2002).

Argument cex specifies the plotting size for each individual study. If this argument is missing the weights from the meta-regression model will be used (which typically is a random effects model). Use cex="common" in order to utilise weights from a common effect model to define the size of the plotted symbols (even for a random effects meta-regression). If a vector with individual study weights is provided, the length of this vector must be of the same length as the number of studies.

Arguments min.cex and max.cex can be used to define the size of the smallest and largest plotting symbol. The plotting size of the most precise study is set to max.cex whereas the plotting size of all studies with a plotting size smaller than min.cex will be set to min.cex.

For a meta-regression with more than one covariate. Only a scatter plot of the first covariate in the regression model is shown. In this case the effect of the first covariate adjusted for other covariates in the meta-regression model is shown.

For a factor or categorial covariate separate bubble plots for each group compared to the baseline group are plotted.

### Author(s)

Guido Schwarzer <sc@imbi.uni-freiburg.de>

#### References

Thompson SG, Higgins JP (2002): How should meta-regression analyses be undertaken and interpreted? *Statistics in Medicine*, **21**, 1559–73

### See Also

```
metagen, metainf
```

### **Examples**

```
data(Fleiss1993cont)

# Add some (fictitious) grouping variables:
Fleiss1993cont$age <- c(55, 65, 52, 65, 58)
Fleiss1993cont$region <- c("Europe", "Europe", "Asia", "Asia", "Europe")

m1 <- metacont(n.psyc, mean.psyc, sd.psyc, n.cont, mean.cont, sd.cont, data = Fleiss1993cont, sm = "MD")

mr1 <- metareg(m1, region)
mr1

bubble(mr1)
bubble(mr1, lwd = 2, col.line = "blue")</pre>
```

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```
mr2 <- metareg(m1, age)
mr2

bubble(mr2, lwd = 2, col.line = "blue", xlim = c(50, 70))
bubble(mr2, lwd = 2, col.line = "blue", xlim = c(50, 70), cex = "common")

# Do not print regression line
#
bubble(mr2, lwd = 2, col.line = "blue", xlim = c(50, 70), regline = FALSE)</pre>
```

ci

Calculation of confidence intervals (based on normal approximation or t-distribution)

### Description

Calculation of confidence intervals; based on normal approximation or t-distribution.

### Usage

```
ci(TE, seTE, level = 0.95, df = NULL, null.effect = 0)
```

### Arguments

TE Estimated treatment effect.

seTE Standard error of treatment estimate.

level The confidence level required.

df Degrees of freedom (for confidence intervals based on t-distribution).

null.effect A numeric value specifying the effect under the null hypothesis.

#### Value

### List with components

TE Estimated treatment effect

seTE Standard error of treatment estimate

lower Lower confidence limits upper Upper confidence limits

statistic Test statistic (either z-score or t-score)

p P-value of text.with null hypothesis TE=0

level The confidence level required

df Degrees of freedom (t-distribution)

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### Note

This function is primarily called from other functions of the library meta, e.g. forest.meta, summary.meta.

### Author(s)

Guido Schwarzer <sc@imbi.uni-freiburg.de>

### **Examples**

```
data.frame(ci(170, 10))
data.frame(ci(170, 10, 0.99))
data.frame(ci(1.959964, 1))
data.frame(ci(2.2621571628, 1, df = 9))
```

cisapride

Cisapride in Non-Ulcer Dispepsia

### Description

Meta-analysis on cisapride in non-ulcer dispepsia.

This meta-analysis is used as a data example in Hartung and Knapp (2001).

### **Format**

A data frame with the following columns:

```
    study
    event.cisa
    n.cisa
    event.plac
    n.plac
    number of events in cisapride group
    number of observations in cisapride group
    number of events in placebo group
    number of observations in placebo group
```

#### **Source**

Hartung J & Knapp G (2001): A refined method for the meta-analysis of controlled clinical trials with binary outcome. *Statistics in Medicine*, **20**, 3875–89

### See Also

```
metabin
```

### **Examples**

```
data(cisapride)
m.or <- metabin(event.cisa, n.cisa, event.plac, n.plac,</pre>
```

```
data = cisapride, sm = "OR",
  method = "Inverse", method.tau = "DL",
  studlab = study, method.incr = "all")
m.or.hakn <- update(m.or, hakn = TRUE)</pre>
m.rr <- update(m.or, sm = "RR")</pre>
m.rr.hakn <- update(m.or, sm = "RR", hakn = TRUE)</pre>
vars.common <- c("TE.common", "lower.common", "upper.common")</pre>
vars.random <- c("TE.random", "lower.random", "upper.random")</pre>
res.common.or <- as.data.frame(m.or[vars.common])</pre>
names(res.common.or) <- vars.random</pre>
res.common.rr <- as.data.frame(m.rr[vars.common])</pre>
names(res.common.rr) <- vars.random</pre>
# Results for log risk ratio - see Table VII in Hartung and Knapp (2001)
#
res.rr <- rbind(res.common.rr,</pre>
  as.data.frame(m.rr[vars.random]),
  as.data.frame(m.rr.hakn[vars.random]))
row.names(res.rr) <- c("CE", "RE", "RE (HaKn)")</pre>
names(res.rr) <- c("Log risk ratio", "CI lower", "CI upper")</pre>
res.rr
# Results for log odds ratio (Table VII in Hartung and Knapp 2001)
res.or <- rbind(res.common.or,</pre>
  as.data.frame(m.or[vars.random]),
  as.data.frame(m.or.hakn[vars.random]))
row.names(res.or) <- c("CE", "RE", "RE (HaKn)")</pre>
names(res.or) <- c("Log odds ratio", "CI lower", "CI upper")</pre>
res.or
```

drapery

Drapery plot

### **Description**

Draw a drapery plot with (scaled) p-value curves for individual studies and meta-analysis estimates.

### Usage

drapery(

```
х,
type = "zvalue",
layout = "grayscale",
study.results = TRUE,
lty.study = 1,
lwd.study = 1,
col.study = "darkgray",
labels,
col.labels = "black",
cex.labels = 0.7,
subset.labels,
srt.labels,
common = x scommon,
random = x$random,
lty.common = 1,
lwd.common = max(3, lwd.study),
col.common = "blue",
lty.random = 1,
lwd.random = lwd.common,
col.random = "red",
sign = NULL,
lty.sign = 1,
lwd.sign = 1,
col.sign = "black",
prediction = random,
col.predict = "lightblue",
alpha = if (type == "zvalue") c(0.001, 0.01, 0.05, 0.1) else c(0.01, 0.05, 0.1),
lty.alpha = 2,
lwd.alpha = 1,
col.alpha = "black",
cex.alpha = 0.7,
col.null.effect = "black",
legend = TRUE,
pos.legend = "topleft",
bg = "white",
bty = "o",
backtransf = x$backtransf,
xlab,
ylab,
xlim,
ylim,
1wd.max = 2.5,
lwd.study.weight = if (random) "random" else "common",
at = NULL,
n.grid = if (type == "zvalue") 10000 else 1000,
mar = c(5.1, 4.1, 4.1, 4.1),
plot = TRUE,
warn.deprecated = gs("warn.deprecated"),
```

```
fixed,
  lwd.fixed,
  lty.fixed,
  col.fixed,
  ...
)
```

## Arguments

alpha

1	guments	
	x	An object of class meta.
	type	A character string indicating whether to plot test statistics ("zvalue") or p-values ("pvalue"), can be abbreviated.
	layout	A character string for the line layout of individual studies: "grayscale", "equal" or "linewidth" (see Details), can be abbreviated.
	study.results	A logical indicating whether results for individual studies should be shown in the figure.
	lty.study	Line type for individual studies.
	lwd.study	Line width for individual studies.
	col.study	Colour of lines for individual studies.
	labels	A logical or character string indicating whether study labels should be shown at the top of the drapery plot; either FALSE, "id", or "studlab"; see Details.
	col.labels	Colour of study labels.
	cex.labels	The magnification for study labels.
	subset.labels	A vector specifying which study labels should be shown in the drapery plot.
	srt.labels	A numerical vector or single numeric (between 0 and 90) specifying the angle to rotate study labels; see Details.
	common	A logical indicating whether to show result for the common effect model.
	random	A logical indicating whether to show result for the random effects model.
	lty.common	Line type for common effect meta-analysis.
	lwd.common	Line width for common effect meta-analysis.
	col.common	Colour of lines for common effect meta-analysis.
	lty.random	Line type for random effects meta-analysis.
	lwd.random	Line width for random effects meta-analysis.
	col.random	Colour of lines for random effects meta-analysis.
	sign	Significance level used to highlight significant values in curves.
	lty.sign	Line type for significant values.
	lwd.sign	Line width for significant values.
	col.sign	Line colour for significant values.
	prediction	A logical indicating whether to show prediction region.
	col.predict	Colour of prediction region

Horizonal lines are printed for the specified alpha values.

Line type of horizonal lines for alpha values. lty.alpha lwd.alpha Line width of horizonal lines for alpha values. col.alpha Colour of horizonal lines for alpha values. cex.alpha The magnification for the text of the alpha col.null.effect Colour of vertical line indicating null effect. legend A logical indicating whether a legend should be printed. A character string with position of legend (see legend). pos.legend Background colour of legend (see legend). Type of the box around the legend; either "o" or "n" (see legend). bty backtransf A logical indicating whether results should be back transformed on the x-axis. For example, if backtransf = FALSE, log odds ratios instead of odds ratios are shown on the x-axis. xlab A label for the x-axis. A label for the y-axis. ylab The x limits (min, max) of the plot. xlim ylim The y limits (min, max) of the plot (ignored if type = "pvalue"). lwd.max The maximum line width (only considered if argument layout is equal to "linewidth"). lwd.study.weight A character string indicating whether to determine line width for individual studies using weights from common effect ("common") or random effects model ("random"), can be abbreviated (only considered if argument layout is equal to "linewidth"). Points at which tick-marks are to be drawn on the x-axis. at n.grid The number of grid points to calculate the p-value or test statistic functions. Physical plot margin, see par. mar plot A logical indicating whether to generate a figure. warn.deprecated A logical indicating whether warnings should be printed if deprecated arguments are used. fixed Deprecated argument (replaced by 'common'). lwd.fixed Deprecated argument (replaced by 'lwd.common'). lty.fixed Deprecated argument (replaced by 'lty.common').

Deprecated argument (replaced by 'col.common').

Graphical arguments as in par may also be passed as arguments.

col.fixed

#### **Details**

The concept of a p-value function, also called confidence curve, goes back to Birnbaum (1961). A drapery plot, showing p-value functions (or a scaled version based on the corresponding test statistics) for individual studies as well as meta-analysis estimates, is drawn in the active graphics window. Furthermore, a prediction region for a single future study is shown as a shaded area. In contrast to a forest plot, a drapery plot does not provide information for a single confidence level however for any confidence level.

Argument type can be used to either show p-value functions (Birnbaum, 1961) or a scaled version (Infanger, 2019) with test statistics (default).

Argument layout determines how curves for individual studies are presented:

- darker gray tones with increasing precision (layout = "grayscale")
- thicker lines with increasing precision (layout = "linewidth")
- equal lines (layout = "equal")

Argument labels determines how curves of individual studies are labelled:

- number of the study in the (unsorted) forest plot / printout of a meta-analysis (labels = "id")
- study labels provided by argument studlab in meta-analysis functions (labels = "studlab")
- no study labels (labels = FALSE)

By default, study labels are used (labels = "studlab") if no label has more than three characters; otherwise IDs are used (labels = "id"). The connection between IDs and study labels (among other information) is part of a data frame which is invisibly returned (if argument study.results = TRUE).

Argument srt.labels can be used to change the rotation of IDs or study labels. By default, study labels are rotated by +/- 45 degrees if at least one study label has more than three characters; otherwise labels are not rotated.

If labels = "studlab", labels are rotated by -45 degrees for studies with a treatment estimate below the common effect estimate and otherwise by 45 degrees.

#### Author(s)

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### References

Birnbaum A (1961): Confidence Curves: An Omnibus Technique for Estimation and Testing Statistical Hypotheses. *Journal of the American Statistical Association*, **56**, 246–9

Infanger D and Schmidt-Trucksäss A (2019): P value functions: An underused method to present research results and to promote quantitative reasoning *Statistics in Medicine*, **38**, 4189–97

#### See Also

forest, radial

Fleiss1993bin 21

### **Examples**

```
data("lungcancer")
m1 <- metainc(d.smokers, py.smokers, d.nonsmokers, py.nonsmokers,</pre>
  data = lungcancer, studlab = study)
# Drapery plot
drapery(m1, xlim = c(0.5, 50))
## Not run:
data(Fleiss1993bin)
m2 <- metabin(d.asp, n.asp, d.plac, n.plac,</pre>
 data = Fleiss1993bin, studlab = paste(study, year),
  sm = "OR", random = FALSE)
# Produce drapery plot and print data frame with connection between
# IDs and study labels
(drapery(m2))
\# For studies with a significant effect (p < 0.05), show
# study labels and print labels and lines in red
drapery(m2,
  labels = "studlab", subset.labels = pval < 0.05,</pre>
  srt.labels = 0, col.labels = "red",
  col.study = ifelse(pval < 0.05, "red", "darkgray"))</pre>
## End(Not run)
```

Fleiss1993bin

Aspirin after Myocardial Infarction

### Description

Meta-analysis on aspirin in preventing death after myocardial infarction.

Data example in Fleiss (1993) for meta-analysis with binary outcomes.

### **Format**

A data frame with the following columns:

```
study
year
d.asp
n.asp
d.plac
number of deaths in aspirin group
number of observations in aspirin group
d.plac
number of deaths in placebo group
number of observations in placebo group
```

Fleiss1993cont

### Source

Fleiss JL (1993): The statistical basis of meta-analysis. *Statistical Methods in Medical Research*, **2**, 121–45

### **Examples**

```
data(Fleiss1993bin)
metabin(d.asp, n.asp, d.plac, n.plac, data = Fleiss1993bin,
    studlab = paste(study, year), sm = "OR", random = FALSE)
```

Fleiss1993cont

Mental Health Treatment

### **Description**

Meta-analysis on the Effect of Mental Health Treatment on Medical Utilisation.

Data example in Fleiss (1993) for meta-analysis with continuous outcomes.

#### **Format**

A data frame with the following columns:

```
    study
    year
    n.psyc
    mean.psyc
    stimated mean in psychotherapy group
    sd.psyc
    number of observations in psychotherapy group
    standard deviation in psychotherapy group
    number of observations in control group
    mean.cont
    sd.cont
    standard deviation in control group
    standard deviation in control group
```

#### Source

Fleiss JL (1993): The statistical basis of meta-analysis. *Statistical Methods in Medical Research*, **2**, 121–45

### See Also

Fleiss1993bin

### **Examples**

```
data(Fleiss1993cont)
metacont(n.psyc, mean.psyc, sd.psyc, n.cont, mean.cont, sd.cont,
  data = Fleiss1993cont, studlab = paste(study, year),
  random = FALSE)
```

forest.meta

Forest plot to display the result of a meta-analysis

### **Description**

Draws a forest plot in the active graphics window (using grid graphics system).

### Usage

```
## S3 method for class 'meta'
forest(
 х,
  sortvar,
  studlab = TRUE,
  layout = gs("layout"),
  common = x scommon,
  random = x$random,
 overall = x$overall,
  text.common = x$text.common,
  text.random = x$text.random,
  lty.common = 2,
  lty.random = 3,
  col.common = "black",
  col.random = "black",
  text.w.common = x$text.w.common,
  text.w.random = x$text.w.random,
  prediction = x$prediction,
  text.predict = x$text.predict,
  subgroup = TRUE,
  subgroup.hetstat = subgroup & (is.character(hetstat) || hetstat),
  print.subgroup.labels = TRUE,
  subgroup.name = x$subgroup.name,
  print.subgroup.name = x$print.subgroup.name,
  sep.subgroup = x$sep.subgroup,
  text.common.w = text.common,
  text.random.w = text.random,
  text.predict.w = text.predict,
  bysort = FALSE,
  pooled.totals = common | random,
  pooled.events = FALSE,
  pooled.times = FALSE,
  study.results = TRUE,
  xlab = "",
  xlab.pos,
  smlab = NULL,
  smlab.pos,
  xlim = "symmetric",
```

```
allstudies = TRUE,
weight.study = NULL,
weight.subgroup,
pscale = x$pscale,
irscale = x$irscale,
irunit = x$irunit,
ref = ifelse(backtransf & is.relative.effect(x$sm), 1, 0),
lower.equi = NA,
upper.equi = NA,
lty.equi = 1,
col.equi = "blue",
fill.equi = "transparent",
leftcols = NULL,
rightcols = NULL,
leftlabs = NULL,
rightlabs = NULL,
label.e = x$label.e,
label.c = x$label.c,
label.e.attach = NULL,
label.c.attach = NULL,
label.right = x$label.right,
label.left = x$label.left,
bottom.lr = TRUE,
lab.NA = ".",
lab.NA.effect,
lab.NA.weight = "--",
lwd = 1,
at = NULL
label = TRUE,
type.study = "square",
type.common = "diamond",
type.random = type.common,
type.subgroup = ifelse(study.results, "diamond", "square"),
type.subgroup.common = type.subgroup,
type.subgroup.random = type.subgroup,
col.study = "black",
col.square = "gray",
col.square.lines = col.square,
col.inside = "white",
col.inside.common = col.inside,
col.inside.random = col.inside,
col.diamond = "gray",
col.diamond.common = col.diamond,
col.diamond.random = col.diamond,
col.diamond.lines = "black",
col.diamond.lines.common = col.diamond.lines,
col.diamond.lines.random = col.diamond.lines,
col.predict = "red",
```

```
col.predict.lines = "black",
col.by = "darkgray",
col.label.right = "black",
col.label.left = "black",
hetstat = common | random | overall.hetstat,
overall.hetstat = x$overall.hetstat,
hetlab = "Heterogeneity: ",
resid.hetstat,
resid.hetlab = "Residual heterogeneity: ",
print.I2,
print.I2.ci = FALSE,
print.tau2,
print.tau2.ci = FALSE,
print.tau = FALSE,
print.tau.ci = FALSE,
print.Q = FALSE,
print.pval.Q,
print.Rb = FALSE,
print.Rb.ci = FALSE,
text.subgroup.nohet = "not applicable",
LRT = FALSE,
test.overall = gs("test.overall"),
test.overall.common = common & overall & test.overall,
test.overall.random = random & overall & test.overall,
label.test.overall.common,
label.test.overall.random,
print.stat = TRUE,
test.subgroup = x$test.subgroup,
test.subgroup.common = test.subgroup & common,
test.subgroup.random = test.subgroup & random,
prediction.subgroup = x$prediction.subgroup,
print.Q.subgroup = TRUE,
label.test.subgroup.common,
label.test.subgroup.random,
test.effect.subgroup = gs("test.effect.subgroup"),
test.effect.subgroup.common,
test.effect.subgroup.random,
label.test.effect.subgroup.common,
label.test.effect.subgroup.random,
text.addline1,
text.addline2,
fontsize = 12,
fontfamily = NULL,
fs.heading = fontsize,
fs.common,
fs.random,
fs.predict,
fs.common.labels,
```

```
fs.random.labels,
fs.predict.labels,
fs.study = fontsize,
fs.study.labels = fs.study,
fs.hetstat,
fs.test.overall,
fs.test.subgroup,
fs.test.effect.subgroup,
fs.addline.
fs.axis = fontsize,
fs.smlab = fontsize,
fs.xlab = fontsize,
fs.lr = fontsize,
ff.heading = "bold",
ff.common,
ff.random,
ff.predict,
ff.common.labels,
ff.random.labels,
ff.predict.labels,
ff.study = "plain",
ff.study.labels = ff.study,
ff.hetstat,
ff.test.overall,
ff.test.subgroup,
ff.test.effect.subgroup,
ff.addline,
ff.axis = "plain",
ff.smlab = "bold",
ff.xlab = "plain",
ff.lr = "plain",
squaresize = 0.8/spacing,
plotwidth = if (layout == "JAMA") "8cm" else "6cm",
colgap = "2mm",
colgap.left = colgap,
colgap.right = colgap,
colgap.studlab = colgap.left,
colgap.forest = colgap,
colgap.forest.left = colgap.forest,
colgap.forest.right = colgap.forest,
calcwidth.pooled = (common | random) & (overall | !is.null(x$subgroup)),
calcwidth.common = calcwidth.pooled,
calcwidth.random = calcwidth.pooled,
calcwidth.predict = FALSE,
calcwidth.hetstat = FALSE,
calcwidth.tests = FALSE,
calcwidth.subgroup = FALSE,
calcwidth.addline = FALSE,
```

```
just = if (layout == "JAMA") "left" else "right",
  just.studlab = "left",
  just.addcols = "center",
  just.addcols.left = just.addcols,
  just.addcols.right = just.addcols,
  spacing = 1,
  addrow,
  addrow.overall,
  addrow.subgroups,
  addrows.below.overall = 0,
  new = TRUE,
  backtransf = x$backtransf,
  digits = gs("digits.forest"),
  digits.se = gs("digits.se"),
  digits.stat = gs("digits.stat"),
  digits.pval = max(gs("digits.pval") - 2, 2),
  digits.pval.Q = max(gs("digits.pval.Q") - 2, 2),
  digits.Q = gs("digits.Q"),
  digits.tau2 = gs("digits.tau2"),
  digits.tau = gs("digits.tau"),
  digits.I2 = max(gs("digits.I2") - 1, 0),
  digits.weight = gs("digits.weight"),
  digits.mean = digits,
  digits.sd = digits.se,
  digits.cor = digits,
  digits.time = digits,
  digits.addcols = digits,
  digits.addcols.right = digits.addcols,
  digits.addcols.left = digits.addcols,
  scientific.pval = gs("scientific.pval"),
  big.mark = gs("big.mark"),
  zero.pval = if (layout == "JAMA") FALSE else gs("zero.pval"),
  JAMA.pval = if (layout == "JAMA") TRUE else gs("JAMA.pval"),
 warn.deprecated = gs("warn.deprecated"),
)
```

#### Arguments

common

X	An object of class meta.
sortvar	An optional vector used to sort the individual studies (must be of same length as $x$ \$TE).
studlab	A logical indicating whether study labels should be printed in the graph. A vector with study labels can also be provided (must be of same length as x\$TE then).
layout	A character string specifying the layout of the forest plot (see Details).

A logical indicating whether common effect estimate should be plotted.

random A logical indicating whether random effects estimate should be plotted.

Overall A logical indicating whether overall summaries should be plotted. This argument is useful in a meta-analysis with subgroups if summaries should only be

plotted on group level.

text.common A character string used in the plot to label the pooled common effect estimate.

text.random A character string used in the plot to label the pooled random effects estimate.

lty.commonLine type (pooled common effect estimate).lty.randomLine type (pooled random effects estimate).col.commonLine colour (pooled common effect estimate).col.randomLine colour (pooled random effects estimate).

text.w.common A character string used to label weights of common effect model.

text.w.random A character string used to label weights of random effects model.

prediction A logical indicating whether a prediction interval should be printed.

text.predict A character string used in the plot to label the prediction interval.

subgroup A single logical or logical vector indicating whether / which subgroup results should be shown in forest plot. This argument is useful in a meta-analysis with

subgroups if summaries should not be plotted for (some) subgroups.

subgroup.hetstat

A single logical or logical vector indicating whether / which information on heterogeneity in subgroups should be shown in forest plot. This argument is useful in a meta-analysis with subgroups if heterogeneity statistics should not be printed for (some) subgroups.

print.subgroup.labels

A logical indicating whether subgroup label should be printed.

subgroup.name A character string with a label for the grouping variable.

print.subgroup.name

A logical indicating whether the name of the grouping variable should be printed in front of the group labels.

sep.subgroup A character string defining the separator between label and levels of grouping variable.

text.common.w A character string to label the pooled common effect estimate within subgroups, or a character vector of same length as number of subgroups with corresponging labels.

text.random.w A character string to label the pooled random effect estimate within subgroups, or a character vector of same length as number of subgroups with corresponging labels.

text.predict.w A character string to label the prediction interval within subgroups, or a character vector of same length as number of subgroups with corresponging labels.

bysort A logical indicating whether groups should be ordered alphabetically.

pooled.totals A logical indicating whether total number of observations should be given in the figure.

pooled. events A logical indicating whether total number of events should be given in the figure.

pooled.times A logical indicating whether total person time at risk should be given in the

figure.

study.results A logical indicating whether results for individual studies should be shown in

the figure (useful to only plot subgroup results).

xlab A label for the x-axis.

xlab.pos A numeric specifying the center of the label on the x-axis. smlab A label for the summary measure (printed at top of figure).

smlab.pos A numeric specifying the center of the label for the summary measure.

xlim The x limits (min,max) of the plot, or the character "s" to produce symmetric

forest plots.

allstudies A logical indicating whether studies with inestimable treatment effects should

be included in the forest plot.

weight.study A character string indicating weighting used to determine size of squares or

diamonds (argument type.study) to plot individual study results. One of missing, "same", "common", or "random", can be abbreviated. Plot symbols have the same size for all studies or represent study weights from common effect or

random effects model.

weight.subgroup

A character string indicating weighting used to determine size of squares or diamonds (argument type.subgroup) to plot subgroup results. One of missing, "same", or "weight", can be abbreviated. Plot symbols have the same size for all subgroup results or represent subgroup weights from common effect or

random effects model.

pscale A numeric giving scaling factor for printing of single event probabilities or risk

differences, i.e. if argument sm is equal to "PLOGIT", "PLN", "PRAW", "PAS",

"PFT", or "RD".

irscale A numeric defining a scaling factor for printing of single incidence rates or in-

cidence rate differences, i.e. if argument sm is equal to "IR", "IRLN", "IRS",

"IRFT", or "IRD".

irunit A character specifying the time unit used to calculate rates, e.g., person-years.

ref A numerical giving the reference value to be plotted as a line in the forest plot.

No reference line is plotted if argument ref is equal to NA.

lower equi A numerical giving the lower limit of equivalence to be plotted as a line in the

forest plot. No line is plotted if argument lower.equi is equal to NA.

upper . equi A numerical giving the upper limit of equivalence to be plotted as a line in the

forest plot. No line is plotted if argument upper . equi is equal to NA.

lty.equi Line type (limits of equivalence).

col.equi Line colour (limits of equivalence).

fill. equi Colour of area between limits of equivalence.

leftcols A character vector specifying (additional) columns to be printed on the left side

of the forest plot or a logical value (see Details).

rightcols A character vector specifying (additional) columns to be printed on the right

side of the forest plot or a logical value (see Details).

leftlabs	A character vector specifying labels for (additional) columns on left side of the forest plot (see Details).
rightlabs	A character vector specifying labels for (additional) columns on right side of the forest plot (see Details).
label.e	Label to be used for experimental group in table heading.
label.c	Label to be used for control group in table heading.
label.e.attach	A character specifying the column name where label label.e should be attached to in table heading.
label.c.attach	A character specifying the column name where label label.c should be attached to in table heading.
label.right	Graph label on right side of forest plot.
label.left	Graph label on left side of forest plot.
bottom.lr	A logical indicating whether labels on right and left side should be printed at bottom or top of forest plot.
lab.NA	A character string to label missing values.
lab.NA.effect	A character string to label missing values in individual treatment estimates and confidence intervals.
lab.NA.weight	A character string to label missing weights.
lwd	The line width, see par.
at	The points at which tick-marks are to be drawn, see grid.xaxis.
label	A logical value indicating whether to draw the labels on the tick marks, or an expression or character vector which specify the labels to use. See grid.xaxis.
type.study	A character string or vector specifying how to plot treatment effects and confidence intervals for individual studies (see Details).
type.common	A character string specifying how to plot treatment effect and confidence interval for common effect meta-analysis (see Details).
type.random	A character string specifying how to plot treatment effect and confidence interval for random effects meta-analysis (see Details).
type.subgroup	A character string specifying how to plot treatment effect and confidence interval for subgroup results (see Details).
type.subgroup.d	
	A character string specifying how to plot treatment effect and confidence interval for subgroup results (common effect model).
type.subgroup.r	
	A character string specifying how to plot treatment effect and confidence interval for subgroup results (random effects model).
col.study	The colour for individual study results and confidence limits.
col.square	The colour for squares reflecting study's weight in the meta-analysis.
col.square.line	
	The colour for the outer lines of squares reflecting study's weight in the meta-

analysis.

col.inside The colour for individual study results and confidence limits if confidence limits are completely within squares.

col.inside.common

The colour for result of common effect meta-analysis if confidence limit lies completely within square.

col.inside.random

The colour for result of random effects meta-analysis if confidence limit lies completely within square.

col.diamond The colour of diamonds representing the results for common effect and random effects models.

col.diamond.common

The colour of diamonds for common effect estimates.

col.diamond.random

The colour of diamonds for random effects estimates.

col.diamond.lines

The colour of the outer lines of diamonds representing the results for common effect and random effects models.

col.diamond.lines.common

The colour of the outer lines of diamond for common effect estimate.

col.diamond.lines.random

The colour of the outer lines of diamond for random effects estimate.

col.predict Background colour of prediction interval.

col.predict.lines

Colour of outer lines of prediction interval.

col.by The colour to print information on subgroups.

col.label.right

The colour for label on right side of null effect.

col.label.left The colour for label on left side of null effect.

hetstat Either a logical value indicating whether to print results for heterogeneity measures at all or a character string (see Details).

overall.hetstat

A logical value indicating whether to print heterogeneity measures for overall treatment comparisons. This argument is useful in a meta-analysis with subgroups if heterogeneity statistics should only be printed on subgroup level.

hetlab Label printed in front of results for heterogeneity measures.

resid.hetstat A logical value indicating whether to print measures of residual heterogeneity in a meta-analysis with subgroups.

resid.hetlab Label printed in front of results for residual heterogeneity measures.

print.12 A logical value indicating whether to print the value of the I-squared statistic.

print.I2.ci A logical value indicating whether to print the confidence interval of the I-squared statistic.

print.tau2 A logical value indicating whether to print the value of the between-study variance  $\tau^2$ .

print.tau2.ci A logical value indicating whether to print the confidence interval of  $\tau^2$ .

print.tau A logical value indicating whether to print  $\tau$ , the square root of the between-study variance  $\tau^2$ .

print.tau.ci A logical value indicating whether to print the confidence interval of  $\tau$ .

print . Q A logical value indicating whether to print the value of the heterogeneity statistic Q.

print.pval.Q A logical value indicating whether to print the p-value of the heterogeneity statistic Q.

print.Rb A logical value indicating whether to print the value of the I-squared statistic.

print.Rb.ci A logical value indicating whether to print the confidence interval of the I-squared statistic.

text.subgroup.nohet

A logical value or character string which is printed to indicate subgroups with less than two studies contributing to meta-analysis (and thus without heterogeneity). If FALSE, heterogeneity statistics are printed (with NAs).

LRT A logical value indicating whether to report Likelihood-Ratio or Wald-type test of heterogeneity for generalized linear mixed models.

test.overall A logical value indicating whether to print results of test for overall effect.

test.overall.common

A logical value indicating whether to print results of test for overall effect (common effect model).

test.overall.random

A logical value indicating whether to print results of test for overall effect (random effects model).

label.test.overall.common

Label printed in front of results of test for overall effect (common effect model).

label.test.overall.random

Label printed in front of results of test for overall effect (random effects model).

print.stat A logical value indicating whether z- or t-value for test of treatment effect should be printed.

test.subgroup A logical value indicating whether to print results of test for subgroup differences.

test.subgroup.common

A logical value indicating whether to print results of test for subgroup differences (common effect model).

test.subgroup.random

A logical value indicating whether to print results of test for subgroup differences (random effects model).

prediction.subgroup

A single logical or logical vector indicating whether / which prediction intervals should be printed for subgroups.

print.Q.subgroup

A logical value indicating whether to print the value of the heterogeneity statistic Q (test for subgroup differences).

label.test.subgroup.common

Label printed in front of results of test for subgroup differences (common effect model).

label.test.subgroup.random

Label printed in front of results of test for subgroup differences (random effects model).

test.effect.subgroup

A single logical or logical vector indicating whether / which tests for effect in subgroups should be printed.

test.effect.subgroup.common

A single logical or logical vector indicating whether / which tests for effect in subgroups should be printed (common effect model).

test.effect.subgroup.random

A single logical or logical vector indicating whether / which tests for effect in subgroups should be printed (random effects model).

label.test.effect.subgroup.common

Label printed in front of results of test for effect in subgroups (common effect model).

label.test.effect.subgroup.random

Label printed in front of results of test for effect in subgroups (random effects model).

text.addline1 Text for first additional line (below meta-analysis results).

text.addline2 Text for second additional line (below meta-analysis results).

fontsize The size of text (in points), see gpar.

fontfamily The font family, see gpar.

fs. heading The size of text for column headings, see gpar.

fs. common The size of text for results of common effect model, see gpar.

fs.random The size of text for results of random effects model, see gpar.

fs.predict The size of text for results of prediction interval, see gpar.

fs.common.labels

The size of text for label of common effect model, see gpar.

fs.random.labels

The size of text for label of random effects model, see gpar.

fs.predict.labels

The size of text for label of prediction interval, see gpar.

fs. study The size of text for results of individual studies, see gpar.

fs.study.labels

The size of text for labels of individual studies, see gpar.

fs.hetstat The size of text for heterogeneity measures, see gpar.

fs.test.overall

The size of text of test for overall effect, see gpar.

fs.test.subgroup

The size of text of test of subgroup differences, see gpar.

fs.test.effect.subgroup The size of text of test of effect in subgroups, see gpar. fs.addline The size of text for additional lines, see gpar. fs.axis The size of text on x-axis, see gpar. fs.smlab The size of text of label for summary measure, see gpar. fs.xlab The size of text of label on x-axis, see gpar. fs.lr The size of text of label on left and right side of forest plot, see gpar. ff.heading The fontface for column headings, see gpar. ff.common The fontface of text for results of common effect model, see gpar. ff.random The fontface of text for results of random effects model, see gpar. ff.predict The fontface of text for results of prediction interval, see gpar. ff.common.labels The fontface of text for label of common effect model, see gpar. ff.random.labels The fontface of text for label of random effects model, see gpar. ff.predict.labels The fontface of text for label of prediction interval, see gpar. ff.study The fontface of text for results of individual studies, see gpar. ff.study.labels The fontface of text for labels of individual studies, see gpar. ff.hetstat The fontface of text for heterogeneity measures, see gpar. ff.test.overall The fontface of text of test for overall effect, see gpar. ff.test.subgroup The fontface of text for test of subgroup differences, see gpar. ff.test.effect.subgroup The fontface of text for test of effect in subgroups, see gpar. ff.addline The fontface of text for additional lines, see gpar. ff.axis The fontface of text on x-axis, see gpar. ff.smlab The fontface of text of label for summary measure, see gpar. ff.xlab The fontface of text of label on x-axis, see gpar. ff.lr The fontface of text of label on left and right side of forest plot, see gpar. A numeric used to increase or decrease the size of squares in the forest plot. squaresize Either a character string, e.g., "8cm", "60mm", or "3inch", or a unit object plotwidth specifying width of the forest plot. Either a character string or a unit object specifying gap between columns printed colgap on left and right side of forest plot. Either a character string or a unit object specifying gap between columns printed colgap.left on left side of forest plot. colgap.right Either a character string or a unit object specifying gap between columns printed on right side of forest plot.

colgap.studlab Either a character string or a unit object specifying gap between column with study labels and subsequent column.

colgap. forest Either a character string or a unit object specifying gap between column adjacent to forest plot and the forest plot.

#### colgap.forest.left

Either a character string or a unit object specifying gap between column on the left side of forest plot and the forest plot.

### colgap.forest.right

Either a character string or a unit object specifying gap between column on the right side of forest plot and the forest plot.

### calcwidth.pooled

A logical indicating whether text for common effect and random effects model should be considered to calculate width of the column with study labels.

#### calcwidth.common

A logical indicating whether text given in arguments text.common and text.common.w should be considered to calculate width of the column with study labels.

### calcwidth.random

A logical indicating whether text given in arguments text.random and text.random.w should be considered to calculate width of the column with study labels.

### calcwidth.predict

A logical indicating whether text given in argument text.predict and text.predict.w should be considered to calculate width of the column with study labels.

#### calcwidth.hetstat

A logical indicating whether text for heterogeneity statistics should be considered to calculate width of the column with study labels.

#### calcwidth.tests

A logical indicating whether text for tests of overall effect or subgroup differences should be considered to calculate width of the column with study labels.

#### calcwidth.subgroup

A logical indicating whether text with subgroup labels should be considered to calculate width of the column with study labels.

#### calcwidth.addline

A logical indicating whether text for additional lines should be considered to calculate width of the column with study labels.

just Justification of text in all columns but columns with study labels and additional variables (possible values: "left", "right", "center").

just.studlab Justification of text for study labels (possible values: "left", "right", "center").

just.addcols Justification of text for additional columns (possible values: "left", "right", "center").

### just.addcols.left

Justification of text for additional columns on left side of forest plot (possible values: "left", "right", "center"). Can be of same length as number of additional columns on left side of forest plot.

just.addcols.right

Justification of text for additional columns on right side of forest plot (possible values: "left", "right", "center"). Can be of same length as number of additional columns on right side of forest plot.

spacing A numeric determining line spacing in a forest plot.

addrow A logical value indicating whether an empty row is printed above and below

study results.

addrow.overall A logical value indicating whether an empty row is printed above overall meta-

analysis results.

addrow.subgroups

A logical value indicating whether an empty row is printed between results for subgroups.

addrows.below.overall

A numeric value indicating how many empty rows are printed between meta-

analysis results and heterogeneity statistics and test results.

new A logical value indicating whether a new figure should be printed in an existing

graphics window.

backtransf A logical indicating whether results should be back transformed in forest plots.

If backtransf = TRUE, results for sm = "OR" are presented as odds ratios rather than log odds ratios and results for sm = "ZCOR" are presented as correlations

rather than Fisher's z transformed correlations, for example.

digits Minimal number of significant digits for treatment effects, see print.default.

digits.se Minimal number of significant digits for standard errors, see print.default.

digits.stat Minimal number of significant digits for z- or t-statistic for test of overall effect,

see print.default.

digits.pval Minimal number of significant digits for p-value of overall treatment effect, see

print.default.

digits.pval.Q Minimal number of significant digits for p-value of heterogeneity test, see print.default.

digits.Q Minimal number of significant digits for heterogeneity statistic Q, see print.default.

digits.tau2 Minimal number of significant digits for between-study variance, see print.default.

digits.tau Minimal number of significant digits for square root of between-study variance,

see print.default.

digits. I2 Minimal number of significant digits for I-squared statistic, see print. default.

digits.weight Minimal number of significant digits for weights, see print.default.

digits.mean Minimal number of significant digits for means; only applies to metacont ob-

jects.

digits.sd Minimal number of significant digits for standard deviations; only applies to

metacont objects.

digits.cor Minimal number of significant digits for correlations; only applies to metacor

objects.

digits.time Minimal number of significant digits for times; only applies to metainc and

metarate objects.

digits.addcols A vector or scalar with minimal number of significant digits for additional columns. digits.addcols.right

A vector or scalar with minimal number of significant digits for additional columns on right side of forest plot.

digits.addcols.left

A vector or scalar with minimal number of significant digits for additional columns on left side of forest plot.

scientific.pval

A logical specifying whether p-values should be printed in scientific notation, e.g., 1.2345e-01 instead of 0.12345.

big.mark A character used as thousands separator.

zero.pval A logical specifying whether p-values should be printed with a leading zero.

JAMA.pval A logical specifying whether p-values for test of overall effect should be printed

according to JAMA reporting standards.

warn.deprecated

A logical indicating whether warnings should be printed if deprecated arguments are used.

. . . Additional graphical arguments.

### **Details**

A forest plot, also called confidence interval plot, is drawn in the active graphics window. The forest functions in R package **meta** are based on the grid graphics system. In order to print the forest plot, resize the graphics window and either use dev.copy2eps or dev.copy2pdf. Another possibility is to create a file using pdf, png, or svg and to specify the width and height of the graphic (see Examples).

### Default layout for studies and pooled effects:

By default, treatment estimates and confidence intervals are plotted in the following way:

- For an individual study, a square with treatment estimate in the center and confidence interval as line extending either side of the square (type.study = "square")
- For meta-analysis results, a diamond with treatment estimate in the center and right and left side corresponding to lower and upper confidence limits (type.common = "diamond", type.random = "diamond", and type.subgroup = "diamond")

In a forest plot, size of the squares typically reflects the precision of individual treatment estimates based either on the common effect (weight.study = "common") or random effects meta-analysis (weight.study = "random"). Information from meta-analysis object x is utilised if argument weight.study is missing. Weights from the common effect model are used if argument x\$common is TRUE; weights from the random effects model are used if argument x\$random is TRUE and x\$common is FALSE. The same square sizes are used if weight.study = "same".

A prediction interval for treatment effect of a new study (Higgins et al., 2009) is given in the forest plot if arguments prediction and random are TRUE. For graphical presentation of prediction intervals the approach by Guddat et al. (2012) is used.

### Columns printed on left side of forest plot:

Argument leftcols can be used to specify columns which are printed on the left side of the forest plot. By default, i.e. if argument leftcols is NULL and layout = "meta", and depending on the class of the meta-analysis object (which is defined by the R function used to generate the object) a different set of *columns* is printed *on the left side of the forest plot*:

```
Function
           Value of argument leftcols
           c("studlab", "event.e", "n.e", "event.c", "n.c")
metabin
           c("studlab", "n.e", "mean.e", "sd.e", "n.c", "mean.c", "sd.c")
metacont
           c("studlab", "n")
metacor
           c("studlab", "TE", "seTE")
metagen
           c("studlab", "event.e", "time.e", "event.c", "time.c")
metainc
metamean c("studlab", "n", "mean", "sd")
           c("studlab", "event", "n")
metaprop
           c("studlab", "event", "time", "n")
metarate
           "studlab"
metacum
           "studlab"
metainf
```

For three-level models, the cluster variable is printed next to the study labels (value "cluster" in argument leftcols).

By default, study labels and labels for pooled estimates and heterogeneity statistics will be printed in the first column on the left side of the forest plot. The character string "studlab" is used to identify study labels as this is the name of the list element of a meta-analysis object.

If the character string "studlab" is not provided in leftcols and rightcols, the first *additional* variable specified by the user is used as study labels (and labels for pooled estimates are printed in this column). Additional variables are any variables not mentioned in the section on predefined column names below. For example, leftcols = "studlab" and leftcols = "study" would result in the same forest plot if the variable "study" was used in the command to conduct the meta-analysis. If no additional variable is provided by the user, no study labels will be printed.

### Overlapping information on left side of forest plot:

Depending on the number of columns printed on the left side of the forest plot, information on heterogeneity measures or statistical tests (see below) can be overlapping with the x-axis. Argument addrows.below.overall can be used to specify the number of empty rows that are printed between meta-analysis results and information on heterogeneity measures and statistical tests. By default, no additional rows are added to the forest plot. If addrows.below.overall = NULL, the function tries to add a sufficient number of empty rows to prevent overlapping text. Another possibility is to manually increase the space between the columns on the left side (argument colgap.left) or between the columns on the left side and the forest plot (argument colgap.forest.left).

### Columns printed on right side of forest plot:

Argument rightcols can be used to specify columns which are printed on the right side of the forest plot. If argument rightcols is FALSE, no columns will be printed on the right side. By default, i.e. if argument rightcols is NULL and layout = "meta", the following *columns* will be printed *on the right side of the forest plot*:

Meta-analysis results
No summary

Value of argument rightcols
c("effect", "ci")

```
Only common effect model c("effect", "ci", "w.common")
Only random effects model c("effect", "ci", "w.random")
Both models c("effect", "ci", "w.common", "w.random")
```

By default, estimated treatment effect and corresponding confidence interval will be printed. Depending on arguments common and random, weights of the common effect and/or random effects model will be given too.

For an object of class metacum or metainf the following columns will be printed: c("effect", "ci", "pval", "tau", "tau", "12"). This information corresponds to the printout with print.meta.

### Predefined column names:

The arguments leftlabs and rightlabs can be used to specify column headings which are printed on left or right side of the forest plot. For certain columns predefined labels exist which are used by default, i.e., if arguments leftlabs and rightlabs are NULL:

Column:	studlab	TE	seTE	cluster	n.e	n.c
Label:	"Study"	"TE"	"seTE"	"Cluster"	"Total"	"Total"
Column:	n	event.e	event.c	event	mean.e	mean.c
Label:	"Total"	"Events"	"Events"	"Events"	"Mean"	"Mean"
Column:	sd.e	sd.c	time.e	time.c	effect	
Label:	"SD"	"SD"	"Time"	"Time"	x\$sm	
Column:	ci	effect.ci	w.common	w.random		
Label:	x\$level"%-CI"	effect+ci	"W(common)"	"W(random)"		

For other columns, the column name will be used as a label if no column label is defined. It is possible to only provide labels for new columns (see Examples). Otherwise the length of leftlabs and rightlabs must be the same as the number of printed columns. The value NA can be used to specify columns which should use default labels (see Examples).

In pairwise meta-analysis comparing two groups (i.e., metabin, metacont, metainc, and metagen depending on the outcome), arguments label.e and label.c are used to label columns belonging to the two treatment groups. By default, labels defined in the meta-analysis object are used. The columns where treatment labels are attached can be changed using arguments label.e.attach and label.c.attach.

## Information on heterogeneity and statistical tests:

Argument hetstat can be a character string to specify where to print heterogeneity information:

- row with results for common effect model (hetstat = "common"),
- row with results for random effects model (hetstat = "random").

Otherwise, information on heterogeneity measures is printed below the meta-analysis results if argument overall.hetstat = TRUE (default). The heterogeneity measures to print can be specified (see list of arguments following overall.hetstat).

In addition, the following arguments can be used to print results for various statistical tests:

Argument

Statistical test

test.overall.common
test.overall.random
test.effect.subgroup.common
test.effect.subgroup.random
test.subgroup.common
test.subgroup.common
test.subgroup.common
test.subgroup.common
Test for overall effect (common effect model)
Test for effect in subgroup (CE model)
Test for effect in subgroup (RE model)
Test for subgroup differences (CE model)
Test for subgroup differences (RE model)

By default, these arguments are FALSE with exception of tests for subgroup differences which are TRUE. R function settings.meta can be used to change this default for the entire R session. For example, use the following command to always print results of tests for an overall effect: settings.meta(test.overall = TRUE).

### Flexible printing of subgroup results:

Argument subgroup determines whether summary results are printed for subgroups. A logical vector of length equal to the number of subgroups can be provided to determine which subgroup summaries are printed. By default, only subgroup results based on at least two studies are printed which is identical to use argument subgroup = k.w > 1. The order of the logical vector corresponds to the order of subgroups in list element 'bylevs' of a meta-analysis object. Argument subgroup = k.w >= 1 can be used to show results for all subgroups (including those with a single study).

The following arguments can be used in a similar way:

- subgroup. hetstat (heterogeneity statistic in subgroups),
- prediction.subgroup (prediction interval in subgroups),
- test.effect.subgroup (test for effect in subgroups),
- test.effect.subgroup.common (test for effect in subgroups, common effect model),
- test.effect.subgroup.random (test for effect in subgroups, random effects model).

## Additional general settings:

Arguments text.common, text.random, and text.predict can be used to change the label to identify overall results (common effect and random effects model as well as prediction interval). By default the following text is printed:

- "Common effect model" (argument text.common)
- "Random effects model" (text.random)
- "Prediction interval" (text.predict)

If confidence interval levels are different for individual studies, meta-analysis, and prediction interval (arguments level, level.ma, level.predict in meta-analysis functions, e.g., metabin), additional information is printed, e.g., " (99%-CI)" for a 99% confidence interval in the meta-analysis.

Argument pscale can be used to rescale single proportions or risk differences, e.g., pscale = 1000 means that proportions are expressed as events per 1000 observations. This is useful in situations with (very) low event probabilities.

Argument irscale can be used to rescale single rates or rate differences, e.g., irscale = 1000 means that rates are expressed as events per 1000 time units, e.g., person-years. This is useful in situations with (very) low rates. Argument irunit can be used to specify the time unit used in individual studies (default: "person-years"). This information is printed in summaries and forest plots if argument irscale is not equal to 1.

### Forest plots in RevMan5 layout:

If argument layout = "RevMan5" (and arguments leftcols and rightcols are NULL), the layout for forest plots used for Cochrane reviews (which are generated with Review Manager 5, https://training.cochrane.org/online-learning/core-software-cochrane-reviews/revman) is reproduced:

- 1. All columns are printed on the left side of the forest plot (see arguments leftcols and rightcols)
- 2. Tests for overall effect and subgroup differences are printed (test.overall, test.effect.subgroup, test.subgroup)
- 3. Diamonds representing meta-analysis results are printed in black (diamond.common, diamond.random)
- 4. Colour of squares depends on the meta-analysis object (col.square, col.square.lines)
- 5. Information on effect measure and meta-analysis method is printed above the forest plot (smlab)
- 6. Label "Study or Subgroup" is printed for meta-analysis with subgroups (leftlabs)

#### Forest plots in JAMA layout:

If argument layout = "JAMA" (and arguments leftcols and rightcols are NULL), instructions for authors of the *Journal of the American Medical Association*, see https://jamanetwork.com/journals/jama/pages/instructions-for-authors/, are taken into account:

- 1. Graph labels on right and left side are printed in bold font at top of forest plot (see arguments bottom.lr and ff.lr)
- 2. Information on effect measure and level of confidence interval is printed at bottom of forest plot (xlab)
- 3. Tests for overall effect are printed (test.overall)
- 4. Diamonds representing meta-analysis results are printed in lightblue (diamond.common, diamond.random)
- 5. Squares representing individual study results are printed in darkblue (col. square, col. square.lines)
- 6. Between-study variance  $\tau^2$  is not printed
- 7. Empty rows are omitted (addrow)
- 8. Label "Source" is printed instead of "Study" (leftlabs)
- 9. P-values are printed without leading zeros (zero.pval)
- 10. P-values are rounded to three digits (for 0.001 ) or two digits (<math>p > 0.01) (JAMA. pval)

Study labels according to JAMA guidelines can be generated using labels.meta.

### Forest plots showing results of subgroups:

The following changes are conducted if argument layout = "subgroup" (and arguments leftcols and rightcols are NULL) and a subgroup analysis was conducted:

- 1. Individual study results are omitted (see argument study.results)
- 2. Total number of observations is not printed (pooled.totals)
- 3. Label "Subgroup" is printed instead of "Study" (leftlabs)

### Author(s)

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### References

Guddat C, Grouven U, Bender R, Skipka G (2012): A note on the graphical presentation of prediction intervals in random-effects meta-analyses. *Systematic Reviews*, **1**, 34

Higgins JPT, Thompson SG, Spiegelhalter DJ (2009): A re-evaluation of random-effects meta-analysis. *Journal of the Royal Statistical Society: Series A*, **172**, 137-59

### See Also

```
metabin, metacont, metagen, forest.metabind, settings.meta, labels.meta
```

```
data(Olkin1995)
m1 <- metabin(ev.exp, n.exp, ev.cont, n.cont,
  data = 01kin1995, subset = c(41, 47, 51, 59),
  sm = "RR", method = "I",
  studlab = paste(author, year))
## Not run:
# Do standard (symmetric) forest plot
forest(m1)
## End(Not run)
# Layout of forest plot similar to Review Manager 5
# Furthermore, add labels on both sides of forest plot and
# prediction interval
forest(m1, layout = "RevMan5", common = FALSE,
  label.right = "Favours control", col.label.right = "red",
  label.left = "Favours experimental", col.label.left = "green",
  prediction = TRUE)
## Not run:
# Create a PDF file forest-m1.pdf with the forest plot
pdf("forest-m1.pdf", width = 10, height = 3)
forest(m1)
dev.off()
# Conduct subgroup meta-analysis
m2 <- update(m1,</pre>
  subgroup = ifelse(year < 1987, "Before 1987", "1987 and later"),</pre>
  print.subgroup.name = FALSE)
# Show summary results for subgroups with at least two studies
```

```
forest(m2, sortvar = -TE, random = FALSE)
# Show results for all subgroups
forest(m2, sortvar = -TE, random = FALSE, subgroup = k.w >= 1)
# Forest plot specifying argument xlim
forest(m1, xlim = c(0.01, 10))
# Print results of test for overall effect
forest(m1, test.overall.common = TRUE, test.overall.random = TRUE)
# Forest plot with 'classic' layout used in R package meta,
# version < 1.6-0
forest(m1, col.square = "black", hetstat = FALSE)
# Change set of columns printed on left side of forest plot
# (resulting in overlapping text)
forest(m1, random = FALSE, leftcols = "studlab")
# Use argument 'calcwidth.hetstat' to consider text for heterogeneity
# measures in width of column with study labels
forest(m1, random = FALSE, leftcols = "studlab",
  calcwidth.hetstat = TRUE)
# Use argument 'addrows.below.overall' to manually add two empty
forest(m1, random = FALSE, leftcols = "studlab", addrows = 2)
# Do not print columns on right side of forest plot
forest(m1, rightcols = FALSE)
# Change study label to "Author"
forest(m1, random = FALSE, leftlabs = c("Author", NA, NA, NA, NA))
# Just give effect estimate and 95% confidence interval on right
# side of forest plot (in one column)
forest(m1, rightcols = c("effect.ci"))
# Just give effect estimate and 95% confidence interval on right
# side of forest plot
forest(m1, rightcols = c("effect", "ci"))
```

```
# 1. Change order of columns on left side
# 2. Attach labels to columns 'event.e' and 'event.c' instead of
    columns 'n.e' and 'n.c'
forest(m1,
 leftcols = c("studlab", "n.e", "event.e", "n.c", "event.c"),
 label.e.attach = "event.e", label.c.attach = "event.c")
# Specify column labels only for variables 'year' and 'author'
# (and define digits for additional variables)
forest(m1,
 leftcols = c("studlab", "event.e", "n.e", "event.c", "n.c", "author", "year"),
 leftlabs = c("Author", "Year of Publ"))
# Center text in all columns
#
forest(m1,
 leftcols = c("studlab", "event.e", "n.e", "event.c", "n.c",
               "author", "year"),
 leftlabs = c("Author", "Year of Publ"), hetstat = FALSE,
 just = "center", just.addcols = "center", just.studlab = "center")
# Same result
forest(m1,
 leftcols = c("studlab", "event.e", "n.e", "event.c", "n.c",
             "author", "year"),
 leftlabs = c("Author", "Year of Publ"), hetstat = FALSE,
 just = "c", just.addcols = "c", just.studlab = "c")
# Change some fontsizes and fontfaces
forest(m1,
 fs.study = 10, ff.study = "italic",
 fs.study.label = 11, ff.study.label = "bold",
 fs.axis = 5, ff.axis = "italic",
 ff.smlab = "bold.italic",
 ff.common = "plain", ff.hetstat = "plain")
# Change some colours
#
forest(m1,
 col.diamond = "green", col.diamond.lines = "red",
 col.study = c("green", "blue", "red", "orange"),
 col.square = "pink", col.square.lines = "black")
# Sort by weight in common effect model
forest(m1, sortvar = 1 / w.common, random = FALSE)
# Sort by decreasing weight in common effect model
```

```
forest(m1, sortvar = -1 / w.common, random = FALSE)
# Sort by size of treatment effect
forest(m1, sortvar = TE, random = FALSE)
# Sort by size of treatment effect
forest(m1, sortvar = -TE, random = FALSE)
# Sort by decreasing year of publication
forest(m1, sortvar = -year, random = FALSE)
# Print results of test for subgroup differences (random effects
# model)
forest(m2, sortvar = -TE, common = FALSE)
# Print only subgroup results
forest(m2, layout = "subgroup", addrows = NULL)
# Print only subgroup results (and consider text for tests of
# subgroup differences in width of subgroup column)
forest(m2, layout = "subgroup", calcwidth.tests = TRUE)
# Print only subgroup results (and consider text for heterogeneity
# in width of subgroup column)
forest(m2, layout = "subgroup", calcwidth.hetstat = TRUE)
## End(Not run)
```

forest.metabind

Forest plot to display the result of a meta-analysis

## Description

Draws a forest plot in the active graphics window (using grid graphics system).

## Usage

```
## S3 method for class 'metabind'
forest(
    x,
    leftcols,
```

```
leftlabs,
  rightcols = c("effect", "ci"),
 rightlabs,
 overall = FALSE,
  subgroup = FALSE,
 hetstat = FALSE,
 overall.hetstat = FALSE,
 lab.NA = "",
 digits = gs("digits.forest"),
 digits.se = gs("digits.se"),
 digits.stat = gs("digits.stat"),
 digits.pval = max(gs("digits.pval") - 2, 2),
 digits.pval.Q = max(gs("digits.pval.Q") - 2, 2),
 digits.Q = gs("digits.Q"),
 digits.tau2 = gs("digits.tau2"),
 digits.tau = gs("digits.tau"),
 digits.I2 = max(gs("digits.I2") - 1, 0),
  scientific.pval = gs("scientific.pval"),
 big.mark = gs("big.mark"),
 print.subgroup.labels = if (any(x$.meta$is.subgroup)) TRUE else FALSE,
  addrow.subgroups = print.subgroup.labels,
 calcwidth.pooled = overall,
 warn.deprecated = gs("warn.deprecated"),
)
```

### **Arguments**

X	An object of class metabind.
leftcols	A character vector specifying (additional) columns to be plotted on the left side of the forest plot or a logical value (see Details).
leftlabs	A character vector specifying labels for (additional) columns on left side of the forest plot (see Details).
rightcols	A character vector specifying (additional) columns to be plotted on the right side of the forest plot or a logical value (see Details).
rightlabs	A character vector specifying labels for (additional) columns on right side of the forest plot (see Details).
overall	A logical indicating whether overall summaries should be plotted. This argument is useful in a meta-analysis with subgroups if summaries should only be plotted on group level.
subgroup	A logical indicating whether subgroup results should be shown in forest plot. This argument is useful in a meta-analysis with subgroups if summaries should not be plotted on group level.
hetstat	Either a logical value indicating whether to print results for heterogeneity measures at all or a character string (see Details).

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A logical value indicating whether to print heterogeneity measures for overall treatment comparisons. This argument is useful in a meta-analysis with subgroups if heterogeneity statistics should only be printed on subgroup level.

lab.NA A character string to label missing values.

digits Minimal number of significant digits for treatment effects, see print.default. digits.se Minimal number of significant digits for standard errors, see print.default. digits.stat Minimal number of significant digits for z- or t-statistic for test of overall effect,

see print.default.

Minimal number of significant digits for p-value of overall treatment effect, see digits.pval

print.default.

digits.pval.Q Minimal number of significant digits for p-value of heterogeneity test, see print. default.

digits.Q Minimal number of significant digits for heterogeneity statistic Q, see print.default. digits.tau2 Minimal number of significant digits for between-study variance, see print.default.

digits.tau Minimal number of significant digits for square root of between-study variance,

see print.default.

digits.I2 Minimal number of significant digits for I-squared statistic, see print.default.

scientific.pval

A logical specifying whether p-values should be printed in scientific notation, e.g., 1.2345e-01 instead of 0.12345.

A character used as thousands separator. big.mark

print.subgroup.labels

A logical indicating whether subgroup label should be printed.

addrow.subgroups

A logical value indicating whether an empty row is printed between results for subgroups.

smlab A label for the summary measurex (printed at top of figure).

calcwidth.pooled

A logical indicating whether text for common effect and random effects model should be considered to calculate width of the column with study labels.

warn.deprecated

A logical indicating whether warnings should be printed if deprecated arguments

Additional graphical arguments (passed on to forest.meta).

### **Details**

A forest plot, also called confidence interval plot, is drawn in the active graphics window. The forest functions in R package **meta** are based on the grid graphics system. In order to print the forest plot, resize the graphics window and either use dev.copy2eps or dev.copy2pdf. Another possibility is to create a file using pdf, png, or svg and to specify the width and height of the graphic (see forest.meta examples).

The arguments leftcols and rightcols can be used to specify columns which are plotted on the left and right side of the forest plot, respectively.

The arguments leftlabs and rightlabs can be used to specify column headings which are plotted on left and right side of the forest plot, respectively. For certain columns predefined labels exist. For other columns, the column name will be used as a label. It is possible to only provide labels for new columns (see <a href="forest.meta">forest.meta</a> examples). Otherwise the length of leftlabs and rightlabs must be the same as the number of printed columns, respectively. The value NA can be used to specify columns which should use default labels.

Argument hetstat can be a character string to specify where to print heterogeneity information:

- row with results for common effect model (hetstat = "common"),
- row with results for random effects model (hetstat = "random"),
- rows with 'study' information (hetstat = "study").

Otherwise, information on heterogeneity is printed in dedicated rows.

### Author(s)

Guido Schwarzer <sc@imbi.uni-freiburg.de>

#### See Also

forest.meta, metabin, metacont, metagen, metabind, settings.meta

```
data(Fleiss1993cont)

# Add some (fictitious) grouping variables:
#
Fleiss1993cont$age <- c(55, 65, 55, 65, 55)
Fleiss1993cont$region <- c("Europe", "Europe", "Asia", "Asia", "Europe")

m1 <- metacont(n.psyc, mean.psyc, sd.psyc, n.cont, mean.cont, sd.cont, data = Fleiss1993cont, sm = "MD")

# Conduct two subgroup analyses
#
mu1 <- update(m1, subgroup = age, bylab = "Age group")
mu2 <- update(m1, subgroup = region, bylab = "Region")

# Combine subgroup meta-analyses and show forest plot with subgroup
# results
#
mb1 <- metabind(mu1, mu2)
mb1
forest(mb1)</pre>
```

funnel.meta

Funnel plot

### **Description**

Draw a funnel plot which can be used to assess small study effects in meta-analysis. A contourenhanced funnel plot can also be produced to assess causes of funnel plot asymmetry.

## Usage

```
## S3 method for class 'meta'
funnel(
  х,
 xlim = NULL,
 ylim = NULL,
 xlab = NULL,
 ylab = NULL,
 common = x scommon,
  random = x$random,
  axes = TRUE,
  pch = if (!inherits(x, "trimfill")) 21 else ifelse(x$trimfill, 1, 21),
  text = NULL,
  cex = 1,
  lty.common = 2,
  lty.random = 9,
  lwd = 1,
  lwd.common = lwd,
  lwd.random = lwd,
  col = "black",
  bg = "darkgray",
  col.common = "black",
  col.random = "black",
  log,
 yaxis,
  contour.levels = NULL,
  col.contour,
  ref = ifelse(is.relative.effect(x$sm), 1, 0),
  level = if (common | random) x$level else NULL,
  studlab = FALSE,
  cex.studlab = 0.8,
  pos.studlab = 2,
  ref.triangle = FALSE,
  lty.ref = 1,
  lwd.ref = lwd,
  col.ref = "black",
  lty.ref.triangle = 5,
  backtransf = x$backtransf,
```

```
warn.deprecated = gs("warn.deprecated"),
    ...
)
```

# Arguments

cex.studlab

х	An object of class meta.
xlim	The x limits (min,max) of the plot.
ylim	The y limits (min,max) of the plot.
xlab	A label for the x-axis.
ylab	A label for the y-axis.
common	A logical indicating whether the common effect estimate should be plotted.
random	A logical indicating whether the random effects estimate should be plotted.
axes	A logical indicating whether axes should be drawn on the plot.
pch	The plotting symbol used for individual studies.
text	A character vector specifying the text to be used instead of plotting symbol.
cex	The magnification to be used for plotting symbol.
lty.common	Line type (common effect estimate).
lty.random	Line type (random effects estimate).
lwd	The line width for confidence intervals (if level is not NULL).
lwd.common	The line width for common effect estimate (if common is not NULL).
lwd.random	The line width for random effects estimate (if random is not NULL).
col	A vector with colour of plotting symbols.
bg	A vector with background colour of plotting symbols (only used if pch in 21:25).
col.common	Colour of line representing common effect estimate.
col.random	Colour of line representing random effects estimate.
log	A character string which contains "x" if the x-axis is to be logarithmic, "y" if the y-axis is to be logarithmic and "xy" or "yx" if both axes are to be logarithmic.
yaxis	A character string indicating which type of weights are to be used. Either "se", "invvar", "invse", code"size", code"invsqrtsize", or code"ess".
contour.levels	A numeric vector specifying contour levels to produce contour-enhanced funnel plot.
col.contour	Colour of contours.
ref	Reference value (null effect) used to produce contour-enhanced funnel plot.
level	The confidence level utilised in the plot. For the funnel plot, confidence limits are not drawn if yaxis="size" or yaxis="invsqrtsize".
studlab	A logical indicating whether study labels should be printed in the graph. A vector with study labels can also be provided (must be of same length as x\$TE then).

Size of study labels, see argument cex in text.

pos.studlab Position of study labels, see argument pos in text.

ref.triangle A logical indicating whether approximate confidence limits should be printed

around reference value (null effect).

lty.ref Line type (reference value).

lwd.ref The line width for the reference value and corresponding confidence intervals

(if ref. triangle is TRUE and level is not NULL).

col.ref Colour of line representing reference value.

lty.ref.triangle

Line type (confidence intervals of reference value).

backtransf A logical indicating whether results for relative summary measures (argument

sm equal to "OR", "RR", "HR", or "IRR") should be back transformed in funnel plots. If backtransf=TRUE, results for sm="OR" are printed as odds ratios rather

than log odds ratios, for example.

warn.deprecated

A logical indicating whether warnings should be printed if deprecated arguments

are used.

... Additional arguments (to catch deprecated arguments). moment).

#### **Details**

A funnel plot (Light & Pillemer, 1984) is drawn in the active graphics window. If common is TRUE, the estimate of the common effect model is plotted as a vertical line. Similarly, if random is TRUE, the estimate of the random effects model is plotted. If level is not NULL, the corresponding approximate confidence limits are drawn around the common effect estimate (if common is TRUE) or the random effects estimate (if random is TRUE and common is FALSE).

In the funnel plot, the standard error of the treatment estimates is plotted on the y-axis by default (yaxis = "se") which is likely to be the best choice (Sterne & Egger, 2001). Only exception is meta-analysis of diagnostic test accuracy studies (Deeks et al., 2005) where the inverse of the square root of the *effective study size* is used (yaxis = "ess"). Other possible choices for yaxis are "invvar" (inverse of the variance), "invse" (inverse of the standard error), "size" (study size), and "invsqrtsize" (1 / sqrt(study size)).

If argument yaxis is not equal to "size", "invsqrtsize" or "ess", contour-enhanced funnel plots can be produced (Peters et al., 2008) by specifying the contour levels (argument contour.levels). By default (argument col.contour missing), suitable gray levels will be used to distinguish the contours. Different colours can be chosen by argument col.contour.

### Author(s)

Guido Schwarzer <sc@imbi.uni-freiburg.de>, Petra Graham <pgraham@efs.mq.edu.au>

### References

Deeks JJ, Macaskill P, Irwig L (2005): The performance of tests of publication bias and other sample size effects in systematic reviews of diagnostic test accuracy was assessed. *Journal of Clinical Epidemiology*, **58**:882–93

Light RJ & Pillemer DB (1984): Summing Up. The Science of Reviewing Research. Cambridge: Harvard University Press

Peters JL, Sutton AJ, Jones DR, Abrams KR, Rushton L (2008): Contour-enhanced meta-analysis funnel plots help distinguish publication bias from other causes of asymmetry. *Journal of Clinical Epidemiology*, **61**, 991–6

Sterne JAC & Egger M (2001): Funnel plots for detecting bias in meta-analysis: Guidelines on choice of axis. *Journal of Clinical Epidemiology*, **54**, 1046–55

## See Also

metabias, metabin, metagen, radial

```
data(Olkin1995)
m1 <- metabin(ev.exp, n.exp, ev.cont, n.cont,</pre>
  data = 01kin1995, subset = c(41, 47, 51, 59),
  studlab = paste(author, year),
  sm = "RR", method = "I")
oldpar \leftarrow par(mfrow = c(2, 2))
# Standard funnel plot
funnel(m1)
# Funnel plot with confidence intervals, common effect estimate and
# contours
cc <- funnel(m1, common = TRUE,</pre>
             level = 0.95, contour = c(0.9, 0.95, 0.99)$col.contour
legend(0.05, 0.05,
  c("0.1 > p > 0.05", "0.05 > p > 0.01", "< 0.01"), fill = cc)
# Contour-enhanced funnel plot with user-chosen colours
#
funnel(m1, common = TRUE,
  level = 0.95, contour = c(0.9, 0.95, 0.99),
  col.contour = c("darkgreen", "green", "lightgreen"),
  lwd = 2, cex = 2, pch = 16, studlab = TRUE, cex.studlab = 1.25)
legend(0.05, 0.05,
  c("0.1 > p > 0.05", "0.05 > p > 0.01", "< 0.01"),
  fill = c("darkgreen", "green", "lightgreen"))
par(oldpar)
```

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gs

Get default for a meta-analysis setting.

## Description

Get default for a meta-analysis setting in R package meta.

## Usage

gs(x)

## **Arguments**

Χ

A character string holding a settings name.

## **Details**

This function can be used to get the default for a meta-analysis setting defined using settings.meta.

This function is primarily used to define default settings in meta-analysis functions, e.g., metabin or metacont. A list of all arguments with current settings is printed using the command settings.meta("print").

## Author(s)

```
Guido Schwarzer <sc@imbi.uni-freiburg.de>
```

### See Also

```
settings.meta
```

```
# Get default setting for Hartung-Knapp method
#
gs("hakn")
# Get default setting for summary measure in metabin()
#
gs("smbin")
```

54 JAMAlabels

JAMAlabels	Create study labels in JAMA layout (deprecated function)

## **Description**

Deprecated function to create study labels in JAMA layout (for forest plot). Replaced by labels.meta.

## Usage

```
JAMAlabels(author, year, citation, data = NULL)
```

## Arguments

author A vector providing study authors.

year A vector providing year of publication.

citation A vector providing citation numbers.

data An optional data frame containing the study information.

### **Details**

This auxiliary function can be used to create study labels in JAMA layout which can be added to a forest plot using argument 'studlab'.

## Author(s)

```
Guido Schwarzer <sc@imbi.uni-freiburg.de>
```

## See Also

```
labels.meta, forest.meta
```

```
data(Fleiss1993bin)

refs <- 20 + 1:7

Fleiss1993bin$mylabs <-
    JAMAlabels(study, year, refs, data = Fleiss1993bin)

m <- metabin(d.asp, n.asp, d.plac, n.plac, data = Fleiss1993bin, studlab = paste(study, year), sm = "OR", random = FALSE)

forest(m, studlab = mylabs, layout = "JAMA", fontfamily = "Times", fontsize = 10)</pre>
```

labbe.metabin

L'Abbé plot for meta-analysis with binary outcomes

### **Description**

Draw a L'Abbé plot for meta-analysis with binary outcomes.

## Usage

```
## S3 method for class 'metabin'
labbe(
  Х,
 xlim,
 ylim,
 xlab = NULL,
 ylab = NULL,
 TE.common = x$TE.common,
  TE.random = x$TE.random,
  common = x scommon,
  random = x$random,
  backtransf = x$backtransf,
  axes = TRUE,
  pch = 21,
  text = NULL,
  cex = 1,
  col = "black",
  bg = "lightgray",
  lwd = 1,
  lwd.common = lwd,
  lwd.random = lwd,
  lty.common = 2,
  lty.random = 9,
  col.common = col,
  col.random = col,
  nulleffect = TRUE,
  lwd.nulleffect = lwd,
  col.nulleffect = "lightgray",
  sm = x\$sm,
  weight,
  studlab = FALSE,
  cex.studlab = 0.8,
  pos.studlab = 2,
  label.e = x$label.e,
  label.c = x$label.c,
  warn.deprecated = gs("warn.deprecated"),
  TE.fixed,
  fixed,
```

```
lwd.fixed,
  lty.fixed,
  col.fixed,
)
## Default S3 method:
labbe(
  Х,
 у,
 xlim,
  ylim,
  xlab = NULL,
 ylab = NULL,
 TE.common = NULL,
  TE.random = NULL,
  common = !is.null(TE.common),
  random = !is.null(TE.random),
  backtransf = TRUE,
  axes = TRUE,
  pch = 21,
  text = NULL,
  cex = 1,
  col = "black",
  bg = "lightgray",
  1wd = 1,
  lwd.common = lwd,
  lwd.random = lwd,
  lty.common = 2,
  lty.random = 9,
  col.common = col,
  col.random = col,
  nulleffect = TRUE,
  lwd.nulleffect = lwd,
  col.nulleffect = "lightgray",
  sm = "",
  weight,
  studlab = FALSE,
  cex.studlab = 0.8,
  pos.studlab = 2,
  label.e = NULL,
  label.c = NULL,
  warn.deprecated = gs("warn.deprecated"),
  TE.fixed,
  fixed,
  lwd.fixed,
  lty.fixed,
  col.fixed,
```

)

### **Arguments**

An object of class metabin. Alternatively, the x coordinates of points of the Х L'Abbé plot.

xlim The x limits (min, max) of the plot. The y limits (min, max) of the plot. vlim

A label for the x-axis. xlab ylab A label for the y-axis.

TE.common A numeric or vector specifying combined common effect estimate(s). TE.random A numeric or vector specifying combined random effects estimate(s).

common A logical indicating whether the common effect estimate should be plotted. random A logical indicating whether the random effects estimate should be plotted. backtransf

A logical indicating which values should be printed on x- and y-axis (see De-

A logical indicating whether axes should be drawn on the plot. axes

The plotting symbol used for individual studies. pch

text A character vector specifying the text to be used instead of plotting symbol.

cex The magnification to be used for plotting symbol.

A vector with colour of plotting symbols. col

A vector with background colour of plotting symbols (only used if pch in 21:25). bg

lwd The line width.

1wd.common The line width(s) for common effect estimate(s) (if common is not NULL or FALSE). lwd.random The line width(s) for random effects estimate(s) (if random is not NULL or FALSE).

lty.common Line type(s) for common effect estimate(s). lty.random Line type(s) for random effects estimate(s). col.common Colour of line(s) for common effect estimate(s). col.random Colour of line(s) for random effects estimate(s).

nulleffect A logical indicating whether line for null effect should be added to the plot..

lwd.nulleffect Width of line for null effect. col.nulleffect Colour of line for null effect.

A character string indicating underlying summary measure, i.e., "RD", "RR",

"OR", or "ASD".

weight Either a numeric vector specifying relative sizes of plotting symbols or a char-

acter string indicating which type of plotting symbols is to be used for individual treatment estimates. One of missing (see Details), "same", "common", or "random", can be abbreviated. Plot symbols have the same size for all studies

or represent study weights from common effect or random effects model.

studlab	A logical indicating whether study labels should be printed in the graph. A vector with study labels can also be provided (must be of same length as $x$ =vent.e then).
cex.studlab	Size of study labels.
pos.studlab	Position of study labels, see argument pos in text.
label.e	Label for experimental group.
label.c	Label for control group.
warn.deprecated	d
	A logical indicating whether warnings should be printed if deprecated arguments are used.
TE.fixed	Deprecated argument (replaced by 'TE.common').
fixed	Deprecated argument (replaced by 'common').
lwd.fixed	Deprecated argument (replaced by 'lwd.common').
lty.fixed	Deprecated argument (replaced by 'lty.common').
col.fixed	Deprecated argument (replaced by 'col.common').
	Graphical arguments as in par may also be passed as arguments.
У	The y coordinates of the L'Abbé plot, if argument x is not an object of class metabin.

## Details

A L'Abbé plot is a scatter plot with the risk in the control group on the x-axis and the risk in the experimental group on the y-axis (L'Abbé et al., 1987). It can be used to evaluate heterogeneity in meta-analysis. Furthermore, this plot can aid to choose a summary measure (odds ratio, risk ratio, risk difference) that will result in more consistent results (Jiménez et al., 1997; Deeks, 2002).

If argument backtransf is TRUE (default), event probabilities will be printed on x- and y-axis. Otherwise, transformed event probabilities will be printed as defined by the summary measure, i.e., log odds of probabilities for odds ratio as summary measure (sm = "OR"), log probabilities for sm = "RR", and arcsine-transformed probabilities for sm = "ASD".

If common is TRUE, the estimate of the common effct model is plotted as a line. If random is TRUE, the estimate of the random effects model is plotted as a line.

Information from object x is utilised if argument weight is missing. Weights from the common effect model are used (weight = "common") if argument x\$common is TRUE; weights from the random effects model are used (weight = "random") if argument x\$random is TRUE and x\$common is FALSE.

### Author(s)

Guido Schwarzer <sc@imbi.uni-freiburg.de>

### References

Deeks JJ (2002): Issues in the selection of a summary statistic for meta-analysis of clinical trials with binary outcomes. *Statistics in Medicine*, **21**, 1575–600

Jiménez FJ, Guallar E, Martín-Moreno JM (1997): A graphical display useful for meta-analysis. *European Journal of Public Health*, **1**, 101–5

L'Abbé KA, Detsky AS, O'Rourke K (1987): Meta-analysis in clinical research. *Annals of Internal Medicine*, **107**, 224–33

### See Also

metabin

```
data(Olkin1995)
m1 <- metabin(ev.exp, n.exp, ev.cont, n.cont,</pre>
  data = Olkin1995, studlab = paste(author, year),
  sm = "RR", method = "I")
# L'Abbe plot for risk ratio
labbe(m1)
# L'Abbe plot for odds ratio
labbe(m1, sm = "OR")
# same plot
labbe(update(m1, sm = "OR"))
# L'Abbe plot for risk difference
labbe(m1, sm = "RD")
# L'Abbe plot on log odds scale
labbe(m1, sm = "OR", backtransf = FALSE)
# L'Abbe plot for odds ratio with coloured lines for various
# treatment effects (defined as log odds ratios)
mycols <- c("blue", "yellow", "green", "red", "green", "yellow", "blue")</pre>
labbe(m1, sm = "OR", random = FALSE,
  TE.common = log(c(1 / 10, 1 / 5, 1 / 2, 1, 2, 5, 10)),
  col.common = mycols, lwd.common = 2)
# L'Abbe plot on log odds scale with coloured lines for various
# treatment effects (defined as log odds ratios)
labbe(m1, sm = "OR", random = FALSE, backtransf = FALSE,
  TE.common = log(c(1 / 10, 1 / 5, 1 / 2, 1, 2, 5, 10)),
  col.common = mycols, lwd.common = 2)
```

60 labels.meta

labels.meta

Create study labels for forest plot

## **Description**

Create study labels for forest plot.

### Usage

```
## S3 method for class 'meta'
labels(
  object,
  author = object$studlab,
  year = "",
  citation = NULL,
  layout = "JAMA",
  data = object$data,
  ...
)
```

## Arguments

object An object of class meta.

author An optional vector providing study authors.

year An optional vector providing year of publication.
citation An optional vector providing citation numbers.

layout A character string specifying layout. Either "JAMA" or "Lancet".

data An optional data frame containing the study information.

... Additional arguments (ignored at the moment).

## **Details**

This auxiliary function can be used to create study labels in JAMA or Lancet layout which can be added to a forest plot using argument 'studlab'.

## Author(s)

```
Guido Schwarzer <sc@imbi.uni-freiburg.de>
```

### See Also

```
forest.meta
```

longarm 61

## **Examples**

```
data(Fleiss1993bin)
refs <- 20 + 1:7

m <- metabin(d.asp, n.asp, d.plac, n.plac, data = Fleiss1993bin,
    studlab = study, sm = "OR", random = FALSE)

forest(m,
    studlab = labels(m, year = year, citation = refs, layout = "JAMA"),
    layout = "JAMA", fontfamily = "Times", fontsize = 10)

forest(m,
    studlab = labels(m, year = year, citation = refs, layout = "Lancet"))</pre>
```

longarm

Transform data from pairwise comparisons to long arm-based format

## Description

This function transforms data from pairwise comparisons to a long arm-based format, i.e., two rows for a pairwise comparison.

## Usage

```
longarm(
  treat1,
  treat2,
  event1,
  n1,
  event2,
 n2,
 mean1,
  sd1,
 mean2,
  sd2,
  time1,
  time2,
  data = NULL,
  studlab,
  append = TRUE,
  keep.duplicated = FALSE,
  keep.internal = FALSE
)
```

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### **Arguments**

treat1 Either label for first treatment or a meta-analysis or pairwise object (see Details).

treat2 Label for second treatment.

event1 Number of events (first treatment).

n1 Number of observations (first treatment).event2 Number of events (second treatment).

n2 Number of observations (second treatment)

mean1 Estimated mean (first treatment).

sd1 Standard deviation (first treatment).

mean2 Estimated mean (second treatment).

sd2 Standard deviation (second treatment).

time1 Person time at risk (first treatment)

time2 Person time at risk (second treatment)

data An optional data frame containing the study information.

studlab A vector with study labels (optional).

append A logical indicating if data frame provided in argument 'data' should be re-

turned.

keep.duplicated

A logical indicating if duplicated rows should be returned (see Details).

keep.internal A logical indicating if variables generated internally should be returned (typi-

cally only relevant for data checking).

### **Details**

This function transforms data given as one pairwise comparison per row to a long arm-based format with one row per treatment arm. The long arm-based format is, for example, the required input format for WinBUGS.

The function can be used to transform data with a binary, continuous or count outcome. The corresponding meta-analysis functions are metabin, metacont and metainc. Accordingly, a meta-analysis object created with one of these functions can be provided as argument treat1. It is also possible to use the longarm function with an R objected created with pairwise from R package netmeta.

Otherwise, arguments treat1 and treat2 are mandatory to identify the individual treatments and, depending on the outcome, the following additional arguments are mandatory:

- event1, n1, event2, n2 (binary outcome);
- n1, mean1, sd1, n2, mean2, sd2 (continuous outcome);
- time1, n1, time2, n2 (count outcome).

Argument studlab must be provided if several pairwise comparisons come from a single study with more than two treatments.

The following variables will be returned:

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```
study label
  studlab
            treatment label
     treat
            group sample size (count outcome only if provided)
        n
            number of events (binary or count outcome)
    events
nonevents
            number of non-events (binary outcome)
            estimated mean (continuous outcome)
    mean
            standard deviation (continuous outcome)
       sd
            person time at risk (count outcome)
     time
```

In addition, the data set provided in argument data will be returned if argument append = TRUE (default).

Argument keep.duplicated can be used to keep duplicated rows from the data set. Duplicated rows can occur, for example, in a three-arm study comparing treatments A and B with placebo. In this situation, the placebo arm will be returned twice in the data set in long arm-based format if keep.duplicated = TRUE. By default, duplicated rows with not be kept in the data set.

#### Value

A data frame in long arm-based format.

#### Note

R function to.long from R package metafor is called internally.

### Author(s)

```
Guido Schwarzer <sc@imbi.uni-freiburg.de>
```

## See Also

```
metabin, metacont, metainc, pairwise
```

```
# Artificial example with three studies
m <- metabin(1:3, 100:102, 4:6, 200:202, studlab = LETTERS[1:3])
# Transform data to long arm-based format
longarm(m)
# Keep internal variables
longarm(m, keep.internal = TRUE)</pre>
```

metabias.meta

Test for funnel plot asymmetry

### **Description**

Test for funnel plot asymmetry, based on rank correlation or linear regression method.

## Usage

```
## S3 method for class 'meta'
metabias(
  х,
 method.bias = x$method.bias,
 plotit = FALSE,
  correct = FALSE,
  k.min = 10,
)
## S3 method for class 'metabias'
print(
  digits = gs("digits"),
  digits.stat = gs("digits.stat"),
  digits.pval = max(gs("digits.pval"), 2),
  digits.se = gs("digits.se"),
  digits.tau2 = gs("digits.tau2"),
  scientific.pval = gs("scientific.pval"),
  big.mark = gs("big.mark"),
  zero.pval = gs("zero.pval"),
  JAMA.pval = gs("JAMA.pval"),
  text.tau2 = gs("text.tau2"),
)
metabias(x, ...)
## Default S3 method:
metabias(
  Х,
  seTE,
  method.bias = "Egger",
 plotit = FALSE,
  correct = FALSE,
  k.min = 10,
)
```

## **Arguments**

X	An object of class meta or estimated treatment effect in individual studies.		
method.bias	A character string indicating which test is to be used (see Details), can be abbreviated.		
plotit	A logical indicating whether a plot should be produced (see Details).		
correct	A logical indicating whether a continuity corrected statistic is used for rank correlation tests.		
k.min	Minimum number of studies to perform test for funnel plot asymmetry.		
	Additional arguments passed on to rma.uni.		
digits	Minimal number of significant digits for estimates, see print.default.		
digits.stat	Minimal number of significant digits for z- or t-value of test for test of funnel plot asymmetry, see print.default.		
digits.pval	Minimal number of significant digits for p-value of test for test of funnel plot asymmetry, see print.default.		
digits.se	Minimal number of significant digits for standard errors, see print.default.		
digits.tau2	Minimal number of significant digits for residual heterogeneity variance, see print.default.		
scientific.pval			
	A logical specifying whether p-values should be printed in scientific notation, e.g., 1.2345e-01 instead of 0.12345.		
big.mark	A character used as thousands separator.		
zero.pval	A logical specifying whether p-values should be printed with a leading zero.		
JAMA.pval	A logical specifying whether p-values for test of overall effect should be printed according to JAMA reporting standards.		
text.tau2	Text printed to identify residual heterogeneity variance $\tau^2$ .		
seTE	Standard error of estimated treatment effect (mandatory if x not of class meta).		

### **Details**

Functions to conduct rank correlation or linear regression tests for funnel plot asymmetry.

**Classic generic tests:** The following tests are generic tests for funnel plot asymmetry which only require estimates of the treatment effect and corresponding standard errors. Accordingly, these are the only tests provided by R function metabias.default.

If argument method.bias is "Begg", the test statistic is based on the rank correlation between standardised treatment estimates and variance estimates of estimated treatment effects; Kendall's tau is used as correlation measure (Begg & Mazumdar, 1994). The test statistic follows a standard normal distribution. By default (if correct is FALSE), no continuity correction is utilised (Kendall & Gibbons, 1990).

If argument method.bias is "Egger", the test statistic is based on a weighted linear regression of the treatment effect on its standard error (Egger et al., 1997). The test statistic follows a t distribution with number of studies -2 degrees of freedom.

If argument method.bias is "Thompson", the test statistic is based on a weighted linear regression of the treatment effect on its standard error using an additive between-study variance component denoted as methods (3a) - (3d) in Thompson & Sharp (1999). The test statistic follows a t distribution with number of studies - 2 degrees of freedom.

**Tests for meta-analysis with binary outcomes:** The following tests for funnel plot asymmetry are only available for meta-analyses comparing two binary outcomes, i.e. meta-analyses generated with the metabin function. The only exception is the test by Peters et al. (2006) which can also be used in a meta-analysis of single proportions generated with metaprop.

If argument method.bias is "Harbord", the test statistic is based on a weighted linear regression utilising efficient score and score variance (Harbord et al., 2006, 2009). The test statistic follows a t distribution with number of studies - 2 degrees of freedom.

In order to calculate an arcsine test for funnel plot asymmetry (Rücker et al., 2008), one has to use the metabin function with argument sm = "ASD" as input to the metabias command. The three arcsine tests described in Rücker et al. (2008) can be calculated by setting method.bias to "Begg", "Egger" and "Thompson", respectively.

If argument method.bias is "Macaskill", the test statistic is based on a weighted linear regression of the treatment effect on the total sample size with weights reciprocal to the variance of the average event probability (Macaskill et al., 2001, *method FPV*). The test statistic follows a t distribution with number of studies - 2 degrees of freedom.

If argument method.bias is "Peters", the test statistic is based on a weighted linear regression of the treatment effect on the inverse of the total sample size with weights reciprocal to the variance of the average event probability (Peters et al., 2006). The test statistic follows at distribution with number of studies – 2 degrees of freedom. Note, this test is a variant of Macaskill et al. (2001), method FPV, using the inverse sample size as covariate.

If argument method.bias is "Schwarzer", the test statistic is based on the rank correlation between a standardised cell frequency and the inverse of the variance of the cell frequency; Kendall's tau is used as correlation measure (Schwarzer et al., 2007). The test statistic follows a standard normal distribution. By default (if correct is FALSE), no continuity correction is utilised (Kendall & Gibbons, 1990).

Finally, for meta-analysis of diagnostic test accuracy studies, if argument method.bias is "Deeks", the test statistic is based on a weighted linear regression of the log diagnostic odds ratio on the inverse of the squared effective sample size using the effective sample size as weights (Deeks et al., 2005). The test statistic follows a t distribution with number of studies -2 degrees of freedom.

**Test for the standardised mean difference:** If argument method.bias is "Pustejovsky", the test statistic is based on a weighted linear regression of the treatment effect on the square root of the sum of the inverse group sample sizes using the treatment effect variance as weights (Pustejovsky & Rodgers, 2019). The test statistic follows a t distribution with number of studies – 2 degrees of freedom.

**Recommendations and default settings:** Following recommendations by Sterne et al. (2011), by default, a test for funnel plot asymmetry is only conducted if the number of studies is ten or larger (argument k.min = 10). This behaviour can be changed by setting a smaller value for argument k.min. Note, the minimum number of studies is three.

If argument method.bias is missing, the Harbord test (method.bias = "Harbord") is used in meta-analysis of binary outcomes for the odds ratio as effect measure and the Egger test (method.bias = "Egger") in all other settings (Sterne et al., 2011).

No test for funnel plot asymmetry is conducted in meta-analyses with subgroups.

If argument plotit = TRUE, a scatter plot is shown if argument method.bias is equal to "Begg", "Egger", "Thompson", "Harbord", or "Deeks".

#### Value

A list with class metabias containing the following components if a test for funnel plot asymmetry is conducted:

statistic Test statistic.

df The degrees of freedom of the test statistic in the case that it follows a t distri-

bution.

pval The p-value for the test.

estimate Estimates used to calculate test statisic.

method A character string indicating what type of test was used.

title Title of Cochrane review.

complab Comparison label.

outclab Outcome label.

var.model A character string indicating whether none, multiplicative, or additive residual

heterogeneity variance was assumed.

method.bias As defined above.

x Meta-analysis object.

version Version of R package **meta** used to create object.

Or a list with the following elements if test is not conducted due to the number of studies:

k Number of studies in meta-analysis.

k.min Minimum number of studies to perform test for funnel plot asymmetry.

version Version of R package **meta** used to create object.

#### Author(s)

Guido Schwarzer <sc@imbi.uni-freiburg.de>

### References

Begg CB & Mazumdar M (1994): Operating characteristics of a rank correlation test for publication bias. *Biometrics*, **50**, 1088–101

Deeks JJ, Macaskill P, Irwig L (2005): The performance of tests of publication bias and other sample size effects in systematic reviews of diagnostic test accuracy was assessed. *Journal of Clinical Epidemiology*, **58**:882–93

Egger M, Smith GD, Schneider M & Minder C (1997): Bias in meta-analysis detected by a simple, graphical test. *British Medical Journal*, **315**, 629–34

Harbord RM, Egger M & Sterne J (2006): A modified test for small-study effects in meta-analyses of controlled trials with binary endpoints. *Statistics in Medicine*, **25**, 3443–57

Harbord RM, Harris RJ, Sterne JAC (2009): Updated tests for small-study effects in meta–analyses. *The Stata Journal*, **9**, 197–210

Kendall M & Gibbons JD (1990): Rank Correlation Methods. London: Edward Arnold

Macaskill P, Walter SD, Irwig L (2001): A comparison of methods to detect publication bias in meta-analysis. *Statistics in Medicine*, **20**, 641–54

Peters JL, Sutton AJ, Jones DR, Abrams KR & Rushton L (2006): Comparison of two methods to detect publication bias in meta-analysis. *Journal of the American Medical Association*, **295**, 676–80

Pustejovsky JE, Rodgers MA (2019): Testing for funnel plot asymmetry of standardized mean differences. *Research Synthesis Methods*, **10**, 57–71

Rücker G, Schwarzer G, Carpenter JR (2008): Arcsine test for publication bias in meta-analyses with binary outcomes. *Statistics in Medicine*, **27**, 746–63

Schwarzer G, Antes G & Schumacher M (2007): A test for publication bias in meta-analysis with sparse binary data. *Statistics in Medicine*, **26**, 721–33

Sterne, JAC et al. (2011): Recommendations for examining and interpreting funnel plot asymmetry in meta-analyses of randomised controlled trials. *BMJ (Clinical research ed.)*, **343**, 1

Thompson SG & Sharp, SJ (1999): Explaining heterogeneity in meta-analysis: a comparison of methods, *Statistics in Medicine*, **18**, 2693–708

#### See Also

funnel, funnel.meta, metabin, metacont, metagen

```
data(Olkin1995)
m1 <- metabin(ev.exp, n.exp, ev.cont, n.cont,</pre>
  data = Olkin1995, subset = 1:10, sm = "RR", method = "I")
metabias(m1)
metabias(m1, plotit = TRUE)
metabias(m1, method.bias = "Begg")
metabias(m1, method.bias = "Begg", correct = TRUE)
metabias(m1, method.bias = "Schwarzer")
metabias(m1, method.bias = "Egger")$pval
# Arcsine test (based on linear regression)
m1.as \leftarrow update(m1, sm = "ASD")
metabias(m1.as)
# Same result (using function metabias.default)
metabias(m1.as$TE, m1.as$seTE)
# No test for funnel plot asymmetry calculated
m2 \leftarrow update(m1, subset = 1:5)
metabias(m2)
```

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```
m3 <- update(m1, subset = 1:2)
metabias(m3)

# Test for funnel plot asymmetry calculated (use of argument k.min)
#
metabias(m2, k.min = 5)</pre>
```

metabias.rm5

Cochrane review: Test for funnel plot asymmetry

## **Description**

Conduct a test for funnel plot asymmetry for all outcomes in a Cochrane review

## Usage

```
## $3 method for class 'rm5'
metabias(
    X,
    comp.no,
    outcome.no,
    method.bias = "linreg",
    method.bias.binary = method.bias,
    method.bias.or = "score",
    k.min = 10,
    ...
)
```

# Arguments ×

An object of class rm5. Comparison number. comp.no outcome.no Outcome number. method.bias A character string indicating which test for small-study effects is to be used for all outcomes. Either "rank", "linreg", or "mm", can be abbreviated. See function metabias method.bias.binary A character string indicating which test is to be used for binary outcomes. Either "rank", "linreg", "mm", "count", "score", or "peters", can be abbreviated. See function metabias method.bias.or A character string indicating which test is to be used for binary outcomes with odds ratio as summary measure. Either "rank", "linreg", "mm", "count", "score", or "peters", can be abbreviated. See function metabias Minimum number of studies to perform test for small-study effects. k.min Additional arguments (ignored at the moment)

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### **Details**

This function can be used to conduct a test for funnel plot asymmetry for all or selected metaanalyses in a Cochrane Review.

Review Manager 5 (RevMan 5) is the current software used for preparing and maintaining Cochrane Reviews (https://training.cochrane.org/online-learning/core-software-cochrane-reviews/revman). In RevMan 5, subgroup analyses can be defined and data from a Cochrane review can be imported to R using the function read.rm5.

The R function metacr is called internally.

### Author(s)

Guido Schwarzer <sc@imbi.uni-freiburg.de>

### References

Higgins, J.P.T and S. Green (2011): Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [Updated March 2011]. The Cochrane Library: http://www.cochrane-handbook.org/

### See Also

```
metabias, metacr, read.rm5, summary.rm5
```

### **Examples**

```
# Locate export data file "Fleiss1993_CR.csv" in sub-directory of
# package "meta"
#
filename <- system.file("extdata", "Fleiss1993_CR.csv", package = "meta")
Fleiss1993_CR <- read.rm5(filename)
# Print results for all tests of small-study effects
# metabias(Fleiss1993_CR, k.min = 5)
# Print result of test of small-study effects for second outcome in
# first comparison
# metabias(Fleiss1993_CR, comp.no = 1, outcome.no = 2, k.min = 5)</pre>
```

metabin

Meta-analysis of binary outcome data

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### **Description**

Calculation of common effect and random effects estimates (risk ratio, odds ratio, risk difference, arcsine difference, or diagnostic odds ratio) for meta-analyses with binary outcome data. Mantel-Haenszel, inverse variance, Peto method, generalised linear mixed model (GLMM), and sample size method are available for pooling. For GLMMs, the rma.glmm function from R package metafor (Viechtbauer, 2010) is called internally.

### **Usage**

```
metabin(
  event.e,
  n.e,
  event.c,
  n.c,
  studlab.
  data = NULL,
  subset = NULL,
  exclude = NULL,
  cluster = NULL,
  method = ifelse(tau.common, "Inverse", gs("method")),
 sm = ifelse(!is.na(charmatch(tolower(method), c("peto", "glmm", "ssw"), nomatch =
    NA)), "OR", gs("smbin")),
  incr = gs("incr"),
  method.incr = gs("method.incr"),
  allstudies = gs("allstudies"),
  MH.exact = gs("MH.exact"),
  RR.Cochrane = gs("RR.Cochrane"),
  Q.Cochrane = gs("Q.Cochrane") & method == "MH" & method.tau == "DL",
  model.glmm = gs("model.glmm"),
  level = gs("level"),
  level.ma = gs("level.ma"),
  common = gs("common"),
  random = gs("random") | !is.null(tau.preset),
  overall = common | random,
  overall.hetstat = common | random,
  hakn = gs("hakn"),
  adhoc.hakn = gs("adhoc.hakn"),
 method.tau = ifelse(!is.na(charmatch(tolower(method), "glmm", nomatch = NA)), "ML",
    gs("method.tau")),
  method.tau.ci = gs("method.tau.ci"),
  tau.preset = NULL,
  TE.tau = NULL,
  tau.common = gs("tau.common"),
  prediction = gs("prediction"),
  level.predict = gs("level.predict"),
  method.bias = ifelse(sm == "OR", "Harbord", ifelse(sm == "DOR", "Deeks",
    gs("method.bias"))),
  backtransf = gs("backtransf"),
```

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```
pscale = 1,
  text.common = gs("text.common"),
  text.random = gs("text.random"),
  text.predict = gs("text.predict"),
  text.w.common = gs("text.w.common"),
  text.w.random = gs("text.w.random"),
  title = gs("title"),
 complab = gs("complab"),
 outclab = "",
 label.e = gs("label.e"),
 label.c = gs("label.c"),
 label.left = gs("label.left"),
  label.right = gs("label.right"),
  subgroup,
  subgroup.name = NULL,
  print.subgroup.name = gs("print.subgroup.name"),
 sep.subgroup = gs("sep.subgroup"),
  test.subgroup = gs("test.subgroup"),
 prediction.subgroup = gs("prediction.subgroup"),
 byvar,
 print.CMH = gs("print.CMH"),
 keepdata = gs("keepdata"),
 warn = gs("warn"),
 warn.deprecated = gs("warn.deprecated"),
 control = NULL,
)
```

### **Arguments**

event.e	Number of events in experimental group or true positives in diagnostic study.
n.e	Number of observations in experimental group or number of ill participants in diagnostic study.
event.c	Number of events in control group or false positives in diagnostic study.
n.c	Number of observations in control group or number of healthy participants in diagnostic study.
studlab	An optional vector with study labels.
data	An optional data frame containing the study information, i.e., event.e, n.e, event.c, and n.c.
subset	An optional vector specifying a subset of studies to be used.
exclude	An optional vector specifying studies to exclude from meta-analysis, however, to include in printouts and forest plots.
cluster	An optional vector specifying which estimates come from the same cluster resulting in the use of a three-level meta-analysis model.
method	A character string indicating which method is to be used for pooling of studies. One of "Inverse", "MH", "Peto", "GLMM", or "SSW", can be abbreviated.

A character string indicating which summary measure ("RR", "OR", "RD", "ASD", sm or "DOR") is to be used for pooling of studies, see Details. incr Could be either a numerical value which is added to cell frequencies for studies with a zero cell count or the character string "TACC" which stands for treatment arm continuity correction, see Details. method.incr A character string indicating which continuity correction method should be used ("only0", "if0all", or "all"), see Details. allstudies A logical indicating if studies with zero or all events in both groups are to be included in the meta-analysis (applies only if sm is equal to "RR", "OR", or "DOR"). A logical indicating if incr is not to be added to cell frequencies for studies with MH.exact a zero cell count to calculate the pooled estimate based on the Mantel-Haenszel RR.Cochrane A logical indicating if 2\*incr instead of 1\*incr is to be added to n.e and n.c in the calculation of the risk ratio (i.e., sm="RR") for studies with a zero cell. This is used in RevMan 5, the program for preparing and maintaining Cochrane reviews. Q.Cochrane A logical indicating if the Mantel-Haenszel estimate is used in the calculation of the heterogeneity statistic Q which is implemented in RevMan 5, the program for preparing and maintaining Cochrane reviews. A character string indicating which GLMM should be used. One of "UM.FS", model.glmm "UM.RS", "CM.EL", and "CM.AL", see Details. level The level used to calculate confidence intervals for individual studies. The level used to calculate confidence intervals for meta-analysis estimates. level.ma common A logical indicating whether a common effect meta-analysis should be conducted. A logical indicating whether a random effects meta-analysis should be conrandom overall A logical indicating whether overall summaries should be reported. This argument is useful in a meta-analysis with subgroups if overall results should not be reported. overall.hetstat A logical value indicating whether to print heterogeneity measures for overall treatment comparisons. This argument is useful in a meta-analysis with subgroups if heterogeneity statistics should only be printed on subgroup level. hakn A logical indicating whether the method by Hartung and Knapp should be used to adjust test statistics and confidence intervals. A character string indicating whether an ad hoc variance correction should be adhoc.hakn applied in the case of an arbitrarily small Hartung-Knapp variance estimate, see Details. method.tau A character string indicating which method is used to estimate the betweenstudy variance  $\tau^2$  and its square root  $\tau$ . Either "DL", "PM", "REML", "ML", "HS", "SJ", "HE", or "EB", can be abbreviated. method.tau.ci A character string indicating which method is used to estimate the confidence interval of  $\tau^2$  and  $\tau$ . Either "QP", "BJ", "J", "PL", or "", can be abbreviated.

Prespecified value for the square root of the between-study variance  $\tau^2$ . tau.preset TE.tau Overall treatment effect used to estimate the between-study variance  $\tau^2$ . A logical indicating whether tau-squared should be the same across subgroups. tau.common prediction A logical indicating whether a prediction interval should be printed. level.predict The level used to calculate prediction interval for a new study. method.bias A character string indicating which test for funnel plot asymmetry is to be used. Either "Begg", "Egger", "Thompson", "Schwarzer", "Harbord", "Peters", or "Deeks", can be abbreviated. See function metabias. A logical indicating whether results for odds ratio (sm="OR"), risk ratio (sm="RR"), backtransf or diagnostic odds ratio (sm="DOR") should be back transformed in printouts and plots. If TRUE (default), results will be presented as odds ratios and risk ratios; otherwise log odds ratios and log risk ratios will be shown. A numeric defining a scaling factor for printing of risk differences. pscale A character string used in printouts and forest plot to label the pooled common text.common effect estimate. A character string used in printouts and forest plot to label the pooled random text.random effects estimate. text.predict A character string used in printouts and forest plot to label the prediction intertext.w.common A character string used to label weights of common effect model. text.w.random A character string used to label weights of random effects model. Title of meta-analysis / systematic review. title complab Comparison label. outclab Outcome label. label.e Label for experimental group. label.c Label for control group. label.left Graph label on left side of forest plot. label.right Graph label on right side of forest plot. subgroup An optional vector to conduct a meta-analysis with subgroups. subgroup.name A character string with a name for the subgroup variable. print.subgroup.name A logical indicating whether the name of the subgroup variable should be printed in front of the group labels. A character string defining the separator between name of subgroup variable and sep.subgroup subgroup label. A logical value indicating whether to print results of test for subgroup differtest.subgroup prediction.subgroup A logical indicating whether prediction intervals should be printed for subgroups.

Deprecated argument (replaced by 'subgroup').

byvar

print.CMH A logical indicating whether result of the Cochran-Mantel-Haenszel test for

overall effect should be printed.

keepdata A logical indicating whether original data (set) should be kept in meta object.

warn A logical indicating whether warnings should be printed (e.g., if incr is added

to studies with zero cell frequencies).

warn.deprecated

A logical indicating whether warnings should be printed if deprecated arguments

are used.

control An optional list to control the iterative process to estimate the between-study

variance  $\tau^2$ . This argument is passed on to rma.uni or rma.glmm, respectively.

... Additional arguments passed on to rma.glmm function and to catch deprecated

arguments.

### **Details**

Calculation of common and random effects estimates for meta-analyses with binary outcome data. The following measures of treatment effect are available (Rücker et al., 2009):

• Risk ratio (sm = "RR")

• Odds ratio (sm = "OR")

• Risk difference (sm = "RD")

• Arcsine difference (sm = "ASD")

• Diagnostic Odds ratio (sm = "DOR")

Note, mathematically, odds ratios and diagnostic odds ratios are identical, however, the labels in printouts and figures differ.

Default settings are utilised for several arguments (assignments using gs function). These defaults can be changed for the current R session using the settings.meta function.

Furthermore, R function update.meta can be used to rerun a meta-analysis with different settings.

# Meta-analysis method:

By default, both common effect (also called common effect) and random effects models are considered (see arguments common and random). If method is "MH" (default), the Mantel-Haenszel method (Greenland & Robins, 1985; Robins et al., 1986) is used to calculate the common effect estimate; if method is "Inverse", inverse variance weighting is used for pooling (Fleiss, 1993); if method is "Peto", the Peto method is used for pooling (Yussuf et al., 1985); if method is "SSW", the sample size method is used for pooling (Bakbergenuly et al., 2020).

While the Mantel-Haenszel and Peto method are defined under the common effect model, random effects variants based on these methods are also implemented in metabin. Following RevMan 5, the Mantel-Haenszel estimator is used in the calculation of the between-study heterogeneity statistic Q which is used in the DerSimonian-Laird estimator. Accordlingly, the results for the random effects meta-analysis using the Mantel-Haenszel or inverse variance method are typically very similar. For the Peto method, Peto's log odds ratio, i.e. (O-E) / V and its standard error sqrt(1 / V) with 0-E and V denoting "Observed minus Expected" and its variance, are utilised in the random effects model. Accordingly, results of a random effects model using sm = "Peto" can be different to results from a random effects model using sm = "Inverse".

A distinctive and frequently overlooked advantage of binary endpoints is that individual patient data (IPD) can be extracted from a two-by-two table. Accordingly, statistical methods for IPD, i.e., logistic regression and generalised linear mixed models, can be utilised in a meta-analysis of binary outcomes (Stijnen et al., 2010; Simmonds et al., 2016). These methods are available (argument method = "GLMM") for the odds ratio as summary measure by calling the rma.glmm function from R package **metafor** internally.

Four different GLMMs are available for meta-analysis with binary outcomes using argument model.glmm (which corresponds to argument model in the rma.glmm function):

- 1. Logistic regression model with common study effects (default) (model.glmm = "UM.FS", i.e., Unconditional Model Fixed Study effects)
- Mixed-effects logistic regression model with random study effects (model.glmm = "UM.RS", i.e., Unconditional Model - Random Study effects)
- 3. Generalised linear mixed model (conditional Hypergeometric-Normal) (model.glmm = "CM.EL", i.e., Conditional Model Exact Likelihood)
- 4. Generalised linear mixed model (conditional Binomial-Normal) (model.glmm = "CM.AL", i.e., Conditional Model Approximate Likelihood)

Details on these four GLMMs as well as additional arguments which can be provided using argument '...' in metabin are described in rma.glmm where you can also find information on the iterative algorithms used for estimation. Note, regardless of which value is used for argument model.glmm, results for two different GLMMs are calculated: common effect model (with fixed treatment effect) and random effects model (with random treatment effects).

#### **Continuity correction:**

Three approaches are available to apply a continuity correction:

- Only studies with a zero cell count (method.incr = "only0")
- All studies if at least one study has a zero cell count (method.incr = "if0all")
- All studies irrespective of zero cell counts (method.incr = "all")

By default, a continuity correction is only applied to studies with a zero cell count (method.incr = "only0"). This method showed the best performance for the odds ratio in a simulation study under the random effects model (Weber et al., 2020).

The continuity correction method is used both to calculate individual study results with confidence limits and to conduct meta-analysis based on the inverse variance method. For the risk difference, the method is only considered to calculate standard errors and confidence limits. For Peto method and GLMMs no continuity correction is used in the meta-analysis. Furthermore, the continuity correction is ignored for individual studies for the Peto method.

For studies with a zero cell count, by default, 0.5 (argument incr) is added to all cell frequencies for the odds ratio or only the number of events for the risk ratio (argument RR.Cochrane = FALSE, default). The increment is added to all cell frequencies for the risk ratio if argument RR.Cochrane = TRUE. For the risk difference, incr is only added to all cell frequencies to calculate the standard error. Finally, a treatment arm continuity correction is used if incr = "TACC" (Sweeting et al., 2004; Diamond et al., 2007).

For odds ratio and risk ratio, treatment estimates and standard errors are only calculated for studies with zero or all events in both groups if allstudies = TRUE.

For the Mantel-Haenszel method, by default (if MH. exact is FALSE), incr is added to cell frequencies of a study with a zero cell count in the calculation of the pooled risk ratio or odds ratio

as well as the estimation of the variance of the pooled risk difference, risk ratio or odds ratio. This approach is also used in other software, e.g. RevMan 5 and the Stata procedure metan. According to Fleiss (in Cooper & Hedges, 1994), there is no need to add 0.5 to a cell frequency of zero to calculate the Mantel-Haenszel estimate and he advocates the exact method (MH.exact = TRUE). Note, estimates based on exact Mantel-Haenszel method or GLMM are not defined if the number of events is zero in all studies either in the experimental or control group.

## **Estimation of between-study variance:**

The following methods to estimate the between-study variance  $\tau^2$  are available for the inverse variance method:

- DerSimonian-Laird estimator (method.tau = "DL")
- Paule-Mandel estimator (method.tau = "PM")
- Restricted maximum-likelihood estimator (method.tau = "REML")
- Maximum-likelihood estimator (method.tau = "ML")
- Hunter-Schmidt estimator (method.tau = "HS")
- Sidik-Jonkman estimator (method.tau = "SJ")
- Hedges estimator (method.tau = "HE")
- Empirical Bayes estimator (method. tau = "EB")

See metagen for more information on these estimators. Note, the maximum-likelihood method is utilized for GLMMs.

# Confidence interval for the between-study variance:

The following methods to calculate a confidence interval for  $\tau^2$  and  $\tau$  are available.

Argument	Method
method.tau.ci = "J"	Method by Jackson (2013)
method.tau.ci = "BJ"	Method by Biggerstaff and Jackson (2008)
<pre>method.tau.ci = "QP"</pre>	Q-Profile method (Viechtbauer, 2007)
<pre>method.tau.ci = "PL"</pre>	Profile-Likelihood method for three-level meta-analysis
	(Van den Noortgate et al., 2013)
method.tau.ci = ""	No confidence interval

See metagen for more information on these methods.

For GLMMs, no confidence intervals for  $\tau^2$  and  $\tau$  are calculated.

### Hartung-Knapp method:

Hartung and Knapp (2001a,b) proposed an alternative method for random effects meta-analysis based on a refined variance estimator for the treatment estimate. Simulation studies (Hartung and Knapp, 2001a,b; IntHout et al., 2014; Langan et al., 2019) show improved coverage probabilities compared to the classic random effects method.

In rare settings with very homogeneous treatment estimates, the Hartung-Knapp variance estimate can be arbitrarily small resulting in a very narrow confidence interval (Knapp and Hartung, 2003; Wiksten et al., 2016). In such cases, an *ad hoc* variance correction has been proposed by utilising the variance estimate from the classic random effects model with the HK method (Knapp and Hartung, 2003; IQWiQ, 2020). An alternative approach is to use the wider confidence interval of classic common or random effects meta-analysis and the HK method (Wiksten et al., 2016; Jackson et al., 2017).

Argument adhoc.hakn can be used to choose the *ad hoc* method:

Argument	Ad hoc method
adhoc.hakn = ""	not used
adhoc.hakn = "se"	use variance correction if HK standard error is smaller
	than standard error from classic random effects
	meta-analysis (Knapp and Hartung, 2003)
adhoc.hakn="iqwig6"	use variance correction if HK confidence interval
	is narrower than CI from classic random effects model
	with DerSimonian-Laird estimator (IQWiG, 2020)
adhoc.hakn = "ci"	use wider confidence interval of classic random effects
	and HK meta-analysis
	(Hybrid method 2 in Jackson et al., 2017)

For GLMMs, a method similar to Knapp and Hartung (2003) is implemented, see description of argument tdist in rma.glmm, and the *ad hoc* variance correction is not available.

### **Prediction interval:**

A prediction interval for the proportion in a new study (Higgins et al., 2009) is calculated if arguments prediction and random are TRUE. Note, the definition of prediction intervals varies in the literature. This function implements equation (12) of Higgins et al., (2009) which proposed a t distribution with K-2 degrees of freedom where K corresponds to the number of studies in the meta-analysis.

### Subgroup analysis:

Argument subgroup can be used to conduct subgroup analysis for a categorical covariate. The metareg function can be used instead for more than one categorical covariate or continuous covariates.

## **Exclusion of studies from meta-analysis:**

Arguments subset and exclude can be used to exclude studies from the meta-analysis. Studies are removed completely from the meta-analysis using argument subset, while excluded studies are shown in printouts and forest plots using argument exclude (see Examples in metagen). Meta-analysis results are the same for both arguments.

# **Presentation of meta-analysis results:**

Internally, both common effect and random effects models are calculated regardless of values choosen for arguments common and random. Accordingly, the estimate for the random effects model can be extracted from component TE.random of an object of class "meta" even if argument random = FALSE. However, all functions in R package **meta** will adequately consider the values for common and random. E.g. function print.meta will not print results for the random effects model if random = FALSE.

# Value

An object of class c("metabin", "meta") with corresponding print, summary, and forest functions. The object is a list containing the following components:

```
event.e, n.e, event.c, n.c, studlab, exclude, cluster, As defined above.
```

sm, method, incr, method.incr,

As defined above.

allstudies, MH.exact, RR.Cochrane, Q.Cochrane, model.glmm,

As defined above.

warn, level, level.ma, common, random,

As defined above.

overall, overall.hetstat,

As defined above.

hakn, adhoc.hakn, method.tau, method.tau.ci,

As defined above.

tau.preset, TE.tau, method.bias,

As defined above.

tau.common, title, complab, outclab,

As defined above.

label.e, label.c, label.left, label.right,

As defined above.

subgroup, subgroup.name,

As defined above.

print.subgroup.name, sep.subgroup, warn,

As defined above.

TE, seTE Estimated treatment effect and standard error of individual studies.

lower, upper Lower and upper confidence interval limits for individual studies.

zval, pval z-value and p-value for test of treatment effect for individual studies.

w.common, w.random

Weight of individual studies (in common effect and random effects model).

TE.common, seTE.common

Estimated overall treatment effect, e.g., log risk ratio or risk difference, and standard error (common effect model).

lower.common, upper.common

Lower and upper confidence interval limits (common effect model).

statistic.common, pval.common

z-value and p-value for test of overall treatment effect (common effect model).

TE.random, seTE.random

Estimated overall treatment effect, e.g., log risk ratio or risk difference, and standard error (random effects model).

lower.random, upper.random

Lower and upper confidence interval limits (random effects model).

statistic.random, pval.random

z-value or t-value and corresponding p-value for test of overall treatment effect (random effects model).

prediction, level.predict

As defined above.

seTE.predict Standard error utilised for prediction interval.

lower.predict, upper.predict

Lower and upper limits of prediction interval.

k Number of estimates combined in meta-analysis.k.study Number of studies combined in meta-analysis.

k.all Number of all studies.

k.TE Number of studies with estimable effects.

Q Heterogeneity statistic Q.

df.Q Degrees of freedom for heterogeneity statistic.

pval.Q P-value of heterogeneity test.

Q.LRT Heterogeneity statistic for likelihood-ratio test (only if method = "GLMM").

df.Q.LRT Degrees of freedom for likelihood-ratio test

pval.Q.LRT P-value of likelihood-ratio test. tau2 Between-study variance  $au^2$ .

se.tau2 Standard error of  $\tau^2$ .

lower.tau2, upper.tau2

Lower and upper limit of confidence interval for  $\tau^2$ .

tau Square-root of between-study variance  $\tau$ .

lower.tau, upper.tau

Lower and upper limit of confidence interval for  $\tau$ .

H Heterogeneity statistic H.

lower.H, upper.H

Lower and upper confidence limit for heterogeneity statistic H.

I2 Heterogeneity statistic I<sup>2</sup>.

lower.I2, upper.I2

Lower and upper confidence limit for heterogeneity statistic  $I^2$ .

Rb Heterogeneity statistic  $R_b$ .

lower.Rb, upper.Rb

Lower and upper confidence limit for heterogeneity statistic  $R_h$ .

O. CMH Cochran-Mantel-Haenszel test statistic for overall effect.

df.Q.CMH Degrees of freedom for Cochran-Mantel-Haenszel test statistic.

pval.Q.CMH P-value of Cochran-Mantel-Haenszel test.

incr.e, incr.c Increment added to cells in the experimental and control group, respectively.

sparse Logical flag indicating if any study included in meta-analysis has any zero cell

frequencies.

doublezeros Logical flag indicating if any study has zero cell frequencies in both treatment

groups.

df.hakn Degrees of freedom for test of treatment effect for Hartung-Knapp method (only

if hakn = TRUE).

k.MH Number of studies combined in meta-analysis using Mantel-Haenszel method.

bylevs Levels of grouping variable - if subgroup is not missing.

TE.common.w, seTE.common.w

Estimated treatment effect and standard error in subgroups (common effect model)

- if subgroup is not missing.

lower.common.w, upper.common.w

Lower and upper confidence interval limits in subgroups (common effect model) - if subgroup is not missing.

statistic.common.w, pval.common.w

z-value and p-value for test of treatment effect in subgroups (common effect model) - if subgroup is not missing.

TE.random.w, seTE.random.w

Estimated treatment effect and standard error in subgroups (random effects model) - if subgroup is not missing.

lower.random.w, upper.random.w

Lower and upper confidence interval limits in subgroups (random effects model) - if subgroup is not missing.

statistic.random.w, pval.random.w

z-value or t-value and corresponding p-value for test of treatment effect in subgroups (random effects model) - if subgroup is not missing.

w.common.w, w.random.w

Weight of subgroups (in common effect and random effects model) - if subgroup is not missing.

df.hakn.w Degrees of freedom for test of treatment effect for Hartung-Knapp method in subgroups - if subgroup is not missing and hakn = TRUE.

event.e.w Number of events in experimental group in subgroups - if subgroup is not missing.

n.e.w Number of observations in experimental group in subgroups - if subgroup is not missing.

event.c.w Number of events in control group in subgroups - if subgroup is not missing.

n.c.w Number of observations in control group in subgroups - if subgroup is not missing.

k.w Number of studies combined within subgroups - if subgroup is not missing.

k.all.w Number of all studies in subgroups - if subgroup is not missing.

Q.w.common Overall within subgroups heterogeneity statistic Q (based on common effect model) - if subgroup is not missing.

Q.w.random Overall within subgroups heterogeneity statistic Q (based on random effects model) - if subgroup is not missing (only calculated if argument tau.common is TRUE).

df.Q.w Degrees of freedom for test of overall within subgroups heterogeneity - if subgroup is not missing.

pval.Q.w.common

P-value of within subgroups heterogeneity statistic Q (based on common effect model) - if subgroup is not missing.

pval.Q.w.random

P-value of within subgroups heterogeneity statistic Q (based on random effects model) - if subgroup is not missing.

Q.b. common Overall between subgroups heterogeneity statistic Q (based on common effect model) - if subgroup is not missing.

Q.b.random Overall between subgroups heterogeneity statistic Q (based on random effects model) - if subgroup is not missing.

df.Q.b Degrees of freedom for test of overall between subgroups heterogeneity - if

subgroup is not missing.

pval.Q.b.common

P-value of between subgroups heterogeneity statistic Q (based on common effect model) - if subgroup is not missing.

pval.Q.b.random

H.w

P-value of between subgroups heterogeneity statistic Q (based on random effects model) - if subgroup is not missing.

tau.w Square-root of between-study variance within subgroups - if subgroup is not missing.

Heterogeneity statistic H within subgroups - if subgroup is not missing.

lower.H.w, upper.H.w

Lower and upper confidence limit for heterogeneity statistic H within subgroups - if subgroup is not missing.

I2. w Heterogeneity statistic  $I^2$  within subgroups - if subgroup is not missing.

lower.I2.w, upper.I2.w

Lower and upper confidence limit for heterogeneity statistic I<sup>2</sup> within subgroups - if subgroup is not missing.

keepdata As defined above.

data Original data (set) used in function call (if keepdata = TRUE).

subset Information on subset of original data used in meta-analysis (if keepdata =

TRUE).

.glmm.common GLMM object generated by call of rma.glmm function (common effect model).
.glmm.random GLMM object generated by call of rma.glmm function (random effects model).

call Function call.

version Version of R package **meta** used to create object.

version.metafor

Version of R package **metafor** used for GLMMs.

# Author(s)

Guido Schwarzer <sc@imbi.uni-freiburg.de>

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## See Also

```
update.meta, forest, funnel, metabias, metacont, metagen, metareg, print.meta
```

# **Examples**

```
# Calculate odds ratio and confidence interval for a single study
metabin(10, 20, 15, 20, sm = "OR")
# Different results (due to handling of studies with double zeros)
metabin(0, 10, 0, 10, sm = "OR")
metabin(0, 10, 0, 10, sm = "OR", all studies = TRUE)
# Use subset of Olkin (1995) to conduct meta-analysis based on
# inverse variance method (with risk ratio as summary measure)
data(Olkin1995)
m1 <- metabin(ev.exp, n.exp, ev.cont, n.cont,</pre>
  data = 01kin1995, subset = c(41, 47, 51, 59),
  studlab = paste(author, year),
  method = "Inverse")
# Show results for individual studies
summary(m1)
# Use different subset of Olkin (1995)
m2 <- metabin(ev.exp, n.exp, ev.cont, n.cont,</pre>
  data = Olkin1995, subset = year < 1970,
  studlab = paste(author, year),
  method = "Inverse")
m2
forest(m2)
# Meta-analysis with odds ratio as summary measure
#
m3 <- metabin(ev.exp, n.exp, ev.cont, n.cont,
 data = Olkin1995, subset = year < 1970,
 studlab = paste(author, year),
  sm = "OR", method = "Inverse")
# Same meta-analysis result using 'update.meta' function
m3 \leftarrow update(m2, sm = "OR")
m3
# Meta-analysis based on Mantel-Haenszel method (with odds ratio as
# summary measure)
m4 <- update(m3, method = "MH")</pre>
m4
# Meta-analysis based on Peto method (only available for odds ratio
```

```
# as summary measure)
m5 <- update(m3, method = "Peto")</pre>
## Not run:
# Meta-analysis using generalised linear mixed models
# (only if R package 'lme4' is available)
\# Logistic regression model with (k = 4) fixed study effects
# (default: model.glmm = "UM.FS")
m6 <- metabin(ev.exp, n.exp, ev.cont, n.cont,</pre>
  studlab = paste(author, year),
  data = Olkin1995, subset = year < 1970, method = "GLMM")
# Same results:
m6 <- update(m2, method = "GLMM")</pre>
m6
# Mixed-effects logistic regression model with random study effects
# (warning message printed due to argument 'nAGQ')
m7 <- update(m6, model.glmm = "UM.RS")
# Use additional argument 'nAGQ' for internal call of 'rma.glmm'
m7 <- update(m6, model.glmm = "UM.RS", nAGQ = 1)
m7
# Generalised linear mixed model (conditional Hypergeometric-Normal)
# (R package 'BiasedUrn' must be available)
m8 <- update(m6, model.glmm = "CM.EL")
m8
# Generalised linear mixed model (conditional Binomial-Normal)
m9 <- update(m6, model.glmm = "CM.AL")</pre>
# Logistic regression model with (k = 70) fixed study effects
# (about 18 seconds with Intel Core i7-3667U, 2.0GHz)
m10 <- metabin(ev.exp, n.exp, ev.cont, n.cont,</pre>
   studlab = paste(author, year),
   data = Olkin1995, method = "GLMM")
m10
# Mixed-effects logistic regression model with random study effects
# - about 50 seconds with Intel Core i7-3667U, 2.0GHz
# - several warning messages, e.g. "failure to converge, ..."
```

```
#
update(m10, model.glmm = "UM.RS")

# Conditional Hypergeometric-Normal GLMM
# - long computation time (about 12 minutes with Intel Core
# i7-3667U, 2.0GHz)
# - estimation problems for this very large dataset:
# * warning that Choleski factorization of Hessian failed
# * confidence interval for treatment effect smaller in random
# effects model compared to common effect model
#
system.time(m11 <- update(m10, model.glmm = "CM.EL"))
m11

# Generalised linear mixed model (conditional Binomial-Normal)
# (less than 1 second with Intel Core i7-3667U, 2.0GHz)
#
update(m10, model.glmm = "CM.AL")

## End(Not run)</pre>
```

metabind

Combine and summarize meta-analysis objects

# Description

This function can be used to combine meta-analysis objects and is, for example, useful to summarize results of various meta-analysis methods or to generate a forest plot with results of several subgroup analyses.

## Usage

```
metabind(..., name = NULL, pooled = NULL, backtransf = NULL, outclab = NULL)
```

# **Arguments**

... Any number of meta-analysis objects or a single list with meta-analyses.

name An optional character vector providing descriptive names for the meta-analysis

objects.

pooled A character string or vector indicating whether results of a common effect or

random effects model should be considered. Either "common" or "random", can

be abbreviated.

backtransf A logical indicating whether results should be back transformed in printouts and

plots. If backtransf=TRUE (default), results for sm="OR" are printed as odds

ratios rather than log odds ratios, for example.

outclab Outcome label for all meta-analyis objects.

### **Details**

This function can be used to combine any number of meta-analysis objects which is useful, for example, to summarize results of various meta-analysis methods or to generate a forest plot with results of several subgroup analyses (see Examples).

Individual study results are not retained with metabind. This is possible using R function metamerge which, however, can only be used to combine results of two meta-analyses.

### Value

An object of class c("metabind", "meta") with corresponding print, summary, and forest functions. See metagen for more information on list elements.

### Author(s)

Guido Schwarzer <sc@imbi.uni-freiburg.de>

#### See Also

```
metagen, forest.metabind, metamerge
```

## **Examples**

```
data(Fleiss1993cont)
# Add some (fictitious) grouping variables:
Fleiss1993cont$age <- c(55, 65, 55, 65, 55)
Fleiss1993cont$region <- c("Europe", "Europe", "Asia", "Asia", "Europe")
m1 <- metacont(n.psyc, mean.psyc, sd.psyc, n.cont, mean.cont, sd.cont,</pre>
  data = Fleiss1993cont, sm = "MD")
# Conduct two subgroup analyses
mu1 <- update(m1, subgroup = age, subgroup.name = "Age group")</pre>
mu2 <- update(m1, subgroup = region, subgroup.name = "Region")</pre>
# Combine subgroup meta-analyses and show forest plot with subgroup
# results
mb1 <- metabind(mu1, mu2)</pre>
mb1
forest(mb1)
# Use various estimation methods for between-study heterogeneity
m1.pm <- update(m1, method.tau = "PM")</pre>
m1.dl <- update(m1, method.tau = "DL")</pre>
m1.ml <- update(m1, method.tau = "ML")</pre>
m1.hs <- update(m1, method.tau = "HS")</pre>
```

```
m1.sj <- update(m1, method.tau = "SJ")</pre>
m1.he <- update(m1, method.tau = "HE")</pre>
m1.eb <- update(m1, method.tau = "EB")</pre>
# Combine meta-analyses and show results
taus <- c("Restricted maximum-likelihood estimator",</pre>
  "Paule-Mandel estimator",
  "DerSimonian-Laird estimator",
  "Maximum-likelihood estimator",
  "Hunter-Schmidt estimator",
  "Sidik-Jonkman estimator",
  "Hedges estimator",
  "Empirical Bayes estimator")
#
m1.taus \leftarrow metabind(m1, m1.pm, m1.dl, m1.ml, m1.hs, m1.sj, m1.he, m1.eb,
  name = taus, pooled = "random")
forest(m1.taus, print.I2 = FALSE, print.pval.Q = FALSE)
```

metacont

Meta-analysis of continuous outcome data

# **Description**

Calculation of common and random effects estimates for meta-analyses with continuous outcome data; inverse variance weighting is used for pooling.

## Usage

```
metacont(
  n.e,
 mean.e,
  sd.e,
  n.c,
 mean.c,
  sd.c,
  studlab,
  data = NULL,
  subset = NULL,
  exclude = NULL,
  cluster = NULL,
  median.e,
  q1.e,
  q3.e,
 min.e,
  max.e,
 median.c,
```

```
q1.c,
q3.c,
min.c,
max.c,
method.mean = "Luo",
method.sd = "Shi",
approx.mean.e,
approx.mean.c = approx.mean.e,
approx.sd.e,
approx.sd.c = approx.sd.e,
sm = gs("smcont"),
pooledvar = gs("pooledvar"),
method.smd = gs("method.smd"),
sd.glass = gs("sd.glass"),
exact.smd = gs("exact.smd"),
method.ci = gs("method.ci.cont"),
level = gs("level"),
level.ma = gs("level.ma"),
common = gs("common"),
random = gs("random") | !is.null(tau.preset),
overall = common | random,
overall.hetstat = common | random,
hakn = gs("hakn"),
adhoc.hakn = gs("adhoc.hakn"),
method.tau = gs("method.tau"),
method.tau.ci = gs("method.tau.ci"),
tau.preset = NULL,
TE.tau = NULL,
tau.common = gs("tau.common"),
prediction = gs("prediction"),
level.predict = gs("level.predict"),
method.bias = gs("method.bias"),
backtransf = gs("backtransf"),
text.common = gs("text.common"),
text.random = gs("text.random"),
text.predict = gs("text.predict"),
text.w.common = gs("text.w.common"),
text.w.random = gs("text.w.random"),
title = gs("title"),
complab = gs("complab"),
outclab = "",
label.e = gs("label.e"),
label.c = gs("label.c"),
label.left = gs("label.left"),
label.right = gs("label.right"),
subgroup,
subgroup.name = NULL,
print.subgroup.name = gs("print.subgroup.name"),
```

```
sep.subgroup = gs("sep.subgroup"),
test.subgroup = gs("test.subgroup"),
prediction.subgroup = gs("prediction.subgroup"),
byvar,
id,
keepdata = gs("keepdata"),
warn = gs("warn"),
warn.deprecated = gs("warn.deprecated"),
control = NULL,
...
)
```

# Arguments

n.e	Number of observations in experimental group.
mean.e	Estimated mean in experimental group.
sd.e	Standard deviation in experimental group.
n.c	Number of observations in control group.
mean.c	Estimated mean in control group.
sd.c	Standard deviation in control group.
studlab	An optional vector with study labels.
data	An optional data frame containing the study information.
subset	An optional vector specifying a subset of studies to be used.
exclude	An optional vector specifying studies to exclude from meta-analysis, however, to include in printouts and forest plots.
cluster	An optional vector specifying which estimates come from the same cluster resulting in the use of a three-level meta-analysis model.
median.e	Median in experimental group (used to estimate the mean and standard deviation).
q1.e	First quartile in experimental group (used to estimate the mean and standard deviation).
q3.e	Third quartile in experimental group (used to estimate the mean and standard deviation).
min.e	Minimum in experimental group (used to estimate the mean and standard deviation).
max.e	Maximum in experimental group (used to estimate the mean and standard deviation).
median.c	Median in control group (used to estimate the mean and standard deviation).
q1.c	First quartile in control group (used to estimate the mean and standard deviation).
q3.c	Third quartile in control group (used to estimate the mean and standard deviation).
min.c	Minimum in control group (used to estimate the mean and standard deviation).

max.c	Maximum in control group (used to estimate the mean and standard deviation).
method.mean	A character string indicating which method to use to approximate the mean from the median and other statistics (see Details).
method.sd	A character string indicating which method to use to approximate the standard deviation from sample size, median, interquartile range and range (see Details).
approx.mean.e	Approximation method to estimate means in experimental group (see Details).
approx.mean.c	Approximation method to estimate means in control group (see Details).
approx.sd.e	Approximation method to estimate standard deviations in experimental group (see Details).
approx.sd.c	Approximation method to estimate standard deviations in control group (see Details).
SM	A character string indicating which summary measure ("MD", "SMD", or "ROM") is to be used for pooling of studies.
pooledvar	A logical indicating if a pooled variance should be used for the mean difference $(sm="MD")$ .
method.smd	A character string indicating which method is used to estimate the standardised mean difference (sm="SMD"). Either "Hedges" for Hedges' g (default), "Cohen" for Cohen's d, or "Glass" for Glass' delta, can be abbreviated.
sd.glass	A character string indicating which standard deviation is used in the denominator for Glass' method to estimate the standardised mean difference. Either "control" using the standard deviation in the control group (sd.c) or "experimental" using the standard deviation in the experimental group (sd.e), can be abbreviated.
exact.smd	A logical indicating whether exact formulae should be used in estimation of the standardised mean difference and its standard error (see Details).
method.ci	A character string indicating which method is used to calculate confidence intervals for individual studies, see Details.
level	The level used to calculate confidence intervals for individual studies.
level.ma	The level used to calculate confidence intervals for meta-analysis estimates.
common	A logical indicating whether a common effect meta-analysis should be conducted.
random	A logical indicating whether a random effects meta-analysis should be conducted.
overall	A logical indicating whether overall summaries should be reported. This argument is useful in a meta-analysis with subgroups if overall results should not be reported.
overall.hetstat	
	A logical value indicating whether to print heterogeneity measures for overall treatment comparisons. This argument is useful in a meta-analysis with subgroups if heterogeneity statistics should only be printed on subgroup level.
hakn	A logical indicating whether the method by Hartung and Knapp should be used to adjust test statistics and confidence intervals.

A character string indicating whether an ad hoc variance correction should be adhoc.hakn applied in the case of an arbitrarily small Hartung-Knapp variance estimate, see Details. method.tau A character string indicating which method is used to estimate the betweenstudy variance  $\tau^2$  and its square root  $\tau$ . Either "DL", "PM", "REML", "ML", "HS", "SJ", "HE", or "EB", can be abbreviated. method.tau.ci A character string indicating which method is used to estimate the confidence interval of  $\tau^2$  and  $\tau$ . Either "QP", "BJ", "J", "PL", or "", can be abbreviated. tau.preset Prespecified value for the square root of the between-study variance  $\tau^2$ . TE.tau Overall treatment effect used to estimate the between-study variance tau-squared. tau.common A logical indicating whether tau-squared should be the same across subgroups. prediction A logical indicating whether a prediction interval should be printed. level.predict The level used to calculate prediction interval for a new study. method.bias A character string indicating which test is to be used. Either "Begg", "Egger", "Thompson", or "Pustejovsky", can be abbreviated. See function metabias. backtransf A logical indicating whether results for ratio of means (sm="ROM") should be back transformed in printouts and plots. If TRUE (default), results will be presented as ratio of means; otherwise log ratio of means will be shown. text.common A character string used in printouts and forest plot to label the pooled common effect estimate. text.random A character string used in printouts and forest plot to label the pooled random effects estimate. text.predict A character string used in printouts and forest plot to label the prediction inter-A character string used to label weights of common effect model. text.w.common text.w.random A character string used to label weights of random effects model. Title of meta-analysis / systematic review. title complab Comparison label. outclab Outcome label. label.e Label for experimental group. label.c Label for control group. label.left Graph label on left side of forest plot. label.right Graph label on right side of forest plot. subgroup An optional vector to conduct a meta-analysis with subgroups. subgroup.name A character string with a name for the subgroup variable. print.subgroup.name A logical indicating whether the name of the subgroup variable should be printed in front of the group labels. sep.subgroup A character string defining the separator between name of subgroup variable and

subgroup label.

test.subgroup A logical value indicating whether to print results of test for subgroup differ-

ences.

prediction.subgroup

A logical indicating whether prediction intervals should be printed for sub-

groups.

byvar Deprecated argument (replaced by 'subgroup').

id Deprecated argument (replaced by 'cluster').

keepdata A logical indicating whether original data (set) should be kept in meta object.

warn A logical indicating whether warnings should be printed (e.g., if studies are

excluded from meta-analysis due to zero standard deviations).

warn.deprecated

A logical indicating whether warnings should be printed if deprecated arguments

are used.

control An optional list to control the iterative process to estimate the between-study

variance  $\tau^2$ . This argument is passed on to rma.uni.

. . . Additional arguments (to catch deprecated arguments).

#### **Details**

Calculation of common and random effects estimates for meta-analyses with continuous outcome data; inverse variance weighting is used for pooling.

Three different types of summary measures are available for continuous outcomes:

• mean difference (argument sm = "MD")

• standardised mean difference (sm = "SMD")

• ratio of means (sm = "ROM")

Default settings are utilised for several arguments (assignments using gs function). These defaults can be changed for the current R session using the settings.meta function.

Furthermore, R function update.meta can be used to rerun a meta-analysis with different settings.

### Standardised mean difference:

For the standardised mean difference three methods are implemented:

- Hedges' g (default, method.smd = "Hedges") see Hedges (1981)
- Cohen's d (method.smd = "Cohen") see Cohen (1988)
- Glass' delta (method.smd = "Glass") see Glass (1976)

Hedges (1981) calculated the exact bias in Cohen's d which is a ratio of gamma distributions with the degrees of freedom, i.e. total sample size minus two, as argument. By default (argument exact.smd = FALSE), an accurate approximation of this bias provided in Hedges (1981) is utilised for Hedges' g as well as its standard error; these approximations are also used in RevMan 5. Following Borenstein et al. (2009) these approximations are not used in the estimation of Cohen's d. White and Thomas (2005) argued that approximations are unnecessary with modern software and accordingly promote to use the exact formulae; this is possible using argument exact.smd = TRUE. For Hedges' g the exact formulae are used to calculate the standardised mean difference as well as the standard error; for Cohen's d the exact formula is only used to calculate the standard

error. In typical applications (with sample sizes above 10), the differences between using the exact formulae and the approximation will be minimal.

For Glass' delta, by default (argument sd.glass = "control"), the standard deviation in the control group (sd.c) is used in the denominator of the standard mean difference. The standard deviation in the experimental group (sd.e) can be used by specifying sd.glass = "experimental".

#### Ratio of means:

Meta-analysis of ratio of means – also called response ratios – is described in Hedges et al. (1999) and Friedrich et al. (2008). Calculations are conducted on the log scale and list elements TE, TE.common, and TE.random contain the logarithm of the ratio of means. In printouts and plots these values are back transformed if argument backtransf = TRUE.

### Approximate means from sample sizes, medians and other statistics:

Missing means in the experimental group (analogously for the control group) can be derived from

- 1. sample size, median, interquartile range and range (arguments n.e, median.e, q1.e, q3.e, min.e, and max.e),
- 2. sample size, median and interquartile range (arguments n.e, median.e, q1.e, and q3.e), or
- 3. sample size, median and range (arguments n.e, median.e, min.e, and max.e).

By default, methods described in Luo et al. (2018) are utilized (argument method. mean = "Luo"):

- equation (15) if sample size, median, interquartile range and range are available,
- equation (11) if sample size, median and interquartile range are available,
- equation (7) if sample size, median and range are available.

Instead the methods described in Wan et al. (2014) are used if argument method. mean = "Wan":

- equation (10) if sample size, median, interquartile range and range are available,
- equation (14) if sample size, median and interquartile range are available,
- equation (2) if sample size, median and range are available.

By default, missing means are replaced successively using interquartile ranges and ranges (if available), interquartile ranges (if available) and finally ranges. Arguments approx.mean.e and approx.mean.c can be used to overwrite this behaviour for each individual study and treatment arm:

- use means directly (entry "" in argument approx.mean.e or approx.mean.c);
- median, interquartile range and range ("iqr.range");
- median and interquartile range ("iqr");
- median and range ("range").

# Approximate standard deviations from sample sizes, medians and other statistics:

Missing standard deviations in the experimental group (analogously for the control group) can be derived from

- 1. sample size, median, interquartile range and range (arguments n.e, median.e, q1.e, q3.e, min.e, and max.e),
- 2. sample size, median and interquartile range (arguments n.e, median.e, q1.e and q3.e), or
- 3. sample size, median and range (arguments n.e, median.e, min.e and max.e).

Wan et al. (2014) describe methods to estimate the standard deviation from the sample size, median and additional statistics. Shi et al. (2020) provide an improved estimate of the standard deviation if the interquartile range and range are available in addition to the sample size and median. Accordingly, equation (11) in Shi et al. (2020) is the default (argument method.sd = "Shi"), if the median, interquartile range and range are provided. The method by Wan et al. (2014) is used if argument method.sd = "Wan" and, depending on the sample size, either equation (12) or (13) is used. If only the interquartile range or range is available, equations (15) / (16) and (7) / (9) in Wan et al. (2014) are used, respectively.

By default, missing standard deviations are replaced successively using these method, i.e., interquartile ranges and ranges are used before interquartile ranges before ranges. Arguments approx.sd.e and approx.sd.c can be used to overwrite this default for each individual study and treatment arms:

- sample size, median, interquartile range and range ("iqr.range");
- sample size, median and interquartile range ("iqr");
- sample size, median and range ("range").

#### Confidence intervals for individual studies:

For the mean difference (argument sm = "MD"), the confidence interval for individual studies can be based on the

- standard normal distribution (method.ci = "z", default), or
- t-distribution (method.ci = "t").

Note, this choice does not affect the results of the common effect and random effects metaanalysis.

# **Estimation of between-study variance:**

The following methods to estimate the between-study variance  $\tau^2$  are available:

- DerSimonian-Laird estimator (method.tau = "DL")
- Paule-Mandel estimator (method.tau = "PM")
- Restricted maximum-likelihood estimator (method.tau = "REML")
- Maximum-likelihood estimator (method.tau = "ML")
- Hunter-Schmidt estimator (method.tau = "HS")
- Sidik-Jonkman estimator (method.tau = "SJ")
- Hedges estimator (method.tau = "HE")
- Empirical Bayes estimator (method.tau = "EB")

See metagen for more information on these estimators.

### Confidence interval for the between-study variance:

The following methods to calculate a confidence interval for  $\tau^2$  and  $\tau$  are available.

Argument	Method
method.tau.ci = "J"	Method by Jackson (2013)
method.tau.ci = "BJ"	Method by Biggerstaff and Jackson (2008)
<pre>method.tau.ci = "QP"</pre>	Q-Profile method (Viechtbauer, 2007)
method.tau.ci = "PL"	Profile-Likelihood method for three-level meta-analysis
	(Van den Noortgate et al., 2013)
<pre>method.tau.ci = ""</pre>	No confidence interval

See metagen for more information on these methods.

# Hartung-Knapp method:

Hartung and Knapp (2001) proposed an alternative method for random effects meta-analysis based on a refined variance estimator for the treatment estimate. Simulation studies (Hartung and Knapp, 2001; IntHout et al., 2014; Langan et al., 2019) show improved coverage probabilities compared to the classic random effects method.

In rare settings with very homogeneous treatment estimates, the Hartung-Knapp variance estimate can be arbitrarily small resulting in a very narrow confidence interval (Knapp and Hartung, 2003; Wiksten et al., 2016). In such cases, an *ad hoc* variance correction has been proposed by utilising the variance estimate from the classic random effects model with the HK method (Knapp and Hartung, 2003; IQWiQ, 2020). An alternative approach is to use the wider confidence interval of classic common or random effects meta-analysis and the HK method (Wiksten et al., 2016; Jackson et al., 2017).

Argument adhoc. hakn can be used to choose the *ad hoc* method:

Argument	Ad hoc method
adhoc.hakn = ""	not used
adhoc.hakn = "se"	use variance correction if HK standard error is smaller
	than standard error from classic random effects
	meta-analysis (Knapp and Hartung, 2003)
adhoc.hakn="iqwig6"	use variance correction if HK confidence interval
	is narrower than CI from classic random effects model
	with DerSimonian-Laird estimator (IQWiG, 2020)
adhoc.hakn = "ci"	use wider confidence interval of classic random effects
	and HK meta-analysis
	(Hybrid method 2 in Jackson et al., 2017)

## **Prediction interval:**

A prediction interval for the proportion in a new study (Higgins et al., 2009) is calculated if arguments prediction and random are TRUE. Note, the definition of prediction intervals varies in the literature. This function implements equation (12) of Higgins et al., (2009) which proposed a t distribution with K-2 degrees of freedom where K corresponds to the number of studies in the meta-analysis.

### **Subgroup analysis:**

Argument subgroup can be used to conduct subgroup analysis for a categorical covariate. The metareg function can be used instead for more than one categorical covariate or continuous covariates.

## **Exclusion of studies from meta-analysis:**

Arguments subset and exclude can be used to exclude studies from the meta-analysis. Studies are removed completely from the meta-analysis using argument subset, while excluded studies are shown in printouts and forest plots using argument exclude (see Examples in metagen). Meta-analysis results are the same for both arguments.

## Presentation of meta-analysis results:

Internally, both common effect and random effects models are calculated regardless of values choosen for arguments common and random. Accordingly, the estimate for the random effects

model can be extracted from component TE.random of an object of class "meta" even if argument random = FALSE. However, all functions in R package **meta** will adequately consider the values for common and random. E.g. function print.meta will not print results for the random effects model if random = FALSE.

#### Value

An object of class c("metacont", "meta") with corresponding print, summary, and forest functions. The object is a list containing the following components:

n.e, mean.e, sd.e,

As defined above.

n.c, mean.c, sd.c,

As defined above.

studlab, exclude, cluster, sm, method.ci,

As defined above.

median.e, q1.e, q3.e, min.e, max.e,

As defined above.

median.c, q1.c, q3.c, min.c, max.c,

As defined above.

method.mean, method.sd,

As defined above.

approx.mean.e, approx.sd.e, approx.mean.c, approx.sd.c,

As defined above.

level, level.ma,

As defined above.

common, random,

As defined above.

overall, overall.hetstat,

As defined above.

pooledvar, method.smd, sd.glass,

As defined above.

hakn, adhoc.hakn, method.tau, method.tau.ci,

As defined above.

tau.preset, TE.tau, method.bias,

As defined above.

tau.common, title, complab, outclab,

As defined above.

label.e, label.c, label.left, label.right,

As defined above.

subgroup, subgroup.name,

As defined above.

print.subgroup.name, sep.subgroup, warn,

As defined above.

TE, seTE Estimated treatment effect and standard error of individual studies.

lower, upper Lower and upper confidence interval limits for individual studies.

statistic, pval

Statistic and p-value for test of treatment effect for individual studies.

w.common, w.random

Weight of individual studies (in common effect and random effects model).

TE.common, seTE.common

Estimated overall treatment effect and standard error (common effect model).

lower.common, upper.common

Lower and upper confidence interval limits (common effect model).

statistic.common, pval.common

Statistic and p-value for test of overall treatment effect (common effect model).

TE.random, seTE.random

Estimated overall treatment effect and standard error (random effects model).

lower.random, upper.random

Lower and upper confidence interval limits (random effects model).

statistic.random, pval.random

Statistic and p-value for test of overall treatment effect (random effects model).

prediction, level.predict

As defined above.

seTE.predict Standard error utilised for prediction interval.

lower.predict, upper.predict

Lower and upper limits of prediction interval.

k Number of estimates combined in meta-analysis.

k.study Number of studies combined in meta-analysis.

k.all Number of all studies.

k.TE Number of studies with estimable effects.

Q Heterogeneity statistic Q.

df.Q Degrees of freedom for heterogeneity statistic.

pval.Q P-value of heterogeneity test. tau2 Between-study variance  $\tau^2$ .

se. tau2 Standard error of  $\tau^2$ .

lower.tau2, upper.tau2

Lower and upper limit of confidence interval for  $\tau^2$ .

tau Square-root of between-study variance  $\tau$ .

lower.tau, upper.tau

Lower and upper limit of confidence interval for  $\tau$ .

H Heterogeneity statistic H.

lower.H, upper.H

Lower and upper confidence limit for heterogeneity statistic H.

Heterogeneity statistic  $I^2$ .

lower.I2, upper.I2

Lower and upper confidence limit for heterogeneity statistic  $I^2$ .

Rb Heterogeneity statistic  $R_b$ .

lower.Rb, upper.Rb

Lower and upper confidence limit for heterogeneity statistic  $R_b$ .

df.hakn Degrees of freedom for test of treatment effect for Hartung-Knapp method (only

if hakn = TRUE).

method Pooling method: "Inverse".

bylevs Levels of grouping variable - if subgroup is not missing.

TE.common.w, seTE.common.w

Estimated treatment effect and standard error in subgroups (common effect model)

- if subgroup is not missing.

lower.common.w, upper.common.w

Lower and upper confidence interval limits in subgroups (common effect model)

- if subgroup is not missing.

statistic.common.w, pval.common.w

Statistics and p-values for test of treatment effect in subgroups (common effect

model) - if subgroup is not missing. TE.random.w, seTE.random.w

Estimated treatment effect and standard error in subgroups (random effects model)

- if subgroup is not missing.

lower.random.w, upper.random.w

Lower and upper confidence interval limits in subgroups (random effects model)

- if subgroup is not missing.

statistic.random.w, pval.random.w

Statistics and p-values for test of treatment effect in subgroups (random effects

model) - if subgroup is not missing.

w.common.w, w.random.w

Weight of subgroups (in common effect and random effects model) - if subgroup

is not missing.

df.hakn.w Degrees of freedom for test of treatment effect for Hartung-Knapp method in

subgroups - if subgroup is not missing and hakn = TRUE.

n.e.w Number of observations in experimental group in subgroups - if subgroup is not

missing.

n.c.w Number of observations in control group in subgroups - if subgroup is not miss-

ing.

k.w Number of studies combined within subgroups - if subgroup is not missing.

k.all.w Number of all studies in subgroups - if subgroup is not missing.

Q.w.common Overall within subgroups heterogeneity statistic Q (based on common effect

model) - if subgroup is not missing.

O.w.random Overall within subgroups heterogeneity statistic O (based on random effects

model) - if subgroup is not missing (only calculated if argument tau. common is

TRUE).

df.Q.w Degrees of freedom for test of overall within subgroups heterogeneity - if subgroup

is not missing.

pval.Q.w.common

P-value of within subgroups heterogeneity statistic Q (based on common effect

model) - if subgroup is not missing.

pval.Q.w.random

P-value of within subgroups heterogeneity statistic Q (based on random effects

model) - if subgroup is not missing.

Q.b.common Overall between subgroups heterogeneity statistic Q (based on common effect

model) - if subgroup is not missing.

Q.b.random Overall between subgroups heterogeneity statistic Q (based on random effects

model) - if subgroup is not missing.

df.Q.b Degrees of freedom for test of overall between subgroups heterogeneity - if

subgroup is not missing.

pval.Q.b.common

P-value of between subgroups heterogeneity statistic Q (based on common effect

model) - if subgroup is not missing.

pval.Q.b.random

P-value of between subgroups heterogeneity statistic Q (based on random effects

model) - if subgroup is not missing.

tau.w Square-root of between-study variance within subgroups - if subgroup is not

missing.

H.w Heterogeneity statistic H within subgroups - if subgroup is not missing.

lower.H.w, upper.H.w

Lower and upper confidence limit for heterogeneity statistic H within subgroups

- if subgroup is not missing.

12.w Heterogeneity statistic I<sup>2</sup> within subgroups - if subgroup is not missing.

lower.I2.w, upper.I2.w

Lower and upper confidence limit for heterogeneity statistic I<sup>2</sup> within subgroups

- if subgroup is not missing.

keepdata As defined above.

data Original data (set) used in function call (if keepdata = TRUE).

subset Information on subset of original data used in meta-analysis (if keepdata =

TRUE).

call Function call.

version Version of R package **meta** used to create object.

### Note

The function metagen is called internally to calculate individual and overall treatment estimates and standard errors.

## Author(s)

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#### See Also

update.meta, metabin, metagen

## **Examples**

```
data(Fleiss1993cont)
# Meta-analysis with Hedges' g as effect measure
m1 <- metacont(n.psyc, mean.psyc, sd.psyc, n.cont, mean.cont, sd.cont,</pre>
  data = Fleiss1993cont, sm = "SMD")
forest(m1)
# Use Cohen's d instead of Hedges' g as effect measure
update(m1, method.smd = "Cohen")
# Use Glass' delta instead of Hedges' g as effect measure
update(m1, method.smd = "Glass")
# Use Glass' delta based on the standard deviation in the experimental group
update(m1, method.smd = "Glass", sd.glass = "experimental")
# Calculate Hedges' g based on exact formulae
update(m1, exact.smd = TRUE)
data(amlodipine)
m2 <- metacont(n.amlo, mean.amlo, sqrt(var.amlo), n.plac, mean.plac, sqrt(var.plac),</pre>
  data = amlodipine, studlab = study)
m2
# Use pooled variance
update(m2, pooledvar = TRUE)
# Meta-analysis of response ratios (Hedges et al., 1999)
```

```
#
data(woodyplants)
m3 <- metacont(n.elev, mean.elev, sd.elev, n.amb, mean.amb, sd.amb,
  data = woodyplants, sm = "ROM")
m3
print(m3, backtransf = FALSE)</pre>
```

metacor

Meta-analysis of correlations

# **Description**

Calculation of common effect and random effects estimates for meta-analyses with correlations; inverse variance weighting is used for pooling.

# Usage

```
metacor(
  cor,
  n,
  studlab,
  data = NULL,
  subset = NULL,
  exclude = NULL,
  cluster = NULL,
  sm = gs("smcor"),
  level = gs("level"),
  level.ma = gs("level.ma"),
  common = gs("common"),
  random = gs("random") | !is.null(tau.preset),
  overall = common | random,
  overall.hetstat = common | random,
  hakn = gs("hakn"),
  adhoc.hakn = gs("adhoc.hakn"),
 method.tau = gs("method.tau"),
 method.tau.ci = gs("method.tau.ci"),
  tau.preset = NULL,
  TE.tau = NULL,
  tau.common = gs("tau.common"),
  prediction = gs("prediction"),
  level.predict = gs("level.predict"),
  null.effect = 0,
  method.bias = gs("method.bias"),
  backtransf = gs("backtransf"),
  text.common = gs("text.common"),
  text.random = gs("text.random"),
```

```
text.predict = gs("text.predict"),
  text.w.common = gs("text.w.common"),
  text.w.random = gs("text.w.random"),
  title = gs("title"),
  complab = gs("complab"),
  outclab = "",
  subgroup,
  subgroup.name = NULL,
  print.subgroup.name = gs("print.subgroup.name"),
  sep.subgroup = gs("sep.subgroup"),
  test.subgroup = gs("test.subgroup"),
  prediction.subgroup = gs("prediction.subgroup"),
  byvar,
  keepdata = gs("keepdata"),
 warn.deprecated = gs("warn.deprecated"),
  control = NULL,
)
```

## **Arguments**

cor	Correlation.
n	Number of observations.
studlab	An optional vector with study labels.
data	An optional data frame containing the study information, i.e., cor and n.
subset	An optional vector specifying a subset of studies to be used.
exclude	An optional vector specifying studies to exclude from meta-analysis, however, to include in printouts and forest plots.
cluster	An optional vector specifying which estimates come from the same cluster resulting in the use of a three-level meta-analysis model.
sm	A character string indicating which summary measure ("ZCOR" or "COR") is to be used for pooling of studies.
level	The level used to calculate confidence intervals for individual studies.
level.ma	The level used to calculate confidence intervals for meta-analysis estimates.
common	A logical indicating whether a common effect meta-analysis should be conducted.
random	A logical indicating whether a random effects meta-analysis should be conducted.
overall	A logical indicating whether overall summaries should be reported. This argument is useful in a meta-analysis with subgroups if overall results should not be reported.
overall.hetstat	

A logical value indicating whether to print heterogeneity measures for overall treatment comparisons. This argument is useful in a meta-analysis with subgroups if heterogeneity statistics should only be printed on subgroup level.

hakn A logical indicating whether the method by Hartung and Knapp should be used to adjust test statistics and confidence intervals. A character string indicating whether an ad hoc variance correction should be adhoc.hakn applied in the case of an arbitrarily small Hartung-Knapp variance estimate, see Details. method.tau A character string indicating which method is used to estimate the betweenstudy variance  $\tau^2$  and its square root  $\tau$ . Either "DL", "PM", "REML", "ML", "HS", "SJ", "HE", or "EB", can be abbreviated. A character string indicating which method is used to estimate the confidence method.tau.ci interval of  $\tau^2$  and  $\tau$ . Either "QP", "BJ", "J", "PL", or "", can be abbreviated. Prespecified value for the square root of the between-study variance  $\tau^2$ . tau.preset TE.tau Overall effect used to estimate the between-study variance tau-squared. tau.common A logical indicating whether tau-squared should be the same across subgroups. prediction A logical indicating whether a prediction interval should be printed. level.predict The level used to calculate prediction interval for a new study. null.effect A numeric value specifying the effect under the null hypothesis. method.bias A character string indicating which test is to be used. Either "Begg", "Egger", or "Thompson", can be abbreviated. See function metabias. backtransf A logical indicating whether results for Fisher's z transformed correlations (sm = "ZCOR") should be back transformed in printouts and plots. If TRUE (default), results will be presented as correlations; otherwise Fisher's z transformed correlations will be shown. A character string used in printouts and forest plot to label the pooled common text.common effect estimate. A character string used in printouts and forest plot to label the pooled random text.random effects estimate. text.predict A character string used in printouts and forest plot to label the prediction intertext.w.common A character string used to label weights of common effect model. A character string used to label weights of random effects model. text.w.random title Title of meta-analysis / systematic review. Comparison label. complab outclab Outcome label. subgroup An optional vector to conduct a meta-analysis with subgroups. subgroup.name A character string with a name for the subgroup variable. print.subgroup.name A logical indicating whether the name of the subgroup variable should be printed in front of the group labels. A character string defining the separator between name of subgroup variable and sep.subgroup subgroup label. test.subgroup A logical value indicating whether to print results of test for subgroup differ-

ences.

prediction.subgroup

A logical indicating whether prediction intervals should be printed for sub-

groups.

byvar Deprecated argument (replaced by 'subgroup').

keepdata A logical indicating whether original data (set) should be kept in meta object.

warn.deprecated

A logical indicating whether warnings should be printed if deprecated arguments

are used.

control An optional list to control the iterative process to estimate the between-study

variance  $\tau^2$ . This argument is passed on to rma.uni.

... Additional arguments (to catch deprecated arguments).

#### **Details**

Common effect and random effects meta-analysis of correlations based either on Fisher's z transformation of correlations (sm = "ZCOR") or direct combination of (untransformed) correlations (sm = "COR") (see Cooper et al., p264-5 and p273-4). Only few statisticians would advocate the use of untransformed correlations unless sample sizes are very large (see Cooper et al., p265). The artificial example given below shows that the smallest study gets the largest weight if correlations are combined directly because the correlation is closest to 1.

Default settings are utilised for several arguments (assignments using gs function). These defaults can be changed for the current R session using the settings.meta function.

Furthermore, R function update.meta can be used to rerun a meta-analysis with different settings.

### **Estimation of between-study variance:**

The following methods to estimate the between-study variance  $\tau^2$  are available:

- DerSimonian-Laird estimator (method.tau = "DL")
- Paule-Mandel estimator (method.tau = "PM")
- Restricted maximum-likelihood estimator (method.tau = "REML")
- Maximum-likelihood estimator (method.tau = "ML")
- Hunter-Schmidt estimator (method.tau = "HS")
- Sidik-Jonkman estimator (method.tau = "SJ")
- Hedges estimator (method.tau = "HE")
- Empirical Bayes estimator (method.tau = "EB")

See metagen for more information on these estimators.

# Confidence interval for the between-study variance:

The following methods to calculate a confidence interval for  $\tau^2$  and  $\tau$  are available.

Argument	Method
method.tau.ci = "J"	Method by Jackson (2013)
method.tau.ci = "BJ"	Method by Biggerstaff and Jackson (2008)
method.tau.ci = "QP"	Q-Profile method (Viechtbauer, 2007)
method.tau.ci = "PL"	Profile-Likelihood method for three-level meta-analysis
	(Van den Noortgate et al., 2013)
<pre>method.tau.ci = ""</pre>	No confidence interval

See metagen for more information on these methods.

# Hartung-Knapp method:

Hartung and Knapp (2001) and Knapp and Hartung (2003) proposed an alternative method for random effects meta-analysis based on a refined variance estimator for the treatment estimate. Simulation studies (Hartung and Knapp, 2001; IntHout et al., 2014; Langan et al., 2019) show improved coverage probabilities compared to the classic random effects method.

In rare settings with very homogeneous treatment estimates, the Hartung-Knapp variance estimate can be arbitrarily small resulting in a very narrow confidence interval (Knapp and Hartung, 2003; Wiksten et al., 2016). In such cases, an *ad hoc* variance correction has been proposed by utilising the variance estimate from the classic random effects model with the HK method (Knapp and Hartung, 2003; IQWiQ, 2020). An alternative approach is to use the wider confidence interval of classic common or random effects meta-analysis and the HK method (Wiksten et al., 2016; Jackson et al., 2017).

Argument adhoc. hakn can be used to choose the *ad hoc* method:

Argument	Ad hoc method
adhoc.hakn = ""	not used
adhoc.hakn = "se"	use variance correction if HK standard error is smaller
	than standard error from classic random effects
	meta-analysis (Knapp and Hartung, 2003)
adhoc.hakn="iqwig6"	use variance correction if HK confidence interval
	is narrower than CI from classic random effects model
	with DerSimonian-Laird estimator (IQWiG, 2020)
adhoc.hakn = "ci"	use wider confidence interval of classic random effects
	and HK meta-analysis
	(Hybrid method 2 in Jackson et al., 2017)

### **Prediction interval:**

A prediction interval for the proportion in a new study (Higgins et al., 2009) is calculated if arguments prediction and random are TRUE. Note, the definition of prediction intervals varies in the literature. This function implements equation (12) of Higgins et al., (2009) which proposed a t distribution with K-2 degrees of freedom where K corresponds to the number of studies in the meta-analysis.

### **Subgroup analysis:**

Argument subgroup can be used to conduct subgroup analysis for a categorical covariate. The metareg function can be used instead for more than one categorical covariate or continuous covariates.

## **Exclusion of studies from meta-analysis:**

Arguments subset and exclude can be used to exclude studies from the meta-analysis. Studies are removed completely from the meta-analysis using argument subset, while excluded studies are shown in printouts and forest plots using argument exclude (see Examples in metagen). Meta-analysis results are the same for both arguments.

## **Presentation of meta-analysis results:**

Internally, both common effect and random effects models are calculated regardless of values choosen for arguments common and random. Accordingly, the estimate for the random effects

model can be extracted from component TE.random of an object of class "meta" even if argument random = FALSE. However, all functions in R package **meta** will adequately consider the values for common and random. E.g. functions print.meta and forest.meta will not print results for the random effects model if random = FALSE.

#### Value

An object of class c("metacor", "meta") with corresponding print, summary, and forest functions. The object is a list containing the following components:

cor, n, studlab, exclude, cluster,

As defined above.

sm, level, level.ma,

As defined above.

common, random,

As defined above.

hakn, adhoc.hakn, method.tau, method.tau.ci,

As defined above.

tau.preset, TE.tau, method.bias,

As defined above.

method.bias, tau.common, title, complab, outclab,

As defined above.

subgroup, subgroup.name, print.subgroup.name, sep.subgroup

As defined above.

TE, seTE Either Fisher's z transformation of correlations (sm = "ZCOR") or correlations

(sm="COR") for individual studies.

lower, upper Lower and upper confidence interval limits for individual studies.

zval, pval z-value and p-value for test of effect in individual studies.

w.common, w.random

Weight of individual studies (in common effect and random effects model).

TE.common, seTE.common

Estimated overall effect (Fisher's z transformation of correlation or correlation) and standard error (common effect model).

lower.common, upper.common

Lower and upper confidence interval limits (common effect model).

statistic.common, pval.common

z-value and p-value for test of overall effect (common effect model).

TE.random, seTE.random

Estimated overall effect (Fisher's z transformation of correlation) and standard error (random effects model).

lower.random, upper.random

Lower and upper confidence interval limits (random effects model).

statistic.random, pval.random

z-value or t-value and corresponding p-value for test of overall effect (random effects model).

prediction, level.predict

As defined above.

seTE.predict Standard error utilised for prediction interval.

lower.predict, upper.predict

Lower and upper limits of prediction interval.

k Number of estimates combined in meta-analysis.

k.study Number of studies combined in meta-analysis.

k.all Number of all studies.

k.TE Number of studies with estimable effects.

Q Heterogeneity statistic Q.

df.Q Degrees of freedom for heterogeneity statistic.

pval.Q P-value of heterogeneity test. tau2 Between-study variance  $\tau^2$ .

se. tau2 Standard error of  $\tau^2$ .

lower.tau2, upper.tau2

Lower and upper limit of confidence interval for  $\tau^2$ .

tau Square-root of between-study variance  $\tau$ .

lower.tau, upper.tau

Lower and upper limit of confidence interval for  $\tau$ .

H Heterogeneity statistic H.

lower.H, upper.H

Lower and upper confidence limit for heterogeneity statistic H.

I2 Heterogeneity statistic I<sup>2</sup>.

lower.I2, upper.I2

Lower and upper confidence limit for heterogeneity statistic  $I^2$ .

Rb Heterogeneity statistic  $R_b$ .

lower.Rb, upper.Rb

Lower and upper confidence limit for heterogeneity statistic  $R_b$ .

df.hakn Degrees of freedom for test of effect for Hartung-Knapp method (only if hakn =

TRUE).

method Pooling method: "Inverse".

bylevs Levels of grouping variable - if subgroup is not missing.

TE.common.w, seTE.common.w

Estimated effect and standard error in subgroups (common effect model) - if subgroup is not missing.

lower.common.w, upper.common.w

Lower and upper confidence interval limits in subgroups (common effect model)

- if subgroup is not missing.

statistic.common.w, pval.common.w

z-value and p-value for test of effect in subgroups (common effect model) - if subgroup is not missing.

TE.random.w, seTE.random.w

Estimated effect and standard error in subgroups (random effects model) - if subgroup is not missing.

lower.random.w, upper.random.w

Lower and upper confidence interval limits in subgroups (random effects model) - if subgroup is not missing.

statistic.random.w, pval.random.w

z-value or t-value and corresponding p-value for test of effect in subgroups (random effects model) - if subgroup is not missing.

w.common.w, w.random.w

Weight of subgroups (in common effect and random effects model) - if subgroup is not missing.

df.hakn.w Degrees of freedom for test of effect for Hartung-Knapp method in subgroups - if subgroup is not missing and hakn = TRUE.

n.e.w Number of observations in experimental group in subgroups - if subgroup is not missing.

n.c.w Number of observations in control group in subgroups - if subgroup is not missing.

k.w Number of studies combined within subgroups - if subgroup is not missing.

k.all.w Number of all studies in subgroups - if subgroup is not missing.

Q.w.common Overall within subgroups heterogeneity statistic Q (based on common effect model) - if subgroup is not missing.

Q.w.random Overall within subgroups heterogeneity statistic Q (based on random effects model) - if subgroup is not missing (only calculated if argument tau.common is TRUE).

df.Q.w Degrees of freedom for test of overall within subgroups heterogeneity - if subgroup is not missing.

pval.Q.w.common

P-value of within subgroups heterogeneity statistic Q (based on common effect model) - if subgroup is not missing.

pval.Q.w.random

P-value of within subgroups heterogeneity statistic Q (based on random effects model) - if subgroup is not missing.

Q.b. common Overall between subgroups heterogeneity statistic Q (based on common effect model) - if subgroup is not missing.

Q.b.random Overall between subgroups heterogeneity statistic Q (based on random effects model) - if subgroup is not missing.

df.Q.b Degrees of freedom for test of overall between subgroups heterogeneity - if subgroup is not missing.

pval.Q.b.common

P-value of between subgroups heterogeneity statistic Q (based on common effect model) - if subgroup is not missing.

pval.Q.b.random

P-value of between subgroups heterogeneity statistic Q (based on random effects model) - if subgroup is not missing.

tau.w Square-root of between-study variance within subgroups - if subgroup is not missing.

H.w Heterogeneity statistic H within subgroups - if subgroup is not missing.

lower.H.w, upper.H.w

Lower and upper confidence limit for heterogeneity statistic H within subgroups

- if subgroup is not missing.

I2. w Heterogeneity statistic  $I^2$  within subgroups - if subgroup is not missing.

lower.I2.w, upper.I2.w

Lower and upper confidence limit for heterogeneity statistic I<sup>2</sup> within subgroups

- if subgroup is not missing.

keepdata As defined above.

data Original data (set) used in function call (if keepdata = TRUE).

subset Information on subset of original data used in meta-analysis (if keepdata =

TRUE).

call Function call.

version Version of R package **meta** used to create object.

#### Note

The function metagen is called internally to calculate individual and overall treatment estimates and standard errors.

#### Author(s)

Guido Schwarzer <sc@imbi.uni-freiburg.de>

#### References

Cooper H, Hedges LV, Valentine JC (2009): *The Handbook of Research Synthesis and Meta-Analysis*, 2nd Edition. New York: Russell Sage Foundation

DerSimonian R & Laird N (1986): Meta-analysis in clinical trials. *Controlled Clinical Trials*, **7**, 177–88

Hartung J & Knapp G (2001): On tests of the overall treatment effect in meta-analysis with normally distributed responses. *Statistics in Medicine*, **20**, 1771–82

Higgins JPT, Thompson SG, Spiegelhalter DJ (2009): A re-evaluation of random-effects meta-analysis. *Journal of the Royal Statistical Society: Series A*, **172**, 137–59

IntHout J, Ioannidis JPA, Borm GF (2014): The Hartung-Knapp-Sidik-Jonkman method for random effects meta-analysis is straightforward and considerably outperforms the standard DerSimonian-Laird method. *BMC Medical Research Methodology*, **14**, 25

IQWiG (2020): General Methods: Version 6.0. https://www.iqwig.de/en/about-us/methods/methods-paper/

Jackson D, Law M, Rücker G, Schwarzer G (2017): The Hartung-Knapp modification for random-effects meta-analysis: A useful refinement but are there any residual concerns? *Statistics in Medicine*, **36**, 3923–34

Knapp G & Hartung J (2003): Improved tests for a random effects meta-regression with a single covariate. *Statistics in Medicine*, **22**, 2693–710

Langan D, Higgins JPT, Jackson D, Bowden J, Veroniki AA, Kontopantelis E, et al. (2019): A comparison of heterogeneity variance estimators in simulated random-effects meta-analyses. *Research Synthesis Methods*, **10**, 83–98

Van den Noortgate W, López-López JA, Marín-Martínez F, Sánchez-Meca J (2013): Three-level meta-analysis of dependent effect sizes. *Behavior Research Methods*, **45**, 576–94

Viechtbauer W (2010): Conducting Meta-Analyses in R with the Metafor Package. *Journal of Statistical Software*, **36**, 1–48

Wiksten A, Rücker G, Schwarzer G (2016): Hartung-Knapp method is not always conservative compared with fixed-effect meta-analysis. *Statistics in Medicine*, **35**, 2503–15

#### See Also

```
update.meta, metacont, metagen, print.meta
```

## **Examples**

```
m1 \leftarrow metacor(c(0.85, 0.7, 0.95), c(20, 40, 10))
# Print correlations (back transformed from Fisher's z
# transformation)
m1
# Print Fisher's z transformed correlations
print(m1, backtransf = FALSE)
# Forest plot with back transformed correlations
forest(m1)
# Forest plot with Fisher's z transformed correlations
forest(m1, backtransf = FALSE)
m2 \leftarrow update(m1, sm = "cor")
m2
# Identical forest plots (as back transformation is the identity
# transformation)
forest(m2)
forest(m2, backtransf = FALSE)
## End(Not run)
```

metacr

Meta-analysis of outcome data from Cochrane review

## **Description**

Wrapper function to perform meta-analysis for a single outcome of a Cochrane Intervention review.

## Usage

```
metacr(
 х,
 comp.no = 1,
 outcome.no = 1,
 method,
  sm,
  level = gs("level"),
 level.ma = gs("level.ma"),
  common,
  random,
  hakn = FALSE,
 method.tau = "DL",
 method.tau.ci = gs("method.tau.ci"),
  tau.common = FALSE,
  prediction = gs("prediction"),
  level.predict = gs("level.predict"),
  swap.events,
  logscale,
  backtransf = gs("backtransf"),
  test.subgroup,
  prediction.subgroup = gs("prediction.subgroup"),
  text.common = gs("text.common"),
  text.random = gs("text.random"),
  text.predict = gs("text.predict"),
  text.w.common = gs("text.w.common"),
  text.w.random = gs("text.w.random"),
  title,
  complab,
  outclab,
  keepdata = gs("keepdata"),
 warn = FALSE,
 warn.deprecated = gs("warn.deprecated"),
)
```

# Arguments x

An object of class rm5 created by R function read.rm5.

Comparison number.
Outcome number.
A character string indicating which method is to be used for pooling of studies. One of "Inverse", "MH", or "Peto", can be abbreviated.
A character string indicating which summary measure ("RR", "OR", "RD", "ASD", "HR", "MD", or "SMD", or "ROM") is to be used for pooling of studies.
The level used to calculate confidence intervals for individual studies.
The level used to calculate confidence intervals for pooled estimates.
A logical indicating whether a common effect meta-analysis should be conducted.
A logical indicating whether a random effects meta-analysis should be conducted.
A logical indicating whether the method by Hartung and Knapp should be used to adjust test statistics and confidence intervals.
A character string indicating which method is used to estimate the between-study variance $\tau^2$ and its square root $\tau$ . Either "DL", "PM", "REML", "ML", "HS", "SJ", "HE", or "EB", can be abbreviated.
A character string indicating which method is used to estimate the confidence interval of $\tau^2$ and $\tau$ . Either "QP", "BJ", or "J", or "", can be abbreviated.
A logical indicating whether tau-squared should be the same across subgroups.
A logical indicating whether a prediction interval should be printed.
The level used to calculate prediction interval for a new study.
A logical indicating whether events and non-events should be interchanged.
A logical indicating whether effect estimates are entered on log-scale.
A logical indicating whether results should be back transformed in printouts and plots. If backtransf=TRUE (default), results for sm="OR" are printed as odds ratios rather than log odds ratios and results for sm="ZCOR" are printed as correlations rather than Fisher's z transformed correlations, for example.
A logical value indicating whether to print results of test for subgroup differences.
group
A logical indicating whether prediction intervals should be printed for subgroups.
A character string used in printouts and forest plot to label the pooled common effect estimate.
A character string used in printouts and forest plot to label the pooled random effects estimate.
A character string used in printouts and forest plot to label the prediction interval.
A character string used to label weights of common effect model.
A character string used to label weights of random effects model.

title Title of meta-analysis / systematic review.

complab Comparison label.
outclab Outcome label.

keepdata A logical indicating whether original data (set) should be kept in meta object.

warn A logical indicating whether warnings should be printed (e.g., if incr is added

to studies with zero cell frequencies).

warn.deprecated

A logical indicating whether warnings should be printed if deprecated arguments

are used.

... Additional arguments (to catch deprecated arguments).

#### **Details**

Cochrane Intervention reviews are based on the comparison of two interventions. Each Cochrane Intervention review can have a variable number of comparisons. For each comparison, a variable number of outcomes can be define. For each outcome, a seperate meta-analysis is conducted. Review Manager 5 (RevMan 5) is the current software used for preparing and maintaining Cochrane Reviews (https://training.cochrane.org/online-learning/core-software-cochrane-reviews/revman).

This wrapper function can be used to perform meta-analysis for a single outcome of a Cochrane Intervention review. Internally, R functions metabin, metacont, and metagen are called - depending on the definition of the outcome in RevMan 5.

Note, it is recommended to choose the RevMan 5 settings before executing metacr, i.e., settings.meta("revman5").

### Value

An object of class "meta" and "metabin", "metacont", or "metagen" depending on outcome type utilised in Cochrane Intervention review for selected outcome.

#### Author(s)

Guido Schwarzer <sc@imbi.uni-freiburg.de>

## References

Review Manager (RevMan) [Computer program]. Version 5.4. The Cochrane Collaboration, 2020

#### See Also

```
metabin, metacont, metagen, read.rm5, settings.meta
```

## **Examples**

```
# Locate export data file "Fleiss1993_CR.csv"
# in sub-directory of package "meta"
#
filename <- system.file("extdata", "Fleiss1993_CR.csv", package = "meta")
#</pre>
```

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```
Fleiss1993_CR <- read.rm5(filename)

# Choose RevMan 5 settings and store old settings
# oldset <- settings.meta("revman5", quietly = FALSE)

# Same result as R command example(Fleiss1993bin)
# metacr(Fleiss1993_CR)

# Same result as R command example(Fleiss1993cont)
# metacr(Fleiss1993_CR, 1, 2)
forest(metacr(Fleiss1993_CR, 1, 2))

# Change summary measure to RR
# m1 <- metacr(Fleiss1993_CR)
update(m1, sm="RR")

# Use old settings
# settings.meta(oldset)</pre>
```

 ${\tt metacum}$ 

Cumulative meta-analysis

## **Description**

Performs a cumulative meta-analysis.

## Usage

```
metacum(x, pooled, sortvar)
```

# Arguments

x An object of class meta.

pooled A character string indicating whether a common effect or random effects model

is used for pooling. Either missing (see Details), "common", or "random", can

be abbreviated.

sortvar An optional vector used to sort the individual studies (must be of same length as

x\$TE).

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#### **Details**

A cumulative meta-analysis is performed. Studies are included sequentially as defined by sortvar.

Information from object x is utilised if argument pooled is missing. A common effect model is assumed (pooled = "common") if argument x\$common is TRUE; a random effects model is assumed (pooled = "random") if argument x\$random is TRUE and x\$common is FALSE.

#### Value

An object of class c("metacum", "meta") with corresponding print, and forest functions. The object is a list containing the following components:

TE, seTE Estimated treatment effect and standard error of pooled estimate in cumulative

meta-analyses.

lower, upper Lower and upper confidence interval limits.

statistic Statistic for test of overall effect.

P-value for test of overall effect.

studlab Study label describing addition of studies.

w Sum of weights from common effect or random effects model.

I2 Heterogeneity statistic  $I^2$ .

Rb Heterogeneity statistic  $R_b$ .

tau Square-root of between-study variance.

df. hakn Degrees of freedom for test of treatment effect for Hartung-Knapp method (only

if hakn = TRUE).

sm Summary measure.

method Method used for pooling.

k Number of studies combined in meta-analysis.

pooled As defined above.

common A logical indicating whether analysis is based on common effect model.

A logical indicating whether analysis is based on random effects model.

TE.common, seTE.common

Value is NA.

TE.random, seTE.random

Value is NA.

Q Value is NA.

level.ma The level used to calculate confidence intervals for pooled estimates.

hakn A logical indicating whether the method by Hartung and Knapp is used to adjust

test statistics and confidence intervals.

adhoc.hakn A character string indicating whether ad hoc variance correction should be used

for Hartung-Knapp method.

method.tau A character string indicating which method is used to estimate the between-

study variance  $\tau^2$ .

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tau.preset Prespecified value for the square root of the between-study variance  $\tau^2$ . TE.tau Overall treatment effect used to estimate the between-study variance  $\tau^2$ . n.harmonic.mean Harmonic mean of number of observations (for back transformation of Freeman-Tukey Double arcsine transformation).

## Author(s)

Guido Schwarzer <sc@imbi.uni-freiburg.de>

#### References

Cooper H & Hedges LV (1994): *The Handbook of Research Synthesis*. Newbury Park, CA: Russell Sage Foundation

## See Also

```
metabin, metacont, print.meta
```

## **Examples**

```
data(Fleiss1993bin)
m1 <- metabin(d.asp, n.asp, d.plac, n.plac,
    data = Fleiss1993bin, studlab = study, sm = "RR", method = "I")
m1
metacum(m1)
metacum(m1, pooled = "random")

forest(metacum(m1))
forest(metacum(m1, pooled = "random"))

metacum(m1, sortvar = study)
metacum(m1, sortvar = 7:1)

m2 <- update(m1, title = "Fleiss1993bin meta-analysis", backtransf = FALSE)
metacum(m2)

data(Fleiss1993cont)
m3 <- metacont(n.psyc, mean.psyc, sd.psyc, n.cont, mean.cont, sd.cont,
    data = Fleiss1993cont, sm = "SMD")
metacum(m3)</pre>
```

metagen

Generic inverse variance meta-analysis

# **Description**

Common effect and random effects meta-analysis based on estimates (e.g. log hazard ratios) and their standard errors. The inverse variance method is used for pooling.

Three-level random effects meta-analysis (Van den Noortgate et al., 2013) is available by internally calling rma.mv function from R package **metafor** (Viechtbauer, 2010).

# Usage

```
metagen(
  TE,
  seTE,
  studlab,
  data = NULL,
  subset = NULL,
  exclude = NULL,
  cluster = NULL,
  sm = "",
  method.ci = if (missing(df)) "z" else "t",
  level = gs("level"),
  level.ma = gs("level.ma"),
  common = gs("common"),
  random = gs("random") | !is.null(tau.preset),
  overall = common | random,
  overall.hetstat = common | random,
  hakn = gs("hakn"),
  adhoc.hakn = gs("adhoc.hakn"),
  method.tau = gs("method.tau"),
  method.tau.ci = gs("method.tau.ci"),
  tau.preset = NULL,
  TE.tau = NULL,
  tau.common = gs("tau.common"),
  detail.tau = "",
  prediction = gs("prediction"),
  level.predict = gs("level.predict"),
  null.effect = 0,
  method.bias = gs("method.bias"),
  n.e = NULL,
  n.c = NULL,
  pval,
  df,
  lower,
  upper,
```

```
level.ci = 0.95,
 median,
 q1,
 q3,
 min,
 max,
 method.mean = "Luo",
 method.sd = "Shi",
  approx.TE,
  approx.seTE,
  backtransf = gs("backtransf"),
  pscale = 1,
  irscale = 1,
  irunit = "person-years",
  text.common = gs("text.common"),
  text.random = gs("text.random"),
  text.predict = gs("text.predict"),
  text.w.common = gs("text.w.common"),
  text.w.random = gs("text.w.random"),
  title = gs("title"),
  complab = gs("complab"),
  outclab = "",
  label.e = gs("label.e"),
  label.c = gs("label.c"),
  label.left = gs("label.left"),
  label.right = gs("label.right"),
  subgroup,
  subgroup.name = NULL,
  print.subgroup.name = gs("print.subgroup.name"),
  sep.subgroup = gs("sep.subgroup"),
  test.subgroup = gs("test.subgroup"),
  prediction.subgroup = gs("prediction.subgroup"),
  byvar,
  id,
  keepdata = gs("keepdata"),
 warn = gs("warn"),
 warn.deprecated = gs("warn.deprecated"),
 control = NULL,
)
```

## **Arguments**

TE	Estimate of treatment effect, e.g., log hazard ratio or risk difference.
seTE	Standard error of treatment estimate.
studlab	An optional vector with study labels.
data	An optional data frame containing the study information.

subset An optional vector specifying a subset of studies to be used (see Details).

exclude An optional vector specifying studies to exclude from meta-analysis, however, to include in printouts and forest plots (see Details). An optional vector specifying which estimates come from the same cluster recluster sulting in the use of a three-level meta-analysis model. A character string indicating underlying summary measure, e.g., "RD", "RR", sm "OR", "ASD", "HR", "MD", "SMD", or "ROM". method.ci A character string indicating which method is used to calculate confidence intervals for individual studies, see Details. The level used to calculate confidence intervals for individual studies. level The level used to calculate confidence intervals for meta-analysis estimates. level.ma common A logical indicating whether a common effect meta-analysis should be conducted. random A logical indicating whether a random effects meta-analysis should be conducted. overall A logical indicating whether overall summaries should be reported. This argument is useful in a meta-analysis with subgroups if overall results should not be reported. overall.hetstat A logical value indicating whether to print heterogeneity measures for overall treatment comparisons. This argument is useful in a meta-analysis with subgroups if heterogeneity statistics should only be printed on subgroup level. A logical indicating whether method by Hartung and Knapp should be used to hakn adjust test statistics and confidence intervals. adhoc.hakn A character string indicating whether an ad hoc variance correction should be applied in the case of an arbitrarily small Hartung-Knapp variance estimate. Either "", "se", "ci", or "iqwig6" (see Details), can be abbreviated. A character string indicating which method is used to estimate the betweenmethod.tau study variance  $\tau^2$  and its square root  $\tau$ . Either "DL", "PM", "REML", "ML", "HS", "SJ", "HE", or "EB", can be abbreviated. A character string indicating which method is used to estimate the confidence method.tau.ci interval of  $\tau^2$  and  $\tau$ . Either "QP", "BJ", "J", "PL", or "", can be abbreviated. Prespecified value for the square root of the between-study variance  $\tau^2$ . tau.preset TE.tau Overall treatment effect used to estimate the between-study variance tau-squared. tau.common A logical indicating whether tau-squared should be the same across subgroups. Detail on between-study variance estimate. detail.tau A logical indicating whether a prediction interval should be printed. prediction level.predict The level used to calculate prediction interval for a new study. null.effect A numeric value specifying the effect under the null hypothesis. method.bias A character string indicating which test is to be used. Either "Begg", "Egger", or "Thompson", can be abbreviated. See function metabias.

Number of observations in experimental group (or total sample size in study).

n.e

n.c Number of observations in control group.pval P-value (used to estimate the standard error).

Degrees of freedom (used in test or to construct confidence interval).

Lower limit of confidence interval (used to estimate the standard error).

Upper limit of confidence interval (used to estimate the standard error).

level.ci Level of confidence interval.

median (used to estimate the treatment effect and standard error).

q1 First quartile (used to estimate the treatment effect and standard error).
q3 Third quartile (used to estimate the treatment effect and standard error).
min Minimum (used to estimate the treatment effect and standard error).

max Maximum (used to estimate the treatment effect and standard error).

method.mean A character string indicating which method to use to approximate the mean from

the median and other statistics (see Details).

method.sd A character string indicating which method to use to approximate the standard

deviation from sample size, median, interquartile range and range (see Details).

approx.TE Approximation method to estimate treatment estimate (see Details).

Approximation method to estimate standard error (see Details).

backtransf A logical indicating whether results should be back transformed in printouts

and plots. If backtransf = TRUE (default), results for sm = "OR" are printed as odds ratios rather than log odds ratios and results for sm = "ZCOR" are printed as

correlations rather than Fisher's z transformed correlations, for example.

pscale A numeric giving scaling factor for printing of single event probabilities or risk

differences, i.e. if argument sm is equal to "PLOGIT", "PLN", "PRAW", "PAS",

"PFT", or "RD".

irscale A numeric defining a scaling factor for printing of single incidence rates or in-

cidence rate differences, i.e. if argument sm is equal to "IR", "IRLN", "IRS",

"IRFT", or "IRD".

irunit A character specifying the time unit used to calculate rates, e.g. person-years.

text.common A character string used in printouts and forest plot to label the pooled common

effect estimate.

text.random A character string used in printouts and forest plot to label the pooled random

effects estimate.

text.predict A character string used in printouts and forest plot to label the prediction inter-

val.

text.w.common A character string used to label weights of common effect model.

text.w.random A character string used to label weights of random effects model.

title Title of meta-analysis / systematic review.

complab Comparison label.
outclab Outcome label.

label.e Label for experimental group.

label.c Label for control group.

label.left Graph label on left side of forest plot.label.right Graph label on right side of forest plot.

subgroup An optional vector to conduct a meta-analysis with subgroups.

subgroup.name A character string with a name for the subgroup variable.

print.subgroup.name

A logical indicating whether the name of the subgroup variable should be printed

in front of the group labels.

sep. subgroup A character string defining the separator between name of subgroup variable and

subgroup label.

test.subgroup A logical value indicating whether to print results of test for subgroup differ-

ences.

prediction.subgroup

A logical indicating whether prediction intervals should be printed for sub-

groups.

byvar Deprecated argument (replaced by 'subgroup').

id Deprecated argument (replaced by 'cluster').

keepdata A logical indicating whether original data (set) should be kept in meta object.

warn A logical indicating whether warnings should be printed (e.g., if studies are

excluded from meta-analysis due to zero standard errors).

warn.deprecated

A logical indicating whether warnings should be printed if deprecated arguments

are used.

control An optional list to control the iterative process to estimate the between-study

variance  $\tau^2$ . This argument is passed on to rma. uni or rma.mv.

... Additional arguments (to catch deprecated arguments).

#### **Details**

This function provides the *generic inverse variance method* for meta-analysis which requires treatment estimates and their standard errors (Borenstein et al., 2010). The method is useful, e.g., for pooling of survival data (using log hazard ratio and standard errors as input). Arguments TE and seTE can be used to provide treatment estimates and standard errors directly. However, it is possible to derive these quantities from other information.

Default settings are utilised for several arguments (assignments using gs function). These defaults can be changed for the current R session using the settings.meta function.

Furthermore, R function update.meta can be used to rerun a meta-analysis with different settings.

## Three-level random effects meta-analysis:

A three-level random effects meta-analysis model (Van den Noortgate et al., 2013) is utilized if argument cluster is used and at least one cluster provides more than one estimate. Internally, rma.mv is called to conduct the analysis and weights.rma.mv with argument type = "rowsum" is used to calculate random effects weights.

#### **Approximate treatment estimates:**

Missing treatment estimates can be derived from

- 1. confidence limits provided by arguments lower and upper;
- 2. median, interquartile range and range (arguments median, q1, q3, min, and max);
- 3. median and interquartile range (arguments median, q1 and q3);
- 4. median and range (arguments median, min and max).

For confidence limits, the treatment estimate is defined as the center of the confidence interval (on the log scale for relative effect measures like the odds ratio or hazard ratio).

If the treatment effect is a mean it can be approximated from sample size, median, interquartile range and range. By default, methods described in Luo et al. (2018) are utilized (argument method.mean = "Luo"):

- equation (7) if sample size, median and range are available,
- equation (11) if sample size, median and interquartile range are available,
- equation (15) if sample size, median, range and interquartile range are available.

Instead the methods described in Wan et al. (2014) are used if argument method. mean = "Wan":

- equation (2) if sample size, median and range are available,
- equation (14) if sample size, median and interquartile range are available,
- equation (10) if sample size, median, range and interquartile range are available.

By default, missing treatment estimates are replaced successively using these method, i.e., confidence limits are utilised before interquartile ranges. Argument approx.TE can be used to overwrite this default for each individual study:

- Use treatment estimate directly (entry "" in argument approx.TE);
- confidence limits ("ci" in argument approx.TE);
- median, interquartile range and range ("iqr.range");
- median and interquartile range ("iqr");
- median and range ("range").

## Approximate standard errors:

Missing standard errors can be derived from

- 1. p-value provided by arguments pval and (optional) df;
- 2. confidence limits (arguments lower, upper, and (optional) df);
- 3. sample size, median, interquartile range and range (arguments n.e and / or n.c, median, q1, q3, min, and max);
- 4. sample size, median and interquartile range (arguments n.e and / or n.c, median, q1 and q3);
- 5. sample size, median and range (arguments n.e and / or n.c, median, min and max).

For p-values and confidence limits, calculations are either based on the standard normal or t distribution if argument df is provided. Furthermore, argument level.ci can be used to provide the level of the confidence interval.

Wan et al. (2014) describe methods to estimate the standard deviation (and thus the standard error by deviding the standard deviation with the square root of the sample size) from the sample size, median and additional statistics. Shi et al. (2020) provide an improved estimate of the standard deviation if the interquartile range and range are available in addition to the sample size

and median. Accordingly, equation (11) in Shi et al. (2020) is the default (argument method.sd = "Shi"), if the median, interquartile range and range are provided (arguments median, q1, q3, min and max). The method by Wan et al. (2014) is used if argument method.sd = "Wan" and, depending on the sample size, either equation (12) or (13) is used. If only the interquartile range or range is available, equations (15) / (16) and (7) / (9) in Wan et al. (2014) are used, respectively. The sample size of individual studies must be provided with arguments n.e and / or n.c. The total sample size is calculated as n.e + n.c if both arguments are provided.

By default, missing standard errors are replaced successively using these method, e.g., p-value before confidence limits before interquartile range and range. Argument approx.seTE can be used to overwrite this default for each individual study:

- Use standard error directly (entry "" in argument approx.seTE);
- p-value ("pval" in argument approx.seTE);
- confidence limits ("ci");
- median, interquartile range and range ("iqr.range");
- median and interquartile range ("iqr");
- median and range ("range").

#### Confidence intervals for individual studies:

For the mean difference (argument sm = "MD"), the confidence interval for individual studies can be based on the

- standard normal distribution (method.ci = "z"), or
- t-distribution (method.ci = "t").

By default, the first method is used if argument df is missing and the second method otherwise. Note, this choice does not affect the results of the common effect and random effects meta-analysis.

#### **Estimation of between-study variance:**

The following methods are available to estimate the between-study variance  $\tau^2$ .

ı	Argument	Method
	method.tau="DL"	DerSimonian-Laird estimator (DerSimonian and Laird, 1986)
	method.tau="PM"	Paule-Mandel estimator (Paule and Mandel, 1982)
	method.tau="REML"	Restricted maximum-likelihood estimator (Viechtbauer, 2005)
	method.tau="ML"	Maximum-likelihood estimator (Viechtbauer, 2005)
	method.tau="HS"	Hunter-Schmidt estimator (Hunter and Schmidt, 2015)
	method.tau="SJ"	Sidik-Jonkman estimator (Sidik and Jonkman, 2005)
	method.tau="HE"	Hedges estimator (Hedges and Olkin, 1985)
	method.tau="EB"	Empirical Bayes estimator (Morris, 1983)

Historically, the DerSimonian-Laird method was the de facto standard to estimate the between-study variance  $\tau^2$  and is still the default in many software packages including Review Manager 5 (RevMan 5) and R package **meta**. However, its role has been challenged and especially the Paule-Mandel and REML estimators have been recommended (Veroniki et al., 2016). Accordingly, the following R command can be used to use the Paule-Mandel estimator in all meta-analyses of the R session: settings.meta(method.tau = "PM")

## Confidence interval for the between-study variance:

The following methods to calculate a confidence interval for  $\tau^2$  and  $\tau$  are available.

Argument	Method
method.tau.ci = "J"	Method by Jackson (2013)
method.tau.ci = "BJ"	Method by Biggerstaff and Jackson (2008)
method.tau.ci = "QP"	Q-Profile method (Viechtbauer, 2007)
method.tau.ci = "PL"	Profile-Likelihood method for three-level
	meta-analysis model (Van den Noortgate et al., 2013)
method.tau.ci = ""	No confidence interval

The first three methods have been recommended by Veroniki et al. (2016). By default, the Jackson method is used for the DerSimonian-Laird estimator of  $\tau^2$  and the Q-profile method for all other estimators of  $\tau^2$ . The Profile-Likelihood method is the only method available for the three-level meta-analysis model.

### **Hartung-Knapp method:**

Hartung and Knapp (2001a,b) proposed an alternative method for random effects meta-analysis based on a refined variance estimator for the treatment estimate. Simulation studies (Hartung and Knapp, 2001a,b; IntHout et al., 2014; Langan et al., 2019) show improved coverage probabilities compared to the classic random effects method. However, in rare settings with very homogeneous treatment estimates, the Hartung-Knapp (HK) variance estimate can be arbitrarily small resulting in a very narrow confidence interval (Knapp and Hartung, 2003; Wiksten et al., 2016). In such cases, an *ad hoc* variance correction has been proposed by utilising the variance estimate from the classic random effects model with the HK method (Knapp and Hartung, 2003; IQWiQ, 2020). An alternative approach is to use the wider confidence interval of classic common or random effects meta-analysis and the HK method (Wiksten et al., 2016; Jackson et al., 2017).

Argument adhoc. hakn can be used to choose the *ad hoc* method:

Argument	Ad hoc method
adhoc.hakn = ""	not used
adhoc.hakn = "se"	use variance correction if HK standard error is smaller
	than standard error from classic random effects
	meta-analysis (Knapp and Hartung, 2003)
adhoc.hakn="iqwig6"	use variance correction if HK confidence interval
	is narrower than CI from classic random effects model
	with DerSimonian-Laird estimator (IQWiG, 2020)
adhoc.hakn = "ci"	use wider confidence interval of classic random effects
	and HK meta-analysis
	(Hybrid method 2 in Jackson et al., 2017)

## **Prediction interval:**

A prediction interval for the treatment effect of a new study (Higgins et al., 2009) is calculated if arguments prediction and random are TRUE. Note, the definition of prediction intervals varies in the literature. This function implements equation (12) of Higgins et al., (2009) which proposed a t distribution with K-2 degrees of freedom where K corresponds to the number of studies in the meta-analysis.

## Subgroup analysis:

Argument subgroup can be used to conduct subgroup analysis for a categorical covariate. The metareg function can be used instead for more than one categorical covariate or continuous covariates.

## Specify the null hypothesis of test for an overall effect:

Argument null.effect can be used to specify the (treatment) effect under the null hypothesis in a test for an overall effect.

By default (null.effect = 0), the null hypothesis corresponds to "no difference" (which is obvious for absolute effect measures like the mean difference (sm = "MD") or standardised mean difference (sm = "SMD")). For relative effect measures, e.g., risk ratio (sm = "RR") or odds ratio (sm = "OR"), the null effect is defined on the log scale, i.e., ln(RR) = 0 or ln(OR) = 0 which is equivalent to testing RR = 1 or OR = 1.

Use of argument null.effect is especially useful for summary measures without a "natural" null effect, i.e., in situations without a second (treatment) group. For example, an overall proportion of 50% could be tested in the meta-analysis of single proportions with argument null.effect = 0.5.

Note, all tests for an overall effect are two-sided with the alternative hypothesis that the effect is unequal to null.effect.

## **Exclusion of studies from meta-analysis:**

Arguments subset and exclude can be used to exclude studies from the meta-analysis. Studies are removed completely from the meta-analysis using argument subset, while excluded studies are shown in printouts and forest plots using argument exclude (see Examples). Meta-analysis results are the same for both arguments.

## Presentation of meta-analysis results:

Internally, both common effect and random effects models are calculated regardless of values choosen for arguments common and random. Accordingly, the estimate for the random effects model can be extracted from component TE.random of an object of class "meta" even if argument random = FALSE. However, all functions in R package **meta** will adequately consider the values for common and random. For example, functions print.meta and forest.meta will not show results for the random effects model if random = FALSE.

Argument pscale can be used to rescale single proportions or risk differences, e.g. pscale = 1000 means that proportions are expressed as events per 1000 observations. This is useful in situations with (very) low event probabilities.

Argument irscale can be used to rescale single rates or rate differences, e.g. irscale = 1000 means that rates are expressed as events per 1000 time units, e.g. person-years. This is useful in situations with (very) low rates. Argument irunit can be used to specify the time unit used in individual studies (default: "person-years"). This information is printed in summaries and forest plots if argument irscale is not equal to 1.

Default settings for common, random, pscale, irscale, irunit and several other arguments can be set for the whole R session using settings.meta.

### Value

An object of class c("metagen", "meta") with corresponding print, summary, and forest functions. The object is a list containing the following components:

TE, seTE, studlab, exclude, n.e, n.c

As defined above.

cluster, sm, method.ci, level, level.ma,

As defined above.

common, random,

As defined above.

overall, overall.hetstat,

As defined above.

hakn, adhoc.hakn, method.tau, method.tau.ci,

As defined above.

tau.preset, TE.tau, method.bias,

As defined above.

tau.common, title, complab, outclab,

As defined above.

label.e, label.c, label.left, label.right,

As defined above.

subgroup, subgroup.name,

As defined above.

print.subgroup.name, sep.subgroup, warn,

As defined above.

lower, upper Lower and upper confidence interval limits for individual studies.

statistic, pval

Statistic and p-value for test of treatment effect for individual studies.

w.common, w.random

Weight of individual studies (in common effect and random effects model).

TE.common, seTE.common

Estimated overall treatment effect and standard error (common effect model).

lower.common, upper.common

Lower and upper confidence interval limits (common effect model).

statistic.common, pval.common

Statistic and p-value for test of overall treatment effect (common effect model).

TE.random, seTE.random

Estimated overall treatment effect and standard error (random effects model).

lower.random, upper.random

Lower and upper confidence interval limits (random effects model).

statistic.random, pval.random

Statistic and p-value for test of overall treatment effect (random effects model).

prediction, level.predict

As defined above.

seTE.predict Standard error utilised for prediction interval.

lower.predict, upper.predict

Lower and upper limits of prediction interval.

null.effect As defined above.

k Number of estimates combined in meta-analysis.

k.study Number of studies combined in meta-analysis.

Number of all studies. k.all k.TE Number of studies with estimable effects. Heterogeneity statistic. df.Q Degrees of freedom for heterogeneity statistic. P-value of heterogeneity test. pval.Q tau2 Between-study variance  $\tau^2$ . Standard error of  $\tau^2$ . se.tau2 lower.tau2, upper.tau2 Lower and upper limit of confidence interval for  $\tau^2$ . tau Square-root of between-study variance  $\tau$ . lower.tau, upper.tau Lower and upper limit of confidence interval for  $\tau$ . Heterogeneity statistic H. lower.H, upper.H Lower and upper confidence limit for heterogeneity statistic H. 12 Heterogeneity statistic  $I^2$ . lower.I2, upper.I2 Lower and upper confidence limit for heterogeneity statistic  $I^2$ . Rb Heterogeneity statistic  $R_b$ . lower.Rb, upper.Rb Lower and upper confidence limit for heterogeneity statistic  $R_h$ . approx.TE, approx.seTE As defined above. method Pooling method: "Inverse". df.hakn Degrees of freedom for test of treatment effect for Hartung-Knapp method (only if hakn = TRUE). seTE.hakn Estimated standard error for Hartung-Knapp method (not taking ad hoc variance correction into account). seTE.hakn.adhoc Estimated standard error for Hartung-Knapp method (taking ad hoc variance correction into account). bylevs Levels of grouping variable - if subgroup is not missing. TE.common.w, seTE.common.w Estimated treatment effect and standard error in subgroups (common effect model) - if subgroup is not missing. lower.common.w, upper.common.w Lower and upper confidence interval limits in subgroups (common effect model)

Statistics and p-values for test of treatment effect in subgroups (common effect

- if subgroup is not missing.

model) - if subgroup is not missing.

statistic.common.w, pval.common.w

TE.random.w, seTE.random.w

Estimated treatment effect and standard error in subgroups (random effects model) - if subgroup is not missing.

lower.random.w, upper.random.w

Lower and upper confidence interval limits in subgroups (random effects model) - if subgroup is not missing.

statistic.random.w, pval.random.w

Statistics and p-values for test of treatment effect in subgroups (random effects model) - if subgroup is not missing.

w.common.w, w.random.w

Weight of subgroups (in common effect and random effects model) - if subgroup is not missing.

df.hakn.w Degrees of freedom for test of treatment effect for Hartung-Knapp method in subgroups - if subgroup is not missing and hakn = TRUE.

n.harmonic.mean.w

Harmonic mean of number of observations in subgroups (for back transformation of Freeman-Tukey Double arcsine transformation) - if subgroup is not missing.

n.e.w Number of observations in experimental group in subgroups - if subgroup is not missing.

n.c.w Number of observations in control group in subgroups - if subgroup is not missing.

k.w Number of studies combined within subgroups - if subgroup is not missing.

k.all.w Number of all studies in subgroups - if subgroup is not missing.

Q.w.common Overall within subgroups heterogeneity statistic Q (based on common effect model) - if subgroup is not missing.

Q.w.random Overall within subgroups heterogeneity statistic Q (based on random effects model) - if subgroup is not missing (only calculated if argument tau.common is TRUE).

df.Q.w Degrees of freedom for test of overall within subgroups heterogeneity - if subgroup is not missing.

pval.Q.w.common

P-value of within subgroups heterogeneity statistic Q (based on common effect model) - if subgroup is not missing.

pval.Q.w.random

P-value of within subgroups heterogeneity statistic Q (based on random effects model) - if subgroup is not missing.

Q.b.common Overall between subgroups heterogeneity statistic Q (based on common effect model) - if subgroup is not missing.

Q.b.random Overall between subgroups heterogeneity statistic Q (based on random effects model) - if subgroup is not missing.

df.Q.b Degrees of freedom for test of overall between subgroups heterogeneity - if subgroup is not missing.

pval.Q.b.common

P-value of between subgroups heterogeneity statistic Q (based on common effect model) - if subgroup is not missing.

pval.Q.b.random

P-value of between subgroups heterogeneity statistic Q (based on random effects model) - if subgroup is not missing.

tau.w Square-root of between-study variance within subgroups - if subgroup is not missing.

H.w Heterogeneity statistic H within subgroups - if subgroup is not missing.

lower.H.w, upper.H.w

Lower and upper confidence limit for heterogeneity statistic H within subgroups - if subgroup is not missing.

I2. w Heterogeneity statistic  $I^2$  within subgroups - if subgroup is not missing.

lower.I2.w, upper.I2.w

Lower and upper confidence limit for heterogeneity statistic I<sup>2</sup> within subgroups - if subgroup is not missing.

keepdata As defined above.

data Original data (set) used in function call (if keepdata = TRUE).

subset Information on subset of original data used in meta-analysis (if keepdata =

TRUE).

call Function call.

version Version of R package **meta** used to create object.

## Note

R function rma.uni from R package **metafor** (Viechtbauer 2010) is called internally to estimate the between-study variance  $\tau^2$ .

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#### See Also

```
update.meta, metabin, metacont, print.meta, settings.meta
```

## **Examples**

```
data(Fleiss1993bin)
m1 <- metabin(d.asp, n.asp, d.plac, n.plac, study,</pre>
  data = Fleiss1993bin, sm = "RR", method = "I")
# Identical results using the generic inverse variance method with
# log risk ratio and its standard error:
# Note, argument 'n.e' in metagen() is used to provide the total
# sample size which is calculated from the group sample sizes n.e
# and n.c in meta-analysis m1.
m1.gen <- metagen(TE, seTE, studlab, n.e = n.e + n.c, data = m1, sm = "RR")
m1.gen
forest(m1.gen, leftcols = c("studlab", "n.e", "TE", "seTE"))
# Meta-analysis with prespecified between-study variance
metagen(m1$TE, m1$seTE, sm = "RR", tau.preset = sqrt(0.1))
# Meta-analysis of survival data:
#
logHR < - log(c(0.95, 1.5))
selogHR <- c(0.25, 0.35)
metagen(logHR, selogHR, sm = "HR")
# Paule-Mandel method to estimate between-study variance for data
# from Paule & Mandel (1982)
average < c(27.044, 26.022, 26.340, 26.787, 26.796)
variance < c(0.003, 0.076, 0.464, 0.003, 0.014)
metagen(average, sqrt(variance), sm = "MD", method.tau = "PM")
# Conduct meta-analysis using hazard ratios and 95% confidence intervals
# Data from Steurer et al. (2006), Analysis 1.1 Overall survival
```

```
# https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD004270.pub2/abstract
study <- c("FCG on CLL 1996", "Leporrier 2001", "Rai 2000", "Robak 2000")
HR \leftarrow c(0.55, 0.92, 0.79, 1.18)
lower.HR \leftarrow c(0.28, 0.79, 0.59, 0.64)
upper.HR \leftarrow c(1.09, 1.08, 1.05, 2.17)
# Input must be log hazard ratios, not hazard ratios
metagen(log(HR), lower = log(lower.HR), upper = log(upper.HR),
  studlab = study, sm = "HR")
# Exclude MRC-1 and MRC-2 studies from meta-analysis, however,
# show them in printouts and forest plots
#
metabin(d.asp, n.asp, d.plac, n.plac, study,
  data = Fleiss1993bin, sm = "RR", method = "I",
  exclude = study %in% c("MRC-1", "MRC-2"))
# Exclude MRC-1 and MRC-2 studies completely from meta-analysis
metabin(d.asp, n.asp, d.plac, n.plac, study,
  data = Fleiss1993bin, sm = "RR", method = "I",
  subset = !(study %in% c("MRC-1", "MRC-2")))
# Exclude studies with total sample size above 1500
metabin(d.asp, n.asp, d.plac, n.plac, study,
  data = Fleiss1993bin, sm = "RR", method = "I",
  exclude = (n.asp + n.plac) > 1500)
\# Exclude studies containing "MRC" in study name
metabin(d.asp, n.asp, d.plac, n.plac, study,
  data = Fleiss1993bin, sm = "RR", method = "I",
  exclude = grep("MRC", study))
# Use both arguments 'subset' and 'exclude'
metabin(d.asp, n.asp, d.plac, n.plac, study,
  data = Fleiss1993bin, sm = "RR", method = "I",
  subset = (n.asp + n.plac) > 1500,
  exclude = grep("MRC", study))
## Not run:
# Three-level model: effects of modified school calendars on
# student achievement
data(dat.konstantopoulos2011, package = "metadat")
metagen(yi, sqrt(vi), studlab = study, data = dat.konstantopoulos2011,
  sm = "SMD"
  cluster = district, detail.tau = c("district", "district/school"))
## End(Not run)
```

metainc

Meta-analysis of incidence rates

## **Description**

Calculation of common effect and random effects estimates (incidence rate ratio or incidence rate difference) for meta-analyses with event counts. Mantel-Haenszel, Cochran, inverse variance method, and generalised linear mixed model (GLMM) are available for pooling. For GLMMs, the rma.glmm function from R package **metafor** (Viechtbauer 2010) is called internally.

# Usage

```
metainc(
  event.e,
  time.e,
  event.c,
  time.c,
  studlab,
  data = NULL,
  subset = NULL,
  exclude = NULL,
  cluster = NULL,
  method = if (sm == "IRSD") "Inverse" else "MH",
  sm = gs("sminc"),
  incr = gs("incr"),
  method.incr = gs("method.incr"),
  model.glmm = "UM.FS",
  level = gs("level"),
  level.ma = gs("level.ma"),
  common = gs("common"),
  random = gs("random") | !is.null(tau.preset),
  overall = common | random,
  overall.hetstat = common | random,
  hakn = gs("hakn"),
  adhoc.hakn = gs("adhoc.hakn"),
 method.tau = ifelse(!is.na(charmatch(tolower(method), "glmm", nomatch = NA)), "ML",
    gs("method.tau")),
  method.tau.ci = gs("method.tau.ci"),
  tau.preset = NULL,
  TE.tau = NULL,
  tau.common = gs("tau.common"),
  prediction = gs("prediction"),
  level.predict = gs("level.predict"),
  method.bias = gs("method.bias"),
  n.e = NULL,
```

```
n.c = NULL,
 backtransf = if (sm == "IRSD") FALSE else gs("backtransf"),
  irscale = 1,
  irunit = "person-years",
  text.common = gs("text.common"),
  text.random = gs("text.random"),
  text.predict = gs("text.predict"),
  text.w.common = gs("text.w.common"),
  text.w.random = gs("text.w.random"),
  title = gs("title"),
  complab = gs("complab"),
  outclab = "",
  label.e = gs("label.e"),
  label.c = gs("label.c"),
  label.left = gs("label.left"),
  label.right = gs("label.right"),
  subgroup,
  subgroup.name = NULL,
  print.subgroup.name = gs("print.subgroup.name"),
  sep.subgroup = gs("sep.subgroup"),
  test.subgroup = gs("test.subgroup"),
  prediction.subgroup = gs("prediction.subgroup"),
  byvar,
  keepdata = gs("keepdata"),
 warn = gs("warn"),
 warn.deprecated = gs("warn.deprecated"),
  control = NULL,
)
```

## **Arguments**

event.e	Number of events in experimental group.
time.e	Person time at risk in experimental group.
event.c	Number of events in control group.
time.c	Person time at risk in control group.
studlab	An optional vector with study labels.
data	An optional data frame containing the study information, i.e., event.e, time.e, event.c, and time.c.
subset	An optional vector specifying a subset of studies to be used.
exclude	An optional vector specifying studies to exclude from meta-analysis, however, to include in printouts and forest plots.
cluster	An optional vector specifying which estimates come from the same cluster resulting in the use of a three-level meta-analysis model.
method	A character string indicating which method is to be used for pooling of studies. One of "MH", "Inverse", "Cochran", or "GLMM" can be abbreviated.

sm

n.c

A character string indicating which summary measure ("IRR", "IRD" or "IRSD") is to be used for pooling of studies, see Details. incr A numerical value which is added to cell frequencies for studies with a zero cell count, see Details. method.incr A character string indicating which continuity correction method should be used ("only0", "if0all", or "all"), see Details. A character string indicating which GLMM should be used. One of "UM.FS", model.glmm "UM. RS", and "CM. EL", see Details. level The level used to calculate confidence intervals for individual studies. level.ma The level used to calculate confidence intervals for meta-analysis estimates. A logical indicating whether a common effect meta-analysis should be concommon ducted. random A logical indicating whether a random effects meta-analysis should be conducted. A logical indicating whether overall summaries should be reported. This arguoverall ment is useful in a meta-analysis with subgroups if overall results should not be reported. overall.hetstat A logical value indicating whether to print heterogeneity measures for overall treatment comparisons. This argument is useful in a meta-analysis with subgroups if heterogeneity statistics should only be printed on subgroup level. hakn A logical indicating whether the method by Hartung and Knapp should be used to adjust test statistics and confidence intervals. adhoc.hakn A character string indicating whether an ad hoc variance correction should be applied in the case of an arbitrarily small Hartung-Knapp variance estimate, see Details. method.tau A character string indicating which method is used to estimate the betweenstudy variance  $\tau^2$  and its square root  $\tau$ . Either "DL", "PM", "REML", "ML", "HS", "SJ", "HE", or "EB", can be abbreviated. method.tau.ci A character string indicating which method is used to estimate the confidence interval of  $\tau^2$  and  $\tau$ . Either "QP", "BJ", "J", "PL", or "", can be abbreviated. Prespecified value for the square root of the between-study variance  $\tau^2$ . tau.preset Overall treatment effect used to estimate the between-study variance  $\tau^2$ . TE.tau tau.common A logical indicating whether tau-squared should be the same across subgroups. A logical indicating whether a prediction interval should be printed. prediction level.predict The level used to calculate prediction interval for a new study. method.bias A character string indicating which test is to be used. Either "Begg", "Egger", or "Thompson", can be abbreviated. See function metabias. Number of observations in experimental group (optional). n.e

Number of observations in control group (optional).

backtransf A logical indicating whether results for incidence rate ratio (sm = "IRR") should

be back transformed in printouts and plots. If TRUE (default), results will be presented as incidence rate ratios; otherwise log incidence rate ratios will be

shown.

irscale A numeric defining a scaling factor for printing of incidence rate differences.

irunit A character string specifying the time unit used to calculate rates, e.g. person-

years.

text.common A character string used in printouts and forest plot to label the pooled common

effect estimate.

text.random A character string used in printouts and forest plot to label the pooled random

effects estimate.

text.predict A character string used in printouts and forest plot to label the prediction inter-

val.

text.w.common A character string used to label weights of common effect model.

text.w.random A character string used to label weights of random effects model.

title Title of meta-analysis / systematic review.

complab Comparison label.
outclab Outcome label.

label.e Label for experimental group.

label.c Label for control group.

label.left Graph label on left side of forest plot.
label.right Graph label on right side of forest plot.

subgroup An optional vector to conduct a meta-analysis with subgroups.

subgroup.name A character string with a name for the subgroup variable.

print.subgroup.name

A logical indicating whether the name of the subgroup variable should be printed

in front of the group labels.

sep. subgroup A character string defining the separator between name of subgroup variable and

subgroup label.

test.subgroup A logical value indicating whether to print results of test for subgroup differ-

ences

prediction.subgroup

A logical indicating whether prediction intervals should be printed for sub-

groups.

byvar Deprecated argument (replaced by 'subgroup').

keepdata A logical indicating whether original data (set) should be kept in meta object.

warn A logical indicating whether warnings should be printed (e.g., if incr is added

to studies with zero cell frequencies).

warn.deprecated

A logical indicating whether warnings should be printed if deprecated arguments

are used.

control	An optional list to control the iterative process to estimate the between-study variance $\tau^2$ . This argument is passed on to rma.uni or rma.glmm, respectively.
	Additional arguments passed on to rma.glmm function and to catch deprecated arguments.

#### **Details**

Calculation of common and random effects estimates for meta-analyses comparing two incidence rates

The following measures of treatment effect are available:

- Incidence Rate Ratio (sm = "IRR")
- Incidence Rate Difference (sm = "IRD")
- Square root transformed Incidence Rate Difference (sm = "IRSD")

Default settings are utilised for several arguments (assignments using gs function). These defaults can be changed for the current R session using the settings.meta function.

Furthermore, R function update.meta can be used to rerun a meta-analysis with different settings.

## **Meta-analysis method:**

By default, both common effect and random effects models are considered (see arguments common and random). If method is "MH" (default), the Mantel-Haenszel method is used to calculate the common effect estimate (Greenland & Robbins, 1985); if method is "Inverse", inverse variance weighting is used for pooling; if method is "Cochran", the Cochran method is used for pooling (Bayne-Jones, 1964, Chapter 8).

A distinctive and frequently overlooked advantage of incidence rates is that individual patient data (IPD) can be extracted from count data. Accordingly, statistical methods for IPD, i.e., generalised linear mixed models, can be utilised in a meta-analysis of incidence rate ratios (Stijnen et al., 2010). These methods are available (argument method = "GLMM") by calling the rma.glmm function from R package **metafor** internally.

Three different GLMMs are available for meta-analysis of incidence rate ratios using argument model.glmm (which corresponds to argument model in the rma.glmm function):

- 1. Poisson regression model with fixed study effects (default) (model.glmm = "UM.FS", i.e., Unconditional Model Fixed Study effects)
- 2. Mixed-effects Poisson regression model with random study effects (model.glmm = "UM.RS", i.e., Unconditional Model Random Study effects)
- 3. Generalised linear mixed model (conditional Poisson-Normal) (model.glmm = "CM.EL", i.e., Conditional Model Exact Likelihood)

Details on these three GLMMs as well as additional arguments which can be provided using argument '...' in metainc are described in rma.glmm where you can also find information on the iterative algorithms used for estimation. Note, regardless of which value is used for argument model.glmm, results for two different GLMMs are calculated: common effect model (with fixed treatment effect) and random effects model (with random treatment effects).

## **Continuity correction:**

Three approaches are available to apply a continuity correction:

- Only studies with a zero cell count (method.incr = "only0", default)
- All studies if at least one study has a zero cell count (method.incr = "if0all")
- All studies irrespective of zero cell counts (method.incr = "all")

For studies with a zero cell count, by default, 0.5 is added to all cell frequencies of these studies (argument incr). This continuity correction is used both to calculate individual study results with confidence limits and to conduct meta-analysis based on the inverse variance method. For Mantel-Haenszel method, Cochran method, and GLMMs, nothing is added to zero cell counts. Accordingly, estimates for these methods are not defined if the number of events is zero in all studies either in the experimental or control group.

## **Estimation of between-study variance:**

The following methods to estimate the between-study variance  $\tau^2$  are available for the inverse variance method:

- DerSimonian-Laird estimator (method.tau = "DL")
- Paule-Mandel estimator (method.tau = "PM")
- Restricted maximum-likelihood estimator (method. tau = "REML")
- Maximum-likelihood estimator (method.tau = "ML")
- Hunter-Schmidt estimator (method. tau = "HS")
- Sidik-Jonkman estimator (method. tau = "SJ")
- Hedges estimator (method.tau = "HE")
- Empirical Bayes estimator (method. tau = "EB")

See metagen for more information on these estimators. Note, the maximum-likelihood method is utilized for GLMMs.

## **Confidence interval for the between-study variance:**

The following methods to calculate a confidence interval for  $\tau^2$  and  $\tau$  are available.

Argument	Method
method.tau.ci = "J"	Method by Jackson (2013)
<pre>method.tau.ci = "BJ"</pre>	Method by Biggerstaff and Jackson (2008)
method.tau.ci = "QP"	Q-Profile method (Viechtbauer, 2007)
method.tau.ci = "PL"	Profile-Likelihood method for three-level meta-analysis
	(Van den Noortgate et al., 2013)
method.tau.ci = ""	No confidence interval

See metagen for more information on these methods.

For GLMMs, no confidence intervals for  $\tau^2$  and  $\tau$  are calculated.

## Hartung-Knapp method:

Hartung and Knapp (2001a,b) proposed an alternative method for random effects meta-analysis based on a refined variance estimator for the treatment estimate. Simulation studies (Hartung and Knapp, 2001a,b; IntHout et al., 2014; Langan et al., 2019) show improved coverage probabilities compared to the classic random effects method.

In rare settings with very homogeneous treatment estimates, the Hartung-Knapp variance estimate can be arbitrarily small resulting in a very narrow confidence interval (Knapp and Hartung, 2003; Wiksten et al., 2016). In such cases, an *ad hoc* variance correction has been proposed by utilising

the variance estimate from the classic random effects model with the HK method (Knapp and Hartung, 2003; IQWiQ, 2020). An alternative approach is to use the wider confidence interval of classic common or random effects meta-analysis and the HK method (Wiksten et al., 2016; Jackson et al., 2017).

Argument adhoc. hakn can be used to choose the *ad hoc* method:

Argument	Ad hoc method
adhoc.hakn = ""	not used
adhoc.hakn = "se"	use variance correction if HK standard error is smaller
	than standard error from classic random effects
	meta-analysis (Knapp and Hartung, 2003)
adhoc.hakn = "iqwig6"	use variance correction if HK confidence interval
	is narrower than CI from classic random effects model
	with DerSimonian-Laird estimator (IQWiG, 2020)
adhoc.hakn = "ci"	use wider confidence interval of classic random effects
	and HK meta-analysis
	(Hybrid method 2 in Jackson et al., 2017)

For GLMMs, a method similar to Knapp and Hartung (2003) is implemented, see description of argument tdist in rma.glmm, and the *ad hoc* variance correction is not available.

#### **Prediction interval:**

A prediction interval for the proportion in a new study (Higgins et al., 2009) is calculated if arguments prediction and random are TRUE. Note, the definition of prediction intervals varies in the literature. This function implements equation (12) of Higgins et al., (2009) which proposed a t distribution with K-2 degrees of freedom where K corresponds to the number of studies in the meta-analysis.

#### Subgroup analysis:

Argument subgroup can be used to conduct subgroup analysis for a categorical covariate. The metareg function can be used instead for more than one categorical covariate or continuous covariates.

## **Exclusion of studies from meta-analysis:**

Arguments subset and exclude can be used to exclude studies from the meta-analysis. Studies are removed completely from the meta-analysis using argument subset, while excluded studies are shown in printouts and forest plots using argument exclude (see Examples in metagen). Meta-analysis results are the same for both arguments.

# Presentation of meta-analysis results:

Internally, both common effect and random effects models are calculated regardless of values choosen for arguments common and random. Accordingly, the estimate for the random effects model can be extracted from component TE.random of an object of class "meta" even if argument random = FALSE. However, all functions in R package **meta** will adequately consider the values for common and random. E.g. function print.meta will not print results for the random effects model if random = FALSE.

#### Value

An object of class c("metainc", "meta") with corresponding print, summary, and forest functions. The object is a list containing the following components:

event.e, time.e, event.c, time.c, studlab, exclude, cluster,

As defined above.

sm, method, incr, method.incr, model.glmm, warn,

As defined above.

level, level.ma, common, random,

As defined above.

overall, overall.hetstat,

As defined above.

hakn, adhoc.hakn, method.tau, method.tau.ci,

As defined above.

tau.preset, TE.tau, method.bias,

As defined above.

tau.common, title, complab, outclab,

As defined above.

label.e, label.c, label.left, label.right,

As defined above.

subgroup, subgroup.name, print.subgroup.name, sep.subgroup

As defined above.

TE, seTE Estimated treatment effect and standard error of individual studies.

lower, upper Lower and upper confidence interval limits for individual studies.

zval, pval z-value and p-value for test of treatment effect for individual studies.

w.common, w.random

Weight of individual studies (in common effect and random effects model).

TE.common, seTE.common

Estimated overall treatment effect and standard error (common effect model).

lower.common, upper.common

Lower and upper confidence interval limits (common effect model).

statistic.common, pval.common

z-value and p-value for test of overall treatment effect (common effect model).

TE.random, seTE.random

Estimated overall treatment effect and standard error (random effects model).

lower.random, upper.random

Lower and upper confidence interval limits (random effects model).

statistic.random, pval.random

z-value or t-value and corresponding p-value for test of overall treatment effect (random effects model).

prediction, level.predict

As defined above.

seTE.predict Standard error utilised for prediction interval.

lower.predict, upper.predict

Lower and upper limits of prediction interval.

k Number of estimates combined in meta-analysis.

k. study Number of studies combined in meta-analysis.

k.all Number of all studies.

k.TE Number of studies with estimable effects.

Q Heterogeneity statistic Q.

df.Q Degrees of freedom for heterogeneity statistic.

pval.Q P-value of heterogeneity test.

Q.LRT Heterogeneity statistic for likelihood-ratio test (only if method = "GLMM").

df.Q.LRT Degrees of freedom for likelihood-ratio test

pval.Q.LRT P-value of likelihood-ratio test. tau2 Between-study variance  $\tau^2$ .

se. tau2 Standard error of  $\tau^2$ .

lower.tau2, upper.tau2

Lower and upper limit of confidence interval for  $\tau^2$ .

tau Square-root of between-study variance  $\tau$ .

lower.tau, upper.tau

Lower and upper limit of confidence interval for  $\tau$ .

H Heterogeneity statistic H.

lower.H, upper.H

Lower and upper confidence limit for heterogeneity statistic H.

I2 Heterogeneity statistic I<sup>2</sup>.

lower.I2, upper.I2

Lower and upper confidence limit for heterogeneity statistic  $I^2$ .

Rb Heterogeneity statistic  $R_b$ .

lower.Rb, upper.Rb

Lower and upper confidence limit for heterogeneity statistic  $R_b$ .

sparse Logical flag indicating if any study included in meta-analysis has any zero cell

frequencies.

incr.event Increment added to number of events.

df . hakn Degrees of freedom for test of treatment effect for Hartung-Knapp method (only

if hakn = TRUE).

k.MH Number of studies combined in meta-analysis using Mantel-Haenszel method.

bylevs Levels of grouping variable - if subgroup is not missing.

TE.common.w, seTE.common.w

Estimated treatment effect and standard error in subgroups (common effect model)

- if subgroup is not missing.

lower.common.w, upper.common.w

Lower and upper confidence interval limits in subgroups (common effect model)

- if subgroup is not missing.

statistic.common.w, pval.common.w

z-value and p-value for test of treatment effect in subgroups (common effect

model) - if subgroup is not missing.

TE.random.w, seTE.random.w

Estimated treatment effect and standard error in subgroups (random effects model) - if subgroup is not missing.

lower.random.w, upper.random.w

Lower and upper confidence interval limits in subgroups (random effects model) - if subgroup is not missing.

statistic.random.w, pval.random.w

z-value or t-value and corresponding p-value for test of treatment effect in subgroups (random effects model) - if subgroup is not missing.

w.common.w, w.random.w

Weight of subgroups (in common effect and random effects model) - if subgroup is not missing.

df.hakn.w Degrees of freedom for test of treatment effect for Hartung-Knapp method in subgroups - if subgroup is not missing and hakn = TRUE.

event.e.w Number of events in experimental group in subgroups - if subgroup is not missing.

time.e.w Total person time in subgroups (experimental group) - if subgroup is not missing.

n.e.w Number of observations in experimental group in subgroups - if subgroup is not missing.

event.c.w Number of events in control group in subgroups - if subgroup is not missing.

time.c.w Total person time in subgroups (control group) - if subgroup is not missing.

n.c.w Number of observations in control group in subgroups - if subgroup is not missing.

k.w Number of studies combined within subgroups - if subgroup is not missing.

k.all.w Number of all studies in subgroups - if subgroup is not missing.

Q.w.common Overall within subgroups heterogeneity statistic Q (based on common effect model) - if subgroup is not missing.

Q.w.random Overall within subgroups heterogeneity statistic Q (based on random effects model) - if subgroup is not missing (only calculated if argument tau.common is TRUE).

df.Q.w Degrees of freedom for test of overall within subgroups heterogeneity - if subgroup is not missing.

pval.Q.w.common

P-value of within subgroups heterogeneity statistic Q (based on common effect model) - if subgroup is not missing.

pval.Q.w.random

P-value of within subgroups heterogeneity statistic Q (based on random effects model) - if subgroup is not missing.

Q.b. common Overall between subgroups heterogeneity statistic Q (based on common effect model) - if subgroup is not missing.

Q.b.random Overall between subgroups heterogeneity statistic Q (based on random effects model) - if subgroup is not missing.

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df.Q.b Degrees of freedom for test of overall between subgroups heterogeneity - if subgroup is not missing.

pval.Q.b.common

P-value of between subgroups heterogeneity statistic Q (based on common effect model) - if subgroup is not missing.

pval.Q.b.random

P-value of between subgroups heterogeneity statistic Q (based on random effects model) - if subgroup is not missing.

tau.w Square-root of between-study variance within subgroups - if subgroup is not missing.

H.w Heterogeneity statistic H within subgroups - if subgroup is not missing.

lower.H.w, upper.H.w

Lower and upper confidence limit for heterogeneity statistic H within subgroups - if subgroup is not missing.

I2. w Heterogeneity statistic  $I^2$  within subgroups - if subgroup is not missing.

lower.I2.w, upper.I2.w

Lower and upper confidence limit for heterogeneity statistic  $I^2$  within subgroups - if subgroup is not missing.

keepdata As defined above.

data Original data (set) used in function call (if keepdata = TRUE).

subset Information on subset of original data used in meta-analysis (if keepdata =

TRUE).

.glmm.common GLMM object generated by call of rma.glmm function (common effect model).
.glmm.random GLMM object generated by call of rma.glmm function (random effects model).

call Function call.

version Version of R package **meta** used to create object.

version.metafor

Version of R package **metafor** used for GLMMs.

# Author(s)

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#### See Also

```
metabin, update.meta, print.meta
```

### **Examples**

```
data(smoking)
m1 <- metainc(d.smokers, py.smokers, d.nonsmokers, py.nonsmokers,</pre>
  data = smoking, studlab = study)
print(m1, digits = 2)
m2 <- update(m1, method = "Cochran")</pre>
print(m2, digits = 2)
data(lungcancer)
m3 <- metainc(d.smokers, py.smokers, d.nonsmokers, py.nonsmokers,
  data = lungcancer, studlab = study)
print(m3, digits = 2)
# Redo Cochran meta-analysis with inflated standard errors
# All cause mortality
TEa <- log((smoking$d.smokers/smoking$py.smokers) /</pre>
  (smoking$d.nonsmokers/smoking$py.nonsmokers))
seTEa <- sqrt(1 / smoking$d.smokers + 1 / smoking$d.nonsmokers +</pre>
  2.5 / smoking$d.nonsmokers)
metagen(TEa, seTEa, sm = "IRR", studlab = smoking$study)
# Lung cancer mortality
TEl <- log((lungcancer$d.smokers/lungcancer$py.smokers) /</pre>
```

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```
(lungcancer$d.nonsmokers/lungcancer$py.nonsmokers))
seTEl <- sqrt(1 / lungcancer$d.smokers + 1 / lungcancer$d.nonsmokers +
2.25 / lungcancer$d.nonsmokers)
metagen(TEl, seTEl, sm = "IRR", studlab = lungcancer$study)

## Not run:
# Meta-analysis using generalised linear mixed models
# (only if R packages 'metafor' and 'lme4' are available)

# Poisson regression model (fixed study effects)
#
# 4 <- metainc(d.smokers, py.smokers, d.nonsmokers, py.nonsmokers,
    data = smoking, studlab = study, method = "GLMM")

# Mixed-effects Poisson regression model (random study effects)
#

# update(m4, model.glmm = "UM.RS", nAGQ = 1)
#
# Generalised linear mixed model (conditional Poisson-Normal)
#

# update(m4, model.glmm = "CM.EL")

## End(Not run)</pre>
```

metainf

Influence analysis in meta-analysis using leave-one-out method

### Description

Performs an influence analysis. Pooled estimates are calculated omitting one study at a time.

# Usage

```
metainf(x, pooled, sortvar)
```

#### **Arguments**

X	An object of class meta.
pooled	A character string indicating whether a common effect or

A character string indicating whether a common effect or random effects model is used for pooling. Either missing (see Details), "common" or "random", can be

abbreviated.

Sortvar An optional vector used to sort the individual studies (must be of same length as

x\$TE).

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#### **Details**

Performs a influence analysis; pooled estimates are calculated omitting one study at a time. Studies are sorted according to sortvar.

Information from object x is utilised if argument pooled is missing. A common effect model is assumed (pooled="common") if argument x\$common is TRUE; a random effects model is assumed (pooled="random") if argument x\$random is TRUE and x\$common is FALSE.

#### Value

An object of class c("metainf", "meta") with corresponding print, and forest functions. The object is a list containing the following components:

TE, seTE Estimated treatment effect and standard error of pooled estimate in influence

analysis.

lower, upper Lower and upper confidence interval limits.

statistic Statistic for test of overall effect.

P-value for test of overall effect.

studlab Study label describing omission of studies.

w Sum of weights from common effect or random effects model.

I2 Heterogeneity statistic  $I^2$ .

Rb Heterogeneity statistic  $R_b$ .

tau Square-root of between-study variance.

df.hakn Degrees of freedom for test of treatment effect for Hartung-Knapp method (only

if hakn = TRUE).

sm Summary measure.
method Method used for pooling.

k Number of studies combined in meta-analysis.

pooled As defined above.

common A logical indicating whether analysis is based on common effect model.

A logical indicating whether analysis is based on random effects model.

TE.common, seTE.common

Value is NA.

TE.random, seTE.random

Value is NA.

Q Value is NA.

level.ma The level used to calculate confidence intervals for pooled estimates.

hakn A logical indicating whether the method by Hartung and Knapp is used to adjust

test statistics and confidence intervals.

adhoc.hakn A character string indicating whether ad hoc variance correction should be used

for Hartung-Knapp method.

method.tau A character string indicating which method is used to estimate the between-

study variance  $\tau^2$ .

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tau.preset Prespecified value for the square root of the between-study variance  $\tau^2$ . TE.tau Overall treatment effect used to estimate the between-study variance  $\tau^2$ . n.harmonic.mean Harmonic mean of number of observations (for back transformation of Freeman-Tukey Double arcsine transformation). Version Version of R package **meta** used to create object.

### Author(s)

Guido Schwarzer <sc@imbi.uni-freiburg.de>

#### References

Cooper H & Hedges LV (1994): *The Handbook of Research Synthesis*. Newbury Park, CA: Russell Sage Foundation

#### See Also

```
metabin, metacont, print.meta
```

# **Examples**

```
data(Fleiss1993bin)
m1 <- metabin(d.asp, n.asp, d.plac, n.plac,</pre>
  data = Fleiss1993bin, studlab = study, sm = "RR", method = "I")
metainf(m1)
metainf(m1, pooled = "random")
forest(metainf(m1))
forest(metainf(m1), layout = "revman5")
forest(metainf(m1, pooled = "random"))
metainf(m1, sortvar = study)
metainf(m1, sortvar = 7:1)
m2 <- update(m1, title = "Fleiss1993bin meta-analysis", backtransf = FALSE)</pre>
metainf(m2)
data(Fleiss1993cont)
m3 <- metacont(n.psyc, mean.psyc, sd.psyc, n.cont, mean.cont, sd.cont,</pre>
  data = Fleiss1993cont, sm = "SMD")
metainf(m3)
```

metamean

Meta-analysis of single means

### **Description**

Calculation of an overall mean from studies reporting a single mean using the inverse variance method for pooling; inverse variance weighting is used for pooling.

# Usage

```
metamean(
 n,
 mean,
 sd,
  studlab,
 data = NULL,
 subset = NULL,
 exclude = NULL,
  cluster = NULL,
 median,
 q1,
  q3,
 min,
 max,
 method.mean = "Luo",
 method.sd = "Shi",
  approx.mean,
  approx.sd,
  sm = gs("smmean"),
 method.ci = gs("method.ci.cont"),
  level = gs("level"),
  level.ma = gs("level.ma"),
  common = gs("common"),
  random = gs("random") | !is.null(tau.preset),
  overall = common | random,
  overall.hetstat = common | random,
  hakn = gs("hakn"),
  adhoc.hakn = gs("adhoc.hakn"),
 method.tau = gs("method.tau"),
 method.tau.ci = gs("method.tau.ci"),
  tau.preset = NULL,
  TE.tau = NULL,
  tau.common = gs("tau.common"),
  prediction = gs("prediction"),
  level.predict = gs("level.predict"),
  null.effect = NA,
 method.bias = gs("method.bias"),
```

```
backtransf = gs("backtransf"),
  text.common = gs("text.common"),
  text.random = gs("text.random"),
  text.predict = gs("text.predict"),
  text.w.common = gs("text.w.common"),
  text.w.random = gs("text.w.random"),
  title = gs("title"),
  complab = gs("complab"),
 outclab = "",
  subgroup,
  subgroup.name = NULL,
  print.subgroup.name = gs("print.subgroup.name"),
  sep.subgroup = gs("sep.subgroup"),
  test.subgroup = gs("test.subgroup"),
  prediction.subgroup = gs("prediction.subgroup"),
  byvar,
  keepdata = gs("keepdata"),
 warn = gs("warn"),
 warn.deprecated = gs("warn.deprecated"),
  control = NULL,
)
```

# **Arguments**

n	Number of observations.
mean	Estimated mean.
sd	Standard deviation.
studlab	An optional vector with study labels.
data	An optional data frame containing the study information.
subset	An optional vector specifying a subset of studies to be used.
exclude	An optional vector specifying studies to exclude from meta-analysis, however, to include in printouts and forest plots.
cluster	An optional vector specifying which estimates come from the same cluster resulting in the use of a three-level meta-analysis model.
median	Median (used to estimate the mean and standard deviation).
q1	First quartile (used to estimate the mean and standard deviation).
q3	Third quartile (used to estimate the mean and standard deviation).
min	Minimum (used to estimate the mean and standard deviation).
max	Maximum (used to estimate the mean and standard deviation).
method.mean	A character string indicating which method to use to approximate the mean from the median and other statistics (see Details).
method.sd	A character string indicating which method to use to approximate the standard deviation from sample size, median, interquartile range and range (see Details).

approx.mean Approximation method to estimate means (see Details). Approximation method to estimate standard deviations (see Details). approx.sd A character string indicating which summary measure ("MRAW" or "MLN") is to be used for pooling of studies. method.ci A character string indicating which method is used to calculate confidence intervals for individual studies, see Details. level The level used to calculate confidence intervals for individual studies. level.ma The level used to calculate confidence intervals for meta-analysis estimates. common A logical indicating whether a common effect meta-analysis should be conducted. random A logical indicating whether a random effects meta-analysis should be conducted. overall A logical indicating whether overall summaries should be reported. This argument is useful in a meta-analysis with subgroups if overall results should not be reported. overall.hetstat A logical value indicating whether to print heterogeneity measures for overall treatment comparisons. This argument is useful in a meta-analysis with subgroups if heterogeneity statistics should only be printed on subgroup level. hakn A logical indicating whether the method by Hartung and Knapp should be used to adjust test statistics and confidence intervals. adhoc.hakn A character string indicating whether an ad hoc variance correction should be applied in the case of an arbitrarily small Hartung-Knapp variance estimate, see Details. A character string indicating which method is used to estimate the betweenmethod.tau study variance  $\tau^2$  and its square root  $\tau$ . Either "DL", "PM", "REML", "ML", "HS", "SJ", "HE", or "EB", can be abbreviated. method.tau.ci A character string indicating which method is used to estimate the confidence interval of  $\tau^2$  and  $\tau$ . Either "QP", "BJ", "J", "PL", or "", can be abbreviated. Prespecified value for the square root of the between-study variance  $\tau^2$ . tau.preset Overall treatment effect used to estimate the between-study variance tau-squared. TE.tau tau.common A logical indicating whether tau-squared should be the same across subgroups. prediction A logical indicating whether a prediction interval should be printed. level.predict The level used to calculate prediction interval for a new study. null.effect A numeric value specifying the effect under the null hypothesis. method.bias A character string indicating which test is to be used. Either "Begg", "Egger", or "Thompson", can be abbreviated. See function metabias. backtransf A logical indicating whether results should be back transformed in printouts and plots for sm = "MLN". If TRUE (default), results will be presented as means; otherwise logarithm of means will be shown. A character string used in printouts and forest plot to label the pooled common text.common effect estimate.

text.random A character string used in printouts and forest plot to label the pooled random

effects estimate.

text.predict A character string used in printouts and forest plot to label the prediction inter-

val.

text.w.common A character string used to label weights of common effect model.

text.w.random A character string used to label weights of random effects model.

title Title of meta-analysis / systematic review.

complab Comparison label.
outclab Outcome label.

subgroup An optional vector to conduct a meta-analysis with subgroups.

subgroup.name A character string with a name for the subgroup variable.

print.subgroup.name

A logical indicating whether the name of the subgroup variable should be printed

in front of the group labels.

sep.subgroup A character string defining the separator between name of subgroup variable and

subgroup label.

test.subgroup A logical value indicating whether to print results of test for subgroup differ-

ences.

prediction.subgroup

A logical indicating whether prediction intervals should be printed for sub-

groups.

byvar Deprecated argument (replaced by 'subgroup').

keepdata A logical indicating whether original data (set) should be kept in meta object.

warn A logical indicating whether warnings should be printed (e.g., if studies are

excluded from meta-analysis due to zero standard deviations).

warn.deprecated

A logical indicating whether warnings should be printed if deprecated arguments

are used.

control An optional list to control the iterative process to estimate the between-study

variance  $\tau^2$ . This argument is passed on to rma.uni.

... Additional arguments (to catch deprecated arguments).

#### Details

Common effect and random effects meta-analysis of single means to calculate an overall mean; inverse variance weighting is used for pooling. The following transformations of means are implemented to calculate an overall mean:

- Raw, i.e. untransformed, means (sm = "MRAW", default)
- Log transformed means (sm = "MLN")

Note, you should use R function metacont to compare means of pairwise comparisons instead of using metamean for each treatment arm separately which will break randomisation in randomised controlled trials.

Calculations are conducted on the log scale if sm = "ROM". Accordingly, list elements TE, TE. common, and TE.random contain the logarithm of means. In printouts and plots these values are back transformed if argument backtransf = TRUE.

Default settings are utilised for several arguments (assignments using gs function). These defaults can be changed for the current R session using the settings.meta function.

Furthermore, R function update.meta can be used to rerun a meta-analysis with different settings.

# Approximate means from sample sizes, medians and other statistics:

Missing means can be derived from

- 1. sample size, median, interquartile range and range (arguments n, median, q1, q3, min, and max),
- 2. sample size, median and interquartile range (arguments n, median, q1, and q3), or
- 3. sample size, median and range (arguments n, median, min, and max).

By default, methods described in Luo et al. (2018) are utilized (argument method. mean = "Luo"):

- equation (15) if sample size, median, interquartile range and range are available,
- equation (11) if sample size, median and interquartile range are available,
- equation (7) if sample size, median and range are available.

Instead the methods described in Wan et al. (2014) are used if argument method. mean = "Wan":

- equation (10) if sample size, median, interquartile range and range are available,
- equation (14) if sample size, median and interquartile range are available,
- equation (2) if sample size, median and range are available.

By default, missing means are replaced successively using interquartile ranges and ranges (if available), interquartile ranges (if available) and finally ranges. Argument approx.mean can be used to overwrite this behaviour for each individual study and treatment arm:

- use means directly (entry "" in argument approx.mean);
- median, interquartile range and range ("iqr.range");
- median and interquartile range ("iqr");
- median and range ("range").

### Approximate standard deviations from sample sizes, medians and other statistics:

Missing standard deviations can be derived from

- 1. sample size, median, interquartile range and range (arguments n, median, q1, q3, min, and max).
- 2. sample size, median and interquartile range (arguments n, median, q1 and q3), or
- 3. sample size, median and range (arguments n, median, min and max).

Wan et al. (2014) describe methods to estimate the standard deviation from the sample size, median and additional statistics. Shi et al. (2020) provide an improved estimate of the standard deviation if the interquartile range and range are available in addition to the sample size and median. Accordingly, equation (11) in Shi et al. (2020) is the default (argument method.sd = "Shi"), if the median, interquartile range and range are provided. The method by Wan et al. (2014) is used if argument method.sd = "Wan" and, depending on the sample size, either equation (12) or (13) is used. If only the interquartile range or range is available, equations (15) / (16) and (7) / (9) in Wan et al. (2014) are used, respectively.

By default, missing standard deviations are replaced successively using these method, i.e., interquartile ranges and ranges are used before interquartile ranges before ranges. Argument approx.sd can be used to overwrite this default for each individual study and treatment arms:

- sample size, median, interquartile range and range ("iqr.range");
- sample size, median and interquartile range ("iqr");
- sample size, median and range ("range").

#### **Confidence intervals for individual studies:**

For untransformed means (argument sm = "MRAW"), the confidence interval for individual studies can be based on the

- standard normal distribution (method.ci = "z", default), or
- t-distribution (method.ci = "t").

### **Estimation of between-study variance:**

The following methods to estimate the between-study variance  $\tau^2$  are available:

- DerSimonian-Laird estimator (method.tau = "DL")
- Paule-Mandel estimator (method.tau = "PM")
- Restricted maximum-likelihood estimator (method.tau = "REML")
- Maximum-likelihood estimator (method. tau = "ML")
- Hunter-Schmidt estimator (method.tau = "HS")
- Sidik-Jonkman estimator (method.tau = "SJ")
- Hedges estimator (method.tau = "HE")
- Empirical Bayes estimator (method.tau = "EB")

See metagen for more information on these estimators.

### Confidence interval for the between-study variance:

The following methods to calculate a confidence interval for  $\tau^2$  and  $\tau$  are available.

Argument	Method
method.tau.ci = "J"	Method by Jackson (2013)
method.tau.ci = "BJ"	Method by Biggerstaff and Jackson (2008)
<pre>method.tau.ci = "QP"</pre>	Q-Profile method (Viechtbauer, 2007)
<pre>method.tau.ci = "PL"</pre>	Profile-Likelihood method for three-level meta-analysis
	(Van den Noortgate et al., 2013)
<pre>method.tau.ci = ""</pre>	No confidence interval

See metagen for more information on these methods.

#### Hartung-Knapp method:

Hartung and Knapp (2001) proposed an alternative method for random effects meta-analysis based on a refined variance estimator for the treatment estimate. Simulation studies (Hartung and Knapp, 2001; IntHout et al., 2014; Langan et al., 2019) show improved coverage probabilities compared to the classic random effects method.

In rare settings with very homogeneous treatment estimates, the Hartung-Knapp variance estimate can be arbitrarily small resulting in a very narrow confidence interval (Knapp and Hartung, 2003;

Wiksten et al., 2016). In such cases, an *ad hoc* variance correction has been proposed by utilising the variance estimate from the classic random effects model with the HK method (Knapp and Hartung, 2003; IQWiQ, 2020). An alternative approach is to use the wider confidence interval of classic common or random effects meta-analysis and the HK method (Wiksten et al., 2016; Jackson et al., 2017).

Argument adhoc. hakn can be used to choose the *ad hoc* method:

Argument	Ad hoc method
adhoc.hakn = ""	not used
adhoc.hakn = "se"	use variance correction if HK standard error is smaller
	than standard error from classic random effects
	meta-analysis (Knapp and Hartung, 2003)
adhoc.hakn="iqwig6"	use variance correction if HK confidence interval
	is narrower than CI from classic random effects model
	with DerSimonian-Laird estimator (IQWiG, 2020)
adhoc.hakn = "ci"	use wider confidence interval of classic random effects
	and HK meta-analysis
	(Hybrid method 2 in Jackson et al., 2017)

#### **Prediction interval:**

A prediction interval for the proportion in a new study (Higgins et al., 2009) is calculated if arguments prediction and random are TRUE. Note, the definition of prediction intervals varies in the literature. This function implements equation (12) of Higgins et al., (2009) which proposed a t distribution with K-2 degrees of freedom where K corresponds to the number of studies in the meta-analysis.

### **Subgroup analysis:**

Argument subgroup can be used to conduct subgroup analysis for a categorical covariate. The metareg function can be used instead for more than one categorical covariate or continuous covariates.

### **Exclusion of studies from meta-analysis:**

Arguments subset and exclude can be used to exclude studies from the meta-analysis. Studies are removed completely from the meta-analysis using argument subset, while excluded studies are shown in printouts and forest plots using argument exclude (see Examples in metagen). Meta-analysis results are the same for both arguments.

## Presentation of meta-analysis results:

Internally, both common effect and random effects models are calculated regardless of values choosen for arguments common and random. Accordingly, the estimate for the random effects model can be extracted from component TE.random of an object of class "meta" even if argument random = FALSE. However, all functions in R package **meta** will adequately consider the values for common and random. E.g. functions print.meta and forest.meta will not print results for the random effects model if random = FALSE.

#### Value

An object of class c("metamean", "meta") with corresponding print, summary, and forest functions. The object is a list containing the following components:

n, mean, sd, As defined above. studlab, exclude, cluster, sm, method.ci, As defined above. median, q1, q3, min, max, As defined above. method.mean, method.sd, As defined above. approx.mean, approx.sd, As defined above. level, level.ma, As defined above. common, random, As defined above. overall, overall.hetstat, As defined above. hakn, adhoc.hakn, method.tau, method.tau.ci, As defined above. tau.preset, TE.tau, method.bias, As defined above. tau.common, title, complab, outclab, As defined above. subgroup, subgroup.name, print.subgroup.name, sep.subgroup, warn As defined above. TE, seTE Estimated effect (mean or log mean) and standard error of individual studies. lower, upper Lower and upper confidence interval limits for individual studies. statistic, pval Statistic and p-value for test of treatment effect for individual studies. w.common, w.random Weight of individual studies (in common effect and random effects model). TE.common, seTE.common Estimated overall effect (mean or log mean) and standard error (common effect model). lower.common, upper.common Lower and upper confidence interval limits (common effect model). statistic.common, pval.common Statistic and p-value for test of overall treatment effect (common effect model). TE.random, seTE.random Estimated overall effect (mean or log mean) and standard error (random effects model). lower.random, upper.random Lower and upper confidence interval limits (random effects model). statistic.random, pval.random Statistic and p-value for test of overall treatment effect (random effects model).

prediction, level.predict

As defined above.

seTE.predict Standard error utilised for prediction interval.

lower.predict, upper.predict

Lower and upper limits of prediction interval.

k Number of estimates combined in meta-analysis.

k.study Number of studies combined in meta-analysis.

k.all Number of all studies.

k.TE Number of studies with estimable effects.

Q Heterogeneity statistic. tau2 Between-study variance  $\tau^2$ .

se. tau2 Standard error of  $\tau^2$ .

lower.tau2, upper.tau2

Lower and upper limit of confidence interval for  $\tau^2$ .

tau Square-root of between-study variance  $\tau$ .

lower.tau, upper.tau

Lower and upper limit of confidence interval for  $\tau$ .

H Heterogeneity statistic H.

lower.H, upper.H

Lower and upper confidence limit for heterogeneity statistic H.

I2 Heterogeneity statistic I<sup>2</sup>.

lower.I2, upper.I2

Lower and upper confidence limit for heterogeneity statistic  $I^2$ .

Rb Heterogeneity statistic  $R_b$ .

lower.Rb, upper.Rb

Lower and upper confidence limit for heterogeneity statistic  $R_b$ .

method Pooling method: "Inverse".

df.hakn Degrees of freedom for test of treatment effect for Hartung-Knapp method (only

if hakn = TRUE).

bylevs Levels of grouping variable - if subgroup is not missing.

TE.common.w, seTE.common.w

Estimated effect and standard error in subgroups (common effect model) - if subgroup is not missing.

subgroup is not missi

lower.common.w, upper.common.w

Lower and upper confidence interval limits in subgroups (common effect model)

- if subgroup is not missing.

statistic.common.w, pval.common.w

Statistics and p-values for test of treatment effect in subgroups (common effect

model) - if subgroup is not missing.

TE.random.w, seTE.random.w

Estimated effect and standard error in subgroups (random effects model) - if subgroup is not missing.

lower.random.w, upper.random.w

Lower and upper confidence interval limits in subgroups (random effects model)

- if subgroup is not missing.

statistic.random.w, pval.random.w

Statistics and p-values for test of treatment effect in subgroups (random effects model) - if subgroup is not missing.

w.common.w, w.random.w

Weight of subgroups (in common effect and random effects model) - if subgroup is not missing.

df.hakn.w Degrees of freedom for test of effect for Hartung-Knapp method in subgroups - if subgroup is not missing and hakn = TRUE.

n.e.w Number of observations in experimental group in subgroups - if subgroup is not missing.

n.c.w Number of observations in control group in subgroups - if subgroup is not missing.

k.w Number of studies combined within subgroups - if subgroup is not missing.

k.all.w Number of all studies in subgroups - if subgroup is not missing.

Q.w.common Overall within subgroups heterogeneity statistic Q (based on common effect model) - if subgroup is not missing.

Q.w.random Overall within subgroups heterogeneity statistic Q (based on random effects model) - if subgroup is not missing (only calculated if argument tau.common is TRUE).

df.Q.w Degrees of freedom for test of overall within subgroups heterogeneity - if subgroup is not missing.

pval.Q.w.common

P-value of within subgroups heterogeneity statistic Q (based on common effect model) - if subgroup is not missing.

pval.Q.w.random

P-value of within subgroups heterogeneity statistic Q (based on random effects model) - if subgroup is not missing.

Q.b. common Overall between subgroups heterogeneity statistic Q (based on common effect model) - if subgroup is not missing.

Q.b.random Overall between subgroups heterogeneity statistic Q (based on random effects model) - if subgroup is not missing.

df.Q.b Degrees of freedom for test of overall between subgroups heterogeneity - if subgroup is not missing.

pval.Q.b.common

P-value of between subgroups heterogeneity statistic Q (based on common effect model) - if subgroup is not missing.

pval.Q.b.random

P-value of between subgroups heterogeneity statistic Q (based on random effects model) - if subgroup is not missing.

tau.w Square-root of between-study variance within subgroups - if subgroup is not missing.

H.w Heterogeneity statistic H within subgroups - if subgroup is not missing. lower.H.w, upper.H.w

Lower and upper confidence limit for heterogeneity statistic H within subgroups - if subgroup is not missing.

I2. w Heterogeneity statistic  $I^2$  within subgroups - if subgroup is not missing.

lower.I2.w, upper.I2.w

Lower and upper confidence limit for heterogeneity statistic I<sup>2</sup> within subgroups

- if subgroup is not missing.

keepdata As defined above.

data Original data (set) used in function call (if keepdata = TRUE).

subset Information on subset of original data used in meta-analysis (if keepdata =

TRUE).

call Function call.

version Version of R package **meta** used to create object.

#### Note

The function metagen is called internally to calculate individual and overall treatment estimates and standard errors.

#### Author(s)

Guido Schwarzer <sc@imbi.uni-freiburg.de>

#### References

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Viechtbauer W (2010): Conducting Meta-Analyses in R with the Metafor Package. *Journal of Statistical Software*, **36**, 1–48

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### See Also

```
update.meta, metamean, metagen
```

# **Examples**

```
m1 <- metamean(rep(100, 3), 1:3, rep(1, 3))
m1

m2 <- update(m1, sm = "MLN")
m2

# With test for overall mean equal to 2
#
update(m1, null.effect = 2)
update(m2, null.effect = 2)

# Print results without back-transformation
#
update(m1, backtransf = FALSE)
update(m2, backtransf = FALSE)
update(m1, null.effect = 2, backtransf = FALSE)
update(m2, null.effect = 2, backtransf = FALSE)</pre>
```

metamerge

Merge pooled results of two meta-analyses

# Description

This function can be used to merge pooled results of two meta-analyses into a single meta-analysis object. This is, for example, useful to produce a forest plot of a random-effects meta-analysis with and without using the Hartung-Knapp method.

## Usage

```
metamerge(
  meta1,
  meta2,
  pooled1,
  pooled2,
  text.pooled1,
  text.w.pooled1,
  text.w.pooled2,
  detail.tau1,
  detail.tau2,
  backtransf
)
```

## **Arguments**

meta1	First meta-analysis object (see Details).
meta2	Second meta-analysis object (see Details).
pooled1	A character string indicating whether results of common effect or random effects model should be considered for first meta-analysis. Either "common" or "random", can be abbreviated.
pooled2	A character string indicating whether results of common effect or random effects model should be considered for second meta-analysis. Either "common" or "random", can be abbreviated.
text.pooled1	A character string used in printouts and forest plot to label the estimate from the first meta-analysis.
text.pooled2	A character string used in printouts and forest plot to label the estimate from the second meta-analysis.
text.w.pooled1	A character string used to label weights of the first meta-analysis.
text.w.pooled2	A character string used to label weights of the second meta-analysis.
detail.tau1	A character string used to label estimate of between-study variance of the first meta-analysis.
detail.tau2	A character string used to label estimate of between-study variance of the second meta-analysis.
backtransf	A logical indicating whether results should be back transformed in printouts and plots. If backtransf=TRUE (default), results for sm="OR" are printed as odds ratios rather than log odds ratios, for example.

#### Details

In R package **meta**, objects of class "meta" contain results of both a common effect and random effects meta-analysis. This function enables the user to keep the results of one of these models and to add results from a second meta-analysis or a sensitivity analysis.

Applications of this function include printing and plotting results of the common effect or random effects meta-analysis and the

- Hartung-Knapp method (see argument hakn in metagen),
- trim-and-fill method (trimfill),
- limit meta-analyis (limitmeta from R package metasens),
- Copas selection model (copas from R package **metasens**),
- robust variance meta-analysis model (robu from R package robumeta).

The first argument must be an object created by a meta-analysis function, e.g., metagen or metabin. It is also possible to provide an object created with limitmeta or copas. In this case, arguments meta2 and pooled2 will be ignored.

The second meta-analysis could be an object created by a meta-analysis function or with trimfill, limitmeta, copas, or robu.

The created meta-analysis object only contains the study results from the first meta-analysis which are shown in printouts and forest plots. This only makes a difference for meta-analysis methods

where individual study results differ, e.g., Mantel-Haenszel and Peto method for binary outcomes (see metabin).

R function metabind can be used to print and plot the results of more than two meta-analyses, however, without showing individual study results.

#### Value

An object of class "meta" and "metamerge" with corresponding print, summary, and forest functions. The following list elements have a different meaning:

TE, seTE, studlab

Treatment estimate, standard error, and study labels (first meta-analyis).

lower, upper Lower and upper confidence interval limits for individual studies (first meta-

analysis).

statistic, pval

Statistic and p-value for test of treatment effect for individual studies (first meta-analysis.

w.common Weight of individual studies (first meta-analysis).

w.random Weight of individual studies (second meta-analysis).

TE.common, seTE.common

Estimated overall treatment effect and standard error (first meta-analysis).

lower.common, upper.common

Lower and upper confidence interval limits (first meta-analysis).

statistic.common, pval.common

Statistic and p-value for test of overall treatment effect (first meta-analysis).

TE.random, seTE.random

Estimated overall treatment effect and standard error (second meta-analysis).

lower.random, upper.random

Lower and upper confidence interval limits (second meta-analysis).

statistic.random, pval.random

Statistic and p-value for test of overall treatment effect (second meta-analysis).

lower.predict, upper.predict

Lower and upper limits of prediction interval (related to first meta-analysis).

k Number of studies combined in first meta-analysis.

Q Heterogeneity statistic (first meta-analysis).

df.Q Degrees of freedom for heterogeneity statistic (first meta-analysis).

pval.Q P-value of heterogeneity test (first meta-analysis).

tau2 Between-study variance(s)  $\tau^2$  (first and second meta-analysis).

lower.tau2, upper.tau2

Lower and upper limit of confidence interval(s) for  $\tau^2$  (first and second meta-analysis).

tau Square-root of between-study variance(s)  $\tau$  (first and second meta-analysis).

lower.tau, upper.tau

Lower and upper limit of confidence interval(s) for  $\tau$  (first and second meta-analysis).

```
text.common Label for the first meta-analysis.

text.random Label for the second meta-analysis.
```

See metagen for information on other list elements.

### Author(s)

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#### See Also

metagen, metabind

# **Examples**

```
data(Fleiss1993cont)
m1 <- metacont(n.psyc, mean.psyc, sd.psyc, n.cont, mean.cont, sd.cont,</pre>
  data = Fleiss1993cont, sm = "MD", common = FALSE,
  text.random = "Classic random effects", text.w.random = "RE")
# Use Hartung-Knapp method
m2 <- update(m1, hakn = TRUE,</pre>
  text.random = "Hartung-Knapp method", text.w.random = "HK")
# Merge results of the two meta-analyses
m12 <- metamerge(m1, m2)</pre>
m12
forest(m12, rightcols = c("effect", "ci", "w.common"))
# Show results for DerSimonian-Laird and REML estimate of
# between-study variance
m3 <- update(m1,
  text.random = "Random effects moded (DL)", text.w.random = "DL")
m4 \leftarrow update(m1, method.tau = "REML",
  text.random = "Random effects moded (REML)", text.w.random = "REML")
m34 <- metamerge(m3, m4)
m34
data(Fleiss1993bin)
# Mantel-Haenszel method
m5 <- metabin(d.asp, n.asp, d.plac, n.plac, data = Fleiss1993bin,</pre>
  studlab = paste(study, year), sm = "OR", random = FALSE,
  text.common = "MH method", text.w.common = "MH")
# Peto method
```

```
#
m6 <- update(m5, method = "Peto", text.common = "Peto method",
    text.w.common = "Peto")
#
# Merge results (show individual results for MH method)
#
m56 <- metamerge(m5, m6)
m56
forest(m56, digits = 4)
#
# Merge results (show individual results for Peto method)
#
m65 <- metamerge(m6, m5)
m65</pre>
```

metaprop

Meta-analysis of single proportions

# **Description**

Calculation of an overall proportion from studies reporting a single proportion. Inverse variance method and generalised linear mixed model (GLMM) are available for pooling. For GLMMs, the rma.glmm function from R package **metafor** (Viechtbauer 2010) is called internally.

### Usage

```
metaprop(
  event,
  n,
  studlab,
  data = NULL,
  subset = NULL,
  exclude = NULL,
  cluster = NULL,
 method,
  sm = gs("smprop"),
  incr = gs("incr"),
  method.incr = gs("method.incr"),
 method.ci = gs("method.ci.prop"),
  level = gs("level"),
  level.ma = gs("level.ma"),
  common = gs("common"),
  random = gs("random") | !is.null(tau.preset),
  overall = common | random,
  overall.hetstat = common | random,
  hakn = gs("hakn"),
  adhoc.hakn = gs("adhoc.hakn"),
```

```
method.tau,
 method.tau.ci = gs("method.tau.ci"),
  tau.preset = NULL,
 TE.tau = NULL,
  tau.common = gs("tau.common"),
  prediction = gs("prediction"),
  level.predict = gs("level.predict"),
  null.effect = NA,
 method.bias = gs("method.bias"),
 backtransf = gs("backtransf"),
 pscale = 1,
  text.common = gs("text.common"),
  text.random = gs("text.random"),
  text.predict = gs("text.predict"),
  text.w.common = gs("text.w.common"),
  text.w.random = gs("text.w.random"),
  title = gs("title"),
  complab = gs("complab"),
  outclab = "",
  subgroup,
  subgroup.name = NULL,
  print.subgroup.name = gs("print.subgroup.name"),
  sep.subgroup = gs("sep.subgroup"),
  test.subgroup = gs("test.subgroup"),
  prediction.subgroup = gs("prediction.subgroup"),
  byvar,
  keepdata = gs("keepdata"),
 warn = gs("warn"),
 warn.deprecated = gs("warn.deprecated"),
 control = NULL,
  . . .
)
```

#### **Arguments**

event	Number of events.
n	Number of observations.
studlab	An optional vector with study labels.
data	An optional data frame containing the study information, i.e., event and n.
subset	An optional vector specifying a subset of studies to be used.
exclude	An optional vector specifying studies to exclude from meta-analysis, however, to include in printouts and forest plots.
cluster	An optional vector specifying which estimates come from the same cluster resulting in the use of a three-level meta-analysis model.
method	A character string indicating which method is to be used for pooling of studies. One of "Inverse" and "GLMM", can be abbreviated.

sm

A character string indicating which summary measure ("PLOGIT", "PAS", "PFT",

"PLN", or "PRAW") is to be used for pooling of studies, see Details. incr A numeric which is added to event number and sample size of studies with zero or all events, i.e., studies with an event probability of either 0 or 1. method.incr A character string indicating which continuity correction method should be used ("only0", "if0all", or "all"), see Details. method.ci A character string indicating which method is used to calculate confidence intervals for individual studies, see Details. level The level used to calculate confidence intervals for individual studies. level.ma The level used to calculate confidence intervals for meta-analysis estimates. common A logical indicating whether a common effect meta-analysis should be conducted. random A logical indicating whether a random effects meta-analysis should be conducted. overall A logical indicating whether overall summaries should be reported. This argument is useful in a meta-analysis with subgroups if overall results should not be reported. overall.hetstat A logical value indicating whether to print heterogeneity measures for overall treatment comparisons. This argument is useful in a meta-analysis with subgroups if heterogeneity statistics should only be printed on subgroup level. hakn A logical indicating whether the method by Hartung and Knapp should be used to adjust test statistics and confidence intervals. A character string indicating whether an ad hoc variance correction should be adhoc.hakn applied in the case of an arbitrarily small Hartung-Knapp variance estimate, see Details. A character string indicating which method is used to estimate the betweenmethod.tau study variance  $\tau^2$  and its square root  $\tau$ . Either "DL", "PM", "REML", "ML", "HS", "SJ", "HE", or "EB", can be abbreviated. method.tau.ci A character string indicating which method is used to estimate the confidence interval of  $\tau^2$  and  $\tau$ . Either "QP", "BJ", "J", "PL", or "", can be abbreviated. Prespecified value for the square root of the between-study variance  $\tau^2$ . tau.preset TE.tau Overall treatment effect used to estimate the between-study variance tau-squared. A logical indicating whether tau-squared should be the same across subgroups. tau.common prediction A logical indicating whether a prediction interval should be printed. level.predict The level used to calculate prediction interval for a new study. null.effect A numeric value specifying the effect under the null hypothesis. method.bias A character string indicating which test is to be used. Either "Begg", "Egger", or "Thompson", can be abbreviated. See function metabias. backtransf A logical indicating whether results for transformed proportions (argument sm != "PRAW") should be back transformed in printouts and plots. If TRUE (de-

fault), results will be presented as proportions; otherwise transformed proportions will be shown. See Details for presentation of confidence intervals.

pscale A numeric defining a scaling factor for printing of single event probabilities.

text.common A character string used in printouts and forest plot to label the pooled common effect estimate.

text.random A character string used in printouts and forest plot to label the pooled random

effects estimate.

text.predict A character string used in printouts and forest plot to label the prediction inter-

val.

text.w.common A character string used to label weights of common effect model.

text.w.random A character string used to label weights of random effects model.

title Title of meta-analysis / systematic review.

complab Comparison label. outclab Outcome label.

subgroup An optional vector to conduct a meta-analysis with subgroups.

subgroup.name A character string with a name for the subgroup variable.

print.subgroup.name

A logical indicating whether the name of the subgroup variable should be printed

in front of the group labels.

sep. subgroup A character string defining the separator between name of subgroup variable and

subgroup label.

test.subgroup A logical value indicating whether to print results of test for subgroup differ-

ences.

prediction.subgroup

A logical indicating whether prediction intervals should be printed for sub-

groups.

byvar Deprecated argument (replaced by 'subgroup').

keepdata A logical indicating whether original data (set) should be kept in meta object.

warn A logical indicating whether the addition of incr to studies with zero or all

events should result in a warning.

warn.deprecated

A logical indicating whether warnings should be printed if deprecated arguments

are used.

control An optional list to control the iterative process to estimate the between-study

variance  $\tau^2$ . This argument is passed on to rma. uni or rma. glmm, respectively.

.. Additional arguments passed on to rma.glmm function and to catch deprecated

arguments.

# Details

This function provides methods for common effect and random effects meta-analysis of single proportions to calculate an overall proportion. Note, you should use R function metabin to compare proportions of pairwise comparisons instead of using metaprop for each treatment arm separately which will break randomisation in randomised controlled trials.

The following transformations of proportions are implemented to calculate an overall proportion:

- Logit transformation (sm = "PLOGIT", default)
- Arcsine transformation (sm = "PAS")
- Freeman-Tukey Double arcsine transformation (sm = "PFT")
- Log transformation (sm = "PLN")
- Raw, i.e. untransformed, proportions (sm = "PRAW")

A generalised linear mixed model (GLMM) - more specific, a random intercept logistic regression model - can be utilised for the meta-analysis of proportions (Stijnen et al., 2010). This is the default method for the logit transformation (argument sm = "PLOGIT"). Internally, the rma.glmm function from R package **metafor** is called to fit a GLMM.

Classic meta-analysis (Borenstein et al., 2010) utilising the (un)transformed proportions and corresponding standard errors in the inverse variance method is conducted by calling the metagen function internally. This is the only available method for all transformations but the logit transformation. The classic meta-analysis model with logit transformed proportions is used by setting argument method = "Inverse".

Default settings are utilised for several arguments (assignments using gs function). These defaults can be changed for the current R session using the settings.meta function.

Furthermore, R function update.meta can be used to rerun a meta-analysis with different settings.

### Choice of transformation / meta-analysis method:

Contradictory recommendations on the use of transformations of proportions have been published in the literature. For example, Barendregt et al. (2013) recommend the use of the Freeman-Tukey double arcsine transformation instead of the logit transformation whereas Warton & Hui (2011) strongly advise to use generalised linear mixed models with the logit transformation instead of the arcsine transformation.

Schwarzer et al. (2019) describe seriously misleading results in a meta-analysis with very different sample sizes due to problems with the back-transformation of the Freeman-Tukey transformation which requires a single sample size (Miller, 1978). Accordingly, Schwarzer et al. (2019) also recommend to use GLMMs for the meta-analysis of single proportions, however, admit that individual study weights are not available with this method. Meta-analysts which require individual study weights should consider the inverse variance method with the arcsine or logit transformation.

In order to prevent misleading conclusions for the Freeman-Tukey double arcsine transformation, sensitivity analyses using other transformations or using a range of sample sizes should be conducted (Schwarzer et al., 2019).

### **Continuity correction:**

Three approaches are available to apply a continuity correction:

- Only studies with a zero cell count (method.incr = "only0")
- All studies if at least one study has a zero cell count (method.incr = "if0all")
- All studies irrespective of zero cell counts (method.incr = "all")

If the summary measure is equal to "PLOGIT", "PLN", or "PRAW", the continuity correction is applied if a study has either zero or all events, i.e., an event probability of either 0 or 1.

By default, 0.5 is used as continuity correction (argument incr). This continuity correction is used both to calculate individual study results with confidence limits and to conduct meta-analysis based on the inverse variance method. For GLMMs no continuity correction is used.

#### Confidence intervals for individual studies:

Various methods are available to calculate confidence intervals for individual study results (see Agresti & Coull 1998 and Newcombe 1988):

- Clopper-Pearson interval also called 'exact' binomial interval (method.ci = "CP", default)
- Wilson Score interval (method.ci = "WS")
- Wilson Score interval with continuity correction (method.ci = "WSCC")
- Agresti-Coull interval (method.ci = "AC")
- Simple approximation interval (method.ci = "SA")
- Simple approximation interval with continuity correction (method.ci = "SACC")
- Normal approximation interval based on summary measure, i.e. defined by argument sm (method.ci = "NAsm")

Note, with exception of the normal approximation based on the summary measure, i.e. method.ci = "NAsm", the same confidence interval is calculated for individual studies for any summary measure (argument sm) as only number of events and observations are used in the calculation disregarding the chosen transformation.

Results will be presented for transformed proportions if argument backtransf = FALSE. In this case, argument method.ci = "NAsm" is used, i.e. confidence intervals based on the normal approximation based on the summary measure.

## Estimation of between-study variance:

The following methods to estimate the between-study variance  $\tau^2$  are available for the inverse variance method:

- DerSimonian-Laird estimator (method.tau = "DL")
- Paule-Mandel estimator (method.tau = "PM")
- Restricted maximum-likelihood estimator (method.tau = "REML")
- Maximum-likelihood estimator (method.tau = "ML")
- Hunter-Schmidt estimator (method.tau = "HS")
- Sidik-Jonkman estimator (method.tau = "SJ")
- Hedges estimator (method.tau = "HE")
- Empirical Bayes estimator (method.tau = "EB")

See metagen for more information on these estimators. Note, the maximum-likelihood method is utilized for GLMMs.

## **Confidence interval for the between-study variance:**

The following methods to calculate a confidence interval for  $\tau^2$  and  $\tau$  are available.

Argument	Method
method.tau.ci = "J"	Method by Jackson (2013)
method.tau.ci = "BJ"	Method by Biggerstaff and Jackson (2008)
method.tau.ci = "QP"	Q-Profile method (Viechtbauer, 2007)
method.tau.ci = "PL"	Profile-Likelihood method for three-level meta-analysis
	(Van den Noortgate et al., 2013)
method.tau.ci = ""	No confidence interval

See metagen for more information on these methods.

For GLMMs, no confidence intervals for  $\tau^2$  and  $\tau$  are calculated.

### Hartung-Knapp method:

Hartung and Knapp (2001a,b) proposed an alternative method for random effects meta-analysis based on a refined variance estimator for the treatment estimate. Simulation studies (Hartung and Knapp, 2001a,b; IntHout et al., 2014; Langan et al., 2019) show improved coverage probabilities compared to the classic random effects method.

In rare settings with very homogeneous treatment estimates, the Hartung-Knapp variance estimate can be arbitrarily small resulting in a very narrow confidence interval (Knapp and Hartung, 2003; Wiksten et al., 2016). In such cases, an *ad hoc* variance correction has been proposed by utilising the variance estimate from the classic random effects model with the HK method (Knapp and Hartung, 2003; IQWiQ, 2020). An alternative approach is to use the wider confidence interval of classic common or random effects meta-analysis and the HK method (Wiksten et al., 2016; Jackson et al., 2017).

Argument adhoc. hakn can be used to choose the *ad hoc* method:

Argument	Ad hoc method
adhoc.hakn = ""	not used
adhoc.hakn = "se"	use variance correction if HK standard error is smaller
	than standard error from classic random effects
	meta-analysis (Knapp and Hartung, 2003)
adhoc.hakn="iqwig6"	use variance correction if HK confidence interval
	is narrower than CI from classic random effects model
	with DerSimonian-Laird estimator (IQWiG, 2020)
adhoc.hakn = "ci"	use wider confidence interval of classic random effects
	and HK meta-analysis
	(Hybrid method 2 in Jackson et al., 2017)

For GLMMs, a method similar to Knapp and Hartung (2003) is implemented, see description of argument tdist in rma.glmm, and the *ad hoc* variance correction is not available.

### **Prediction interval:**

A prediction interval for the proportion in a new study (Higgins et al., 2009) is calculated if arguments prediction and random are TRUE. Note, the definition of prediction intervals varies in the literature. This function implements equation (12) of Higgins et al., (2009) which proposed a t distribution with K-2 degrees of freedom where K corresponds to the number of studies in the meta-analysis.

#### **Subgroup analysis:**

Argument subgroup can be used to conduct subgroup analysis for a categorical covariate. The metareg function can be used instead for more than one categorical covariate or continuous covariates.

## Specify the null hypothesis of test for an overall proportion:

Argument null.effect can be used to specify the proportion used under the null hypothesis in a test for an overall effect.

By default (null.effect = NA), no hypothesis test is conducted as it is unclear which value is a sensible choice for the data at hand. An overall proportion of 50%, for example, could be tested by setting argument null.effect = 0.5.

Note, all tests for an overall effect are two-sided with the alternative hypothesis that the effect is unequal to null.effect.

### **Exclusion of studies from meta-analysis:**

Arguments subset and exclude can be used to exclude studies from the meta-analysis. Studies are removed completely from the meta-analysis using argument subset, while excluded studies are shown in printouts and forest plots using argument exclude (see Examples in metagen). Meta-analysis results are the same for both arguments.

## Presentation of meta-analysis results:

Internally, both common effect and random effects models are calculated regardless of values choosen for arguments common and random. Accordingly, the estimate for the random effects model can be extracted from component TE.random of an object of class "meta" even if argument random = FALSE. However, all functions in R package **meta** will adequately consider the values for common and random. E.g. function print.meta will not print results for the random effects model if random = FALSE.

Argument pscale can be used to rescale proportions, e.g. pscale = 1000 means that proportions are expressed as events per 1000 observations. This is useful in situations with (very) low event probabilities.

### Value

lower, upper zval, pval

An object of class c("metaprop", "meta") with corresponding print, summary, and forest functions. The object is a list containing the following components:

Lower and upper confidence interval limits for individual studies.

z-value and p-value for test of treatment effect for individual studies.

```
event, n, studlab, exclude, cluster,
                 As defined above.
sm, incr, method.incr, method.ci,
                 As defined above.
level, level.ma,
                 As defined above.
common, random,
                 As defined above.
overall, overall.hetstat,
                 As defined above.
hakn, adhoc.hakn, method.tau, method.tau.ci,
                 As defined above.
tau.preset, TE.tau, null.hypothesis,
                 As defined above.
method.bias, tau.common, title, complab, outclab,
                 As defined above.
subgroup, subgroup.name, print.subgroup.name, sep.subgroup, warn
                 As defined above.
TE, seTE
                 Estimated (un)transformed proportion and its standard error for individual stud-
```

w.common, w.random

Weight of individual studies (in common effect and random effects model).

TE.common, seTE.common

Estimated overall (un)transformed proportion and standard error (common effect model).

lower.common, upper.common

Lower and upper confidence interval limits (common effect model).

statistic.common, pval.common

z-value and p-value for test of overall effect (common effect model).

TE.random, seTE.random

Estimated overall (un)transformed proportion and standard error (random effects model).

lower.random, upper.random

Lower and upper confidence interval limits (random effects model).

statistic.random, pval.random

z-value or t-value and corresponding p-value for test of overall effect (random effects model).

prediction, level.predict

As defined above.

seTE.predict Standard error utilised for prediction interval.

lower.predict, upper.predict

Lower and upper limits of prediction interval.

k Number of estimates combined in meta-analysis.

k. study Number of studies combined in meta-analysis.

k.all Number of all studies.

k.TE Number of studies with estimable effects.

Q Heterogeneity statistic Q.

df.Q Degrees of freedom for heterogeneity statistic.

pval.Q P-value of heterogeneity test.

Q.LRT Heterogeneity statistic for likelihood-ratio test (only if method = "GLMM").

df.Q.LRT Degrees of freedom for likelihood-ratio test

pval.Q.LRT P-value of likelihood-ratio test. tau2 Between-study variance  $\tau^2$ .

se. tau2 Standard error of  $\tau^2$ .

lower.tau2, upper.tau2

Lower and upper limit of confidence interval for  $\tau^2$ .

tau Square-root of between-study variance  $\tau$ .

lower.tau, upper.tau

Lower and upper limit of confidence interval for  $\tau$ .

H Heterogeneity statistic H.

lower.H, upper.H

Lower and upper confidence limit for heterogeneity statistic H.

Heterogeneity statistic  $I^2$ .

lower.I2, upper.I2

Lower and upper confidence limit for heterogeneity statistic  $I^2$ .

Rb Heterogeneity statistic  $R_b$ .

lower.Rb, upper.Rb

Lower and upper confidence limit for heterogeneity statistic  $R_b$ .

method A character string indicating method used for pooling: "Inverse"

df.hakn Degrees of freedom for test of treatment effect for Hartung-Knapp method (only

if hakn=TRUE).

bylevs Levels of grouping variable - if subgroup is not missing.

TE.common.w, seTE.common.w

Estimated treatment effect and standard error in subgroups (common effect model)

- if subgroup is not missing.

lower.common.w, upper.common.w

Lower and upper confidence interval limits in subgroups (common effect model)

- if subgroup is not missing.

statistic.common.w, pval.common.w

z-value and p-value for test of treatment effect in subgroups (common effect model) - if subgroup is not missing.

TE.random.w, seTE.random.w

Estimated treatment effect and standard error in subgroups (random effects model)

- if subgroup is not missing.

lower.random.w, upper.random.w

Lower and upper confidence interval limits in subgroups (random effects model)

- if subgroup is not missing.

statistic.random.w, pval.random.w

z-value or t-value and corresponding p-value for test of treatment effect in sub-

groups (random effects model) - if subgroup is not missing.

w.common.w, w.random.w

Weight of subgroups (in common effect and random effects model) - if subgroup

is not missing.

df.hakn.w Degrees of freedom for test of treatment effect for Hartung-Knapp method in

subgroups - if subgroup is not missing and hakn=TRUE.

n.harmonic.mean.w

Harmonic mean of number of observations in subgroups (for back transfor-

mation of Freeman-Tukey Double arcsine transformation) - if subgroup is not

missing.

event.w Number of events in subgroups - if subgroup is not missing.

n.w Number of observations in subgroups - if subgroup is not missing.

k.w Number of studies combined within subgroups - if subgroup is not missing.

k.all.w Number of all studies in subgroups - if subgroup is not missing.

Q.w.common Overall within subgroups heterogeneity statistic Q (based on common effect

model) - if subgroup is not missing.

Q.w.random Overall within subgroups heterogeneity statistic Q (based on random effects model) - if subgroup is not missing (only calculated if argument tau. common is TRUE). df.Q.w Degrees of freedom for test of overall within subgroups heterogeneity - if subgroup is not missing. pval.Q.w.common P-value of within subgroups heterogeneity statistic Q (based on common effect model) - if subgroup is not missing. pval.Q.w.random P-value of within subgroups heterogeneity statistic Q (based on random effects model) - if subgroup is not missing. Q.b.common Overall between subgroups heterogeneity statistic Q (based on common effect model) - if subgroup is not missing. Q.b.random Overall between subgroups heterogeneity statistic Q (based on random effects model) - if subgroup is not missing. df.Q.b Degrees of freedom for test of overall between subgroups heterogeneity - if subgroup is not missing. pval.Q.b.common P-value of between subgroups heterogeneity statistic Q (based on common effect model) - if subgroup is not missing. pval.Q.b.random P-value of between subgroups heterogeneity statistic Q (based on random effects model) - if subgroup is not missing. Square-root of between-study variance within subgroups - if subgroup is not tau.w Heterogeneity statistic H within subgroups - if subgroup is not missing. H.w lower.H.w, upper.H.w Lower and upper confidence limit for heterogeneity statistic H within subgroups - if subgroup is not missing. I2.w Heterogeneity statistic  $I^2$  within subgroups - if subgroup is not missing. lower.I2.w, upper.I2.w Lower and upper confidence limit for heterogeneity statistic I<sup>2</sup> within subgroups - if subgroup is not missing. incr.event Increment added to number of events. As defined above. keepdata data Original data (set) used in function call (if keepdata=TRUE). subset Information on subset of original data used in meta-analysis (if keepdata=TRUE). GLMM object generated by call of rma. glmm function (common effect model). .glmm.common .glmm.random GLMM object generated by call of rma. glmm function (random effects model). call Function call.

Version of R package **metafor** used for GLMMs.

Version of R package **meta** used to create object.

version

version.metafor

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### See Also

```
update.meta, metacont, metagen, print.meta, forest.meta
```

# **Examples**

```
# Meta-analysis using generalised linear mixed model
metaprop(4:1, 10 * 1:4)
# Apply various classic meta-analysis methods to estimate
# proportions
m1 \leftarrow metaprop(4:1, 10 * 1:4, method = "Inverse")
m2 <- update(m1, sm = "PAS")</pre>
m3 <- update(m1, sm = "PRAW")
m4 <- update(m1, sm = "PLN")</pre>
m5 <- update(m1, sm = "PFT")</pre>
m1
m2
m3
m4
m5
#
forest(m1)
## Not run:
forest(m2)
forest(m3)
forest(m3, pscale = 100)
forest(m4)
forest(m5)
## End(Not run)
# Do not back transform results, e.g. print logit transformed
# proportions if sm = "PLOGIT" and store old settings
#
```

```
oldset <- settings.meta(backtransf = FALSE)</pre>
m6 <- metaprop(4:1, c(10, 20, 30, 40), method = "Inverse")
m7 <- update(m6, sm = "PAS")</pre>
m8 <- update(m6, sm = "PRAW")
m9 <- update(m6, sm = "PLN")</pre>
m10 <- update(m6, sm = "PFT")</pre>
forest(m6)
## Not run:
forest(m7)
forest(m8)
forest(m8, pscale = 100)
forest(m9)
forest(m10)
## End(Not run)
# Use old settings
settings.meta(oldset)
# Examples with zero events
m1 \leftarrow metaprop(c(0, 0, 10, 10), rep(100, 4), method = "Inverse")
m2 \leftarrow metaprop(c(0, 0, 10, 10), rep(100, 4), incr = 0.1, method = "Inverse")
m1
m2
## Not run:
forest(m1)
forest(m2)
## End(Not run)
# Example from Miller (1978):
death <- c(3, 6, 10, 1)
animals <- c(11, 17, 21, 6)
m3 <- metaprop(death, animals, sm = "PFT")
forest(m3)
# Data examples from Newcombe (1998)
# - apply various methods to estimate confidence intervals for
   individual studies
event <- c(81, 15, 0, 1)
n <- c(263, 148, 20, 29)
m1 <- metaprop(event, n, method.ci = "SA", method = "Inverse")</pre>
m2 <- update(m1, method.ci = "SACC")</pre>
```

```
m3 <- update(m1, method.ci = "WS")</pre>
m4 <- update(m1, method.ci = "WSCC")</pre>
m5 <- update(m1, method.ci = "CP")</pre>
lower <- round(rbind(NA, m1$lower, m2$lower, NA, m3$lower,</pre>
  m4$lower, NA, m5$lower), 4)
upper <- round(rbind(NA, m1$upper, m2$upper, NA, m3$upper,</pre>
  m4$upper, NA, m5$upper), 4)
tab1 <- data.frame(</pre>
  scen1 = meta:::formatCI(lower[, 1], upper[, 1]),
  scen2 = meta:::formatCI(lower[, 2], upper[, 2]),
  scen3 = meta:::formatCI(lower[, 3], upper[, 3]),
  scen4 = meta:::formatCI(lower[, 4], upper[, 4])
  )
names(tab1) \leftarrow c("r=81, n=263", "r=15, n=148",
  "r=0, n=20", "r=1, n=29")
row.names(tab1) <- c("Simple", "- SA", "- SACC",</pre>
  "Score", "- WS", "- WSCC", "Binomial", "- CP")
tab1[is.na(tab1)] <- ""
# Newcombe (1998), Table I, methods 1-5:
tab1
# Same confidence interval, i.e. unaffected by choice of summary
# measure
print(metaprop(event, n, method.ci = "WS", method = "Inverse"), ma = FALSE)
print(metaprop(event, n, sm = "PLN", method.ci = "WS"), ma = FALSE)
print(metaprop(event, n, sm = "PFT", method.ci = "WS"), ma = FALSE)
print(metaprop(event, n, sm = "PAS", method.ci = "WS"), ma = FALSE)
print(metaprop(event, n, sm = "PRAW", method.ci = "WS"), ma = FALSE)
# Different confidence intervals as argument sm = "NAsm"
print(metaprop(event, n, method.ci = "NAsm", method = "Inverse"), ma = FALSE)
print(metaprop(event, n, sm = "PLN", method.ci = "NAsm"), ma = FALSE)
print(metaprop(event, n, sm = "PFT", method.ci = "NAsm"), ma = FALSE)
print(metaprop(event, n, sm = "PAS", method.ci = "NAsm"), ma = FALSE)
print(metaprop(event, n, sm = "PRAW", method.ci = "NAsm"), ma = FALSE)
# Different confidence intervals as argument backtransf = FALSE.
# Accordingly, method.ci = "NAsm" used internally.
print(metaprop(event, n, method.ci = "WS", method = "Inverse"),
  ma = FALSE, backtransf = FALSE)
print(metaprop(event, n, sm = "PLN", method.ci = "WS"),
  ma = FALSE, backtransf = FALSE)
print(metaprop(event, n, sm = "PFT", method.ci = "WS"),
  ma = FALSE, backtransf = FALSE)
print(metaprop(event, n, sm = "PAS", method.ci = "WS"),
  ma = FALSE, backtransf = FALSE)
print(metaprop(event, n, sm = "PRAW", method.ci = "WS"),
  ma = FALSE, backtransf = FALSE)
```

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```
# Same results (printed on original and log scale, respectively)
#
print(metaprop(event, n, sm = "PLN", method.ci = "NAsm"), ma = FALSE)
print(metaprop(event, n, sm = "PLN"), ma = FALSE, backtransf = FALSE)
# Results for first study (on log scale)
round(log(c(0.3079848, 0.2569522, 0.3691529)), 4)
# Print results as events per 1000 observations
#
print(metaprop(6:8, c(100, 1200, 1000), method = "Inverse"),
    pscale = 1000, digits = 1)
```

metarate

Meta-analysis of single incidence rates

# **Description**

Calculation of an overall incidence rate from studies reporting a single incidence rate. Inverse variance method and generalised linear mixed model (GLMM) are available for pooling. For GLMMs, the rma.glmm function from R package **metafor** (Viechtbauer 2010) is called internally.

### Usage

```
metarate(
  event,
  time,
  studlab,
  data = NULL,
  subset = NULL,
  exclude = NULL,
  cluster = NULL,
  n = NULL,
 method = "Inverse",
  sm = gs("smrate"),
  incr = gs("incr"),
 method.incr = gs("method.incr"),
 method.ci = gs("method.ci.rate"),
  level = gs("level"),
  level.ma = gs("level.ma"),
  common = gs("common"),
  random = gs("random") | !is.null(tau.preset),
  overall = common | random,
  overall.hetstat = common | random,
  hakn = gs("hakn"),
  adhoc.hakn = gs("adhoc.hakn"),
  method.tau,
```

```
method.tau.ci = gs("method.tau.ci"),
  tau.preset = NULL,
 TE.tau = NULL,
  tau.common = gs("tau.common"),
  prediction = gs("prediction"),
  level.predict = gs("level.predict"),
  null.effect = NA,
 method.bias = gs("method.bias"),
 backtransf = gs("backtransf"),
  irscale = 1,
  irunit = "person-years",
  text.common = gs("text.common"),
  text.random = gs("text.random"),
  text.predict = gs("text.predict"),
  text.w.common = gs("text.w.common"),
  text.w.random = gs("text.w.random"),
  title = gs("title"),
  complab = gs("complab"),
  outclab = "",
  subgroup,
  subgroup.name = NULL,
  print.subgroup.name = gs("print.subgroup.name"),
  sep.subgroup = gs("sep.subgroup"),
  test.subgroup = gs("test.subgroup"),
  prediction.subgroup = gs("prediction.subgroup"),
  byvar,
  keepdata = gs("keepdata"),
 warn = gs("warn"),
 warn.deprecated = gs("warn.deprecated"),
 control = NULL,
  . . .
)
```

#### **Arguments**

event	Number of events.
time	Person time at risk.
studlab	An optional vector with study labels.
data	An optional data frame containing the study information, i.e., event and time.
subset	An optional vector specifying a subset of studies to be used.
exclude	An optional vector specifying studies to exclude from meta-analysis, however, to include in printouts and forest plots.
cluster	An optional vector specifying which estimates come from the same cluster resulting in the use of a three-level meta-analysis model.
n	Number of observations.
method	A character string indicating which method is to be used for pooling of studies. One of "Inverse" and "GLMM", can be abbreviated.

A character string indicating which summary measure ("IR", "IRLN", "IRS", or sm "IRFT") is to be used for pooling of studies, see Details. A numeric which is added to the event number of studies with zero events, i.e., incr studies with an incidence rate of 0. method.incr A character string indicating which continuity correction method should be used ("only0", "if0all", or "all"), see Details. method.ci A character string indicating whether to use approximate normal ("NAsm") or exact Poisson ("Poisson") confidence limits. level The level used to calculate confidence intervals for individual studies. The level used to calculate confidence intervals for meta-analysis estimates. level.ma A logical indicating whether a common effect meta-analysis should be concommon ducted. random A logical indicating whether a random effects meta-analysis should be conoverall A logical indicating whether overall summaries should be reported. This argument is useful in a meta-analysis with subgroups if overall results should not be reported. overall.hetstat A logical value indicating whether to print heterogeneity measures for overall treatment comparisons. This argument is useful in a meta-analysis with subgroups if heterogeneity statistics should only be printed on subgroup level. hakn A logical indicating whether the method by Hartung and Knapp should be used to adjust test statistics and confidence intervals. adhoc.hakn A character string indicating whether an ad hoc variance correction should be applied in the case of an arbitrarily small Hartung-Knapp variance estimate, see Details. method.tau A character string indicating which method is used to estimate the betweenstudy variance  $\tau^2$  and its square root  $\tau$ . Either "DL", "PM", "REML", "ML", "HS", "SJ", "HE", or "EB", can be abbreviated. method.tau.ci A character string indicating which method is used to estimate the confidence interval of  $\tau^2$  and  $\tau$ . Either "QP", "BJ", "J", "PL", or "", can be abbreviated. Prespecified value for the square root of the between-study variance  $\tau^2$ . tau.preset Overall treatment effect used to estimate the between-study variance tau-squared. TE.tau tau.common A logical indicating whether tau-squared should be the same across subgroups. prediction A logical indicating whether a prediction interval should be printed. level.predict The level used to calculate prediction interval for a new study. null.effect A numeric value specifying the effect under the null hypothesis. method.bias A character string indicating which test is to be used. Either "Begg", "Egger", or "Thompson", can be abbreviated. See function metabias. backtransf A logical indicating whether results for transformed rates (argument sm != "IR") should be back transformed in printouts and plots. If TRUE (default), results will be presented as incidence rates; otherwise transformed rates will be shown.

irscale A numeric defining a scaling factor for printing of rates.

irunit A character string specifying the time unit used to calculate rates, e.g. person-

years.

text.common A character string used in printouts and forest plot to label the pooled common

effect estimate.

text.random A character string used in printouts and forest plot to label the pooled random

effects estimate.

text.predict A character string used in printouts and forest plot to label the prediction inter-

val

text.w.common A character string used to label weights of common effect model. text.w.random A character string used to label weights of random effects model.

title Title of meta-analysis / systematic review.

complab Comparison label. outclab Outcome label.

subgroup An optional vector to conduct a meta-analysis with subgroups.

subgroup.name A character string with a name for the subgroup variable.

print.subgroup.name

A logical indicating whether the name of the subgroup variable should be printed

in front of the group labels.

sep. subgroup A character string defining the separator between name of subgroup variable and

subgroup label.

test.subgroup A logical value indicating whether to print results of test for subgroup differ-

ences.

prediction.subgroup

A logical indicating whether prediction intervals should be printed for sub-

groups.

byvar Deprecated argument (replaced by 'subgroup').

keepdata A logical indicating whether original data (set) should be kept in meta object.

warn A logical indicating whether the addition of incr to studies with zero events

should result in a warning.

warn.deprecated

A logical indicating whether warnings should be printed if deprecated arguments

are used.

control An optional list to control the iterative process to estimate the between-study

variance  $\tau^2$ . This argument is passed on to rma. uni or rma. glmm, respectively.

.. Additional arguments passed on to rma.glmm function and to catch deprecated

arguments.

# Details

This function provides methods for common effect and random effects meta-analysis of single incidence rates to calculate an overall rate. Note, you should use R function metainc to compare incidence rates of pairwise comparisons instead of using metarate for each treatment arm separately which will break randomisation in randomised controlled trials.

The following transformations of incidence rates are implemented to calculate an overall rate:

- Log transformation (sm = "IRLN", default)
- Square root transformation (sm = "IRS")
- Freeman-Tukey Double arcsine transformation (sm = "IRFT")
- No transformation (sm = "IR")

By default (argument method = "Inverse"), the inverse variance method (Borenstein et al., 2010) is used for pooling by calling metagen internally. A random intercept Poisson regression model (Stijnen et al., 2010) can be utilised instead with argument method = "GLMM" which calls the rma.glmm function from R package metafor.

Default settings are utilised for several arguments (assignments using gs function). These defaults can be changed for the current R session using the settings.meta function.

Furthermore, R function update.meta can be used to rerun a meta-analysis with different settings.

#### **Continuity correction:**

Three approaches are available to apply a continuity correction:

- Only studies with a zero cell count (method.incr = "only0")
- All studies if at least one study has a zero cell count (method.incr = "if0all")
- All studies irrespective of zero cell counts (method.incr = "all")

If the summary measure (argument sm) is equal to "IR" or "IRLN", the continuity correction is applied if a study has zero events, i.e., an incidence rate of 0.

By default, 0.5 is used as continuity correction (argument incr). This continuity correction is used both to calculate individual study results with confidence limits and to conduct meta-analysis based on the inverse variance method.

For the Freeman-Tukey (Freeman & Tukey, 1950) and square root transformation as well as GLMMs no continuity correction is used.

### **Estimation of between-study variance:**

The following methods to estimate the between-study variance  $\tau^2$  are available for the inverse variance method:

- DerSimonian-Laird estimator (method.tau = "DL")
- Paule-Mandel estimator (method.tau = "PM")
- Restricted maximum-likelihood estimator (method.tau = "REML")
- Maximum-likelihood estimator (method.tau = "ML")
- Hunter-Schmidt estimator (method.tau = "HS")
- Sidik-Jonkman estimator (method.tau = "SJ")
- Hedges estimator (method.tau = "HE")
- Empirical Bayes estimator (method.tau = "EB")

See metagen for more information on these estimators. Note, the maximum-likelihood method is utilized for GLMMs.

## Confidence interval for the between-study variance:

The following methods to calculate a confidence interval for  $\tau^2$  and  $\tau$  are available.

Argument Method

```
method.tau.ci = "J" Method by Jackson (2013)

method.tau.ci = "BJ" Method by Biggerstaff and Jackson (2008)

method.tau.ci = "QP" Q-Profile method (Viechtbauer, 2007)

method.tau.ci = "PL" Profile-Likelihood method for three-level meta-analysis (Van den Noortgate et al., 2013)

method.tau.ci = "" No confidence interval
```

See metagen for more information on these methods.

For GLMMs, no confidence intervals for  $\tau^2$  and  $\tau$  are calculated.

### Hartung-Knapp method:

Hartung and Knapp (2001a,b) proposed an alternative method for random effects meta-analysis based on a refined variance estimator for the treatment estimate. Simulation studies (Hartung and Knapp, 2001a,b; IntHout et al., 2014; Langan et al., 2019) show improved coverage probabilities compared to the classic random effects method.

In rare settings with very homogeneous treatment estimates, the Hartung-Knapp variance estimate can be arbitrarily small resulting in a very narrow confidence interval (Knapp and Hartung, 2003; Wiksten et al., 2016). In such cases, an *ad hoc* variance correction has been proposed by utilising the variance estimate from the classic random effects model with the HK method (Knapp and Hartung, 2003; IQWiQ, 2020). An alternative approach is to use the wider confidence interval of classic common or random effects meta-analysis and the HK method (Wiksten et al., 2016; Jackson et al., 2017).

Argument adhoc. hakn can be used to choose the *ad hoc* method:

Argument	Ad hoc method
adhoc.hakn = ""	not used
adhoc.hakn = "se"	use variance correction if HK standard error is smaller
	than standard error from classic random effects
	meta-analysis (Knapp and Hartung, 2003)
adhoc.hakn="iqwig6"	use variance correction if HK confidence interval
	is narrower than CI from classic random effects model
	with DerSimonian-Laird estimator (IQWiG, 2020)
adhoc.hakn = "ci"	use wider confidence interval of classic random effects
	and HK meta-analysis
	(Hybrid method 2 in Jackson et al., 2017)

For GLMMs, a method similar to Knapp and Hartung (2003) is implemented, see description of argument tdist in rma.glmm, and the *ad hoc* variance correction is not available.

#### **Prediction interval:**

A prediction interval for the proportion in a new study (Higgins et al., 2009) is calculated if arguments prediction and random are TRUE. Note, the definition of prediction intervals varies in the literature. This function implements equation (12) of Higgins et al., (2009) which proposed a t distribution with K-2 degrees of freedom where K corresponds to the number of studies in the meta-analysis.

### **Subgroup analysis:**

Argument subgroup can be used to conduct subgroup analysis for a categorical covariate. The metareg function can be used instead for more than one categorical covariate or continuous covariates.

#### Specify the null hypothesis of test for an overall effect:

Argument null.effect can be used to specify the rate used under the null hypothesis in a test for an overall effect.

By default (null.effect = NA), no hypothesis test is conducted as it is unclear which value is a sensible choice for the data at hand. An overall rate of 2, for example, could be tested by setting argument null.effect = 2.

Note, all tests for an overall effect are two-sided with the alternative hypothesis that the effect is unequal to null.effect.

### **Exclusion of studies from meta-analysis:**

Arguments subset and exclude can be used to exclude studies from the meta-analysis. Studies are removed completely from the meta-analysis using argument subset, while excluded studies are shown in printouts and forest plots using argument exclude (see Examples in metagen). Meta-analysis results are the same for both arguments.

#### Presentation of meta-analysis results:

Internally, both common effect and random effects models are calculated regardless of values choosen for arguments common and random. Accordingly, the estimate for the random effects model can be extracted from component TE.random of an object of class "meta" even if argument random = FALSE. However, all functions in R package **meta** will adequately consider the values for common and random. E.g. function print.meta will not print results for the random effects model if random = FALSE.

Argument irscale can be used to rescale rates, e.g. irscale = 1000 means that rates are expressed as events per 1000 time units, e.g. person-years. This is useful in situations with (very) low rates. Argument irunit can be used to specify the time unit used in individual studies (default: "person-years"). This information is printed in summaries and forest plots if argument irscale is not equal to 1.

### Value

An object of class c("metarate", "meta") with corresponding print, summary, and forest functions. The object is a list containing the following components:

tau.preset, TE.tau, null.hypothesis,

As defined above.

method.bias, tau.common, title, complab, outclab,

As defined above.

subgroup, subgroup.name, print.subgroup.name, sep.subgroup, warn

As defined above.

TE, seTE Estimated (un)transformed incidence rate and its standard error for individual

studies.

lower, upper Lower and upper confidence interval limits for individual studies.

zval, pval z-value and p-value for test of treatment effect for individual studies.

w.common, w.random

Weight of individual studies (in common effect and random effects model).

TE.common, seTE.common

Estimated overall (un)transformed incidence rate and standard error (common effect model).

lower.common, upper.common

Lower and upper confidence interval limits (common effect model).

statistic.common, pval.common

z-value and p-value for test of overall effect (common effect model).

TE.random, seTE.random

Estimated overall (un)transformed incidence rate and standard error (random effects model).

lower.random, upper.random

Lower and upper confidence interval limits (random effects model).

statistic.random, pval.random

z-value or t-value and corresponding p-value for test of overall effect (random effects model).

prediction, level.predict

As defined above.

seTE.predict Standard error utilised for prediction interval.

lower.predict, upper.predict

Lower and upper limits of prediction interval.

k Number of estimates combined in meta-analysis.

k. study Number of studies combined in meta-analysis.

k.all Number of all studies.

k. TE Number of studies with estimable effects.

Q Heterogeneity statistic Q.

df.Q Degrees of freedom for heterogeneity statistic.

pval.Q P-value of heterogeneity test.

Q.LRT Heterogeneity statistic for likelihood-ratio test (only if method = "GLMM").

df.Q.LRT Degrees of freedom for likelihood-ratio test

pval.Q.LRT P-value of likelihood-ratio test.

tau2 Between-study variance  $\tau^2$ .

se. tau2 Standard error of  $\tau^2$ .

lower.tau2, upper.tau2

Lower and upper limit of confidence interval for  $\tau^2$ .

tau Square-root of between-study variance  $\tau$ .

lower.tau, upper.tau

Lower and upper limit of confidence interval for  $\tau$ .

H Heterogeneity statistic H.

lower.H, upper.H

Lower and upper confidence limit for heterogeneity statistic H.

Heterogeneity statistic  $I^2$ .

lower.I2, upper.I2

Lower and upper confidence limit for heterogeneity statistic  $I^2$ .

Rb Heterogeneity statistic  $R_b$ .

lower.Rb, upper.Rb

Lower and upper confidence limit for heterogeneity statistic  $R_b$ .

method A character string indicating method used for pooling: "Inverse"

df.hakn Degrees of freedom for test of treatment effect for Hartung-Knapp method (only

if hakn = TRUE).

bylevs Levels of grouping variable - if subgroup is not missing.

TE.common.w, seTE.common.w

Estimated treatment effect and standard error in subgroups (common effect model)

- if subgroup is not missing.

lower.common.w, upper.common.w

Lower and upper confidence interval limits in subgroups (common effect model)

- if subgroup is not missing.

statistic.common.w, pval.common.w

z-value and p-value for test of treatment effect in subgroups (common effect model) - if subgroup is not missing.

TE.random.w, seTE.random.w

Estimated treatment effect and standard error in subgroups (random effects model)

- if subgroup is not missing.

lower.random.w, upper.random.w

Lower and upper confidence interval limits in subgroups (random effects model)

- if subgroup is not missing.

statistic.random.w, pval.random.w

z-value or t-value and corresponding p-value for test of treatment effect in subgroups (random effects model) - if subgroup is not missing.

w.common.w, w.random.w

Weight of subgroups (in common effect and random effects model) - if subgroup is not missing.

df.hakn.w Degrees

Degrees of freedom for test of treatment effect for Hartung-Knapp method in subgroups - if subgroup is not missing and hakn = TRUE.

#### n.harmonic.mean.w

Harmonic mean of number of observations in subgroups (for back transformation of Freeman-Tukey Double arcsine transformation) - if subgroup is not missing.

event.w Number of events in subgroups - if subgroup is not missing.

n.w Number of observations in subgroups - if subgroup is not missing.

k.w Number of studies combined within subgroups - if subgroup is not missing.

k.all.w Number of all studies in subgroups - if subgroup is not missing.

Q.w.common Overall within subgroups heterogeneity statistic Q (based on common effect

model) - if subgroup is not missing.

Q.w.random Overall within subgroups heterogeneity statistic Q (based on random effects

model) - if subgroup is not missing (only calculated if argument tau. common is

TRUE).

df.Q.w Degrees of freedom for test of overall within subgroups heterogeneity - if subgroup

is not missing.

pval.Q.w.common

P-value of within subgroups heterogeneity statistic Q (based on common effect model) - if subgroup is not missing.

pval.Q.w.random

P-value of within subgroups heterogeneity statistic Q (based on random effects model) - if subgroup is not missing.

Q.b.common Overall between subgroups heterogeneity statistic Q (based on common effect

model) - if subgroup is not missing.

Q.b.random Overall between subgroups heterogeneity statistic Q (based on random effects

model) - if subgroup is not missing.

df.Q.b Degrees of freedom for test of overall between subgroups heterogeneity - if

subgroup is not missing.

pval.Q.b.common

P-value of between subgroups heterogeneity statistic Q (based on common effect

model) - if subgroup is not missing.

pval.Q.b.random

P-value of between subgroups heterogeneity statistic Q (based on random effects

model) - if subgroup is not missing.

tau.w Square-root of between-study variance within subgroups - if subgroup is not

missing.

H.w Heterogeneity statistic H within subgroups - if subgroup is not missing.

lower.H.w, upper.H.w

Lower and upper confidence limit for heterogeneity statistic H within subgroups - if subgroup is not missing.

I2. w Heterogeneity statistic  $I^2$  within subgroups - if subgroup is not missing.

lower.I2.w, upper.I2.w

Lower and upper confidence limit for heterogeneity statistic  $I^2$  within subgroups - if subgroup is not missing.

incr. event Increment added to number of events.

keepdata As defined above.

data Original data (set) used in function call (if keepdata = TRUE).

subset Information on subset of original data used in meta-analysis (if keepdata =

TRUE).

.glmm.common GLMM object generated by call of rma.glmm function (common effect model).
.glmm.random GLMM object generated by call of rma.glmm function (random effects model).

call Function call.

version Version of R package meta used to create object.

version.metafor

Version of R package **metafor** used for GLMMs.

#### Author(s)

Guido Schwarzer <sc@imbi.uni-freiburg.de>

#### References

Borenstein M, Hedges LV, Higgins JP, Rothstein HR (2010): A basic introduction to fixed-effect and random-effects models for meta-analysis. *Research Synthesis Methods*, **1**, 97–111

Freeman MF & Tukey JW (1950): Transformations related to the angular and the square root. *Annals of Mathematical Statistics*, **21**, 607–11

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Hartung J, Knapp G (2001a): On tests of the overall treatment effect in meta-analysis with normally distributed responses. *Statistics in Medicine*, **20**, 1771–82

Hartung J, Knapp G (2001b): A refined method for the meta-analysis of controlled clinical trials with binary outcome. *Statistics in Medicine*, **20**, 3875–89

IntHout J, Ioannidis JPA, Borm GF (2014): The Hartung-Knapp-Sidik-Jonkman method for random effects meta-analysis is straightforward and considerably outperforms the standard DerSimonian-Laird method. *BMC Medical Research Methodology*, **14**, 25

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Langan D, Higgins JPT, Jackson D, Bowden J, Veroniki AA, Kontopantelis E, et al. (2019): A comparison of heterogeneity variance estimators in simulated random-effects meta-analyses. *Research Synthesis Methods*, **10**, 83–98

Stijnen T, Hamza TH, Ozdemir P (2010): Random effects meta-analysis of event outcome in the framework of the generalized linear mixed model with applications in sparse data. *Statistics in Medicine*, **29**, 3046–67

Van den Noortgate W, López-López JA, Marín-Martínez F, Sánchez-Meca J (2013): Three-level meta-analysis of dependent effect sizes. *Behavior Research Methods*, **45**, 576–94

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Viechtbauer W (2010): Conducting Meta-Analyses in R with the Metafor Package. *Journal of Statistical Software*, **36**, 1–48

Wiksten A, Rücker G, Schwarzer G (2016): Hartung-Knapp method is not always conservative compared with fixed-effect meta-analysis. *Statistics in Medicine*, **35**, 2503–15

#### See Also

```
update.meta, metacont, metagen, print.meta
```

## **Examples**

```
# Apply various meta-analysis methods to estimate incidence rates
m1 <- metarate(4:1, c(10, 20, 30, 40))
m2 \leftarrow update(m1, sm = "IR")
m3 <- update(m1, sm = "IRS")</pre>
m4 <- update(m1, sm = "IRFT")</pre>
m1
m2
m3
m4
forest(m1)
forest(m1, irscale = 100)
forest(m1, irscale = 100, irunit = "person-days")
forest(m1, backtransf = FALSE)
## Not run:
forest(m2)
forest(m3)
forest(m4)
## End(Not run)
m5 <- metarate(40:37, c(100, 200, 300, 400), sm = "IRFT")
m5
```

metareg

Meta-regression

## Description

Meta-regression for objects of class meta. This is a wrapper function for the R function rma.uni in the R package **metafor** (Viechtbauer 2010).

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### Usage

```
metareg(
    x,
    formula,
    method.tau = x$method.tau,
    hakn = x$hakn,
    level.ma = x$level.ma,
    intercept = TRUE,
    ...
)
```

### **Arguments**

An object of class meta.

Either a character string or a formula object.

Method.tau

A character string indicating which method is used to estimate the between-study variance tau-squared. Either "FE", "DL", "REML", "ML", "HS", "SJ", "HE", or "EB", can be abbreviated.

A logical indicating whether the method by Hartung and Knapp should be used to adjust test statistics and confidence intervals.

Ievel.ma

The level used to calculate confidence intervals for parameter estimates in the meta-regression model.

intercept A logical indicating whether an intercept should be included in the meta-regression

model.

... Additional arguments passed to R function rma.uni.

#### **Details**

This R function is a wrapper function for R function rma.uni in the R package **metafor** (Viechtbauer 2010).

Note, results are not back-transformed in printouts of meta-analyses using summary measures with transformations, e.g., log risk ratios are printed instead of the risk ratio if argument sm = "RR" and logit transformed proportions are printed if argument sm = "PLOGIT".

Argument '...' can be used to pass additional arguments to R function rma.uni. For example, argument control to provide a list of control values for the iterative estimation algorithm. See help page of R function rma.uni for more details.

### Value

An object of class c("metareg", "rma.uni", "rma"). Please look at the help page of R function rma.uni for more details on the output from this function.

In addition, a list .meta is added to the output containing the following components:

```
x, formula, method.tau, hakn, level.ma, intercept
As defined above.

dots

Information provided in argument '...'.
```

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```
call Function call.

version Version of R package meta used to create object.

version.metafor Version of R package metafor used to create object.
```

#### Author(s)

```
Guido Schwarzer <sc@imbi.uni-freiburg.de>
```

#### References

Viechtbauer W (2010): Conducting Meta-Analyses in R with the Metafor Package. *Journal of Statistical Software*, **36**, 1–48

#### See Also

```
bubble, summary.meta, metagen
```

## **Examples**

```
data(Fleiss1993cont)
# Add some (fictitious) grouping variables:
Fleiss1993cont$age <- c(55, 65, 55, 65, 55)
Fleiss1993cont$region <- c("Europe", "Europe", "Asia", "Asia", "Europe")
m1 <- metacont(n.psyc, mean.psyc, sd.psyc, n.cont, mean.cont, sd.cont,</pre>
  data = Fleiss1993cont, sm = "MD")
## Not run:
# Warnings due to wrong ordering of arguments (order has changed
# with version 3.0-0 of R package meta)
metareg(~ region, m1)
metareg(~ region, data = m1)
# Warning as no information on covariate is available
metareg(m1)
## End(Not run)
# Do meta-regression for covariate region
mu2 <- update(m1, subgroup = region, tau.common = TRUE, common = FALSE)</pre>
metareg(mu2)
# Same result for
# - tau-squared
# - test of heterogeneity
# - test for subgroup differences
# (as argument 'tau.common' was used to create mu2)
```

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```
metareg(mu2, intercept = FALSE)
metareg(m1, region)
# Different result for
# - tau-squared
# - test of heterogeneity
# - test for subgroup differences
# (as argument 'tau.common' is - by default - FALSE)
mu1 <- update(m1, subgroup = region)</pre>
mu1
# Generate bubble plot
bubble(metareg(mu2))
# Do meta-regression with two covariates
#
metareg(mu1, region + age)
# Do same meta-regressions using formula notation
metareg(m1, \sim region)
metareg(mu1, ~ region + age)
# Do meta-regression using REML method and print intermediate
# results for iterative estimation algorithm; furthermore print
# results with three digits.
metareg(mu1, region, method.tau = "REML",
  control = list(verbose = TRUE), digits = 3)
# Use Hartung-Knapp method
mu3 <- update(mu2, hakn = TRUE)</pre>
mu3
metareg(mu3, intercept = FALSE)
```

nnt

Calculate the number needed to treat (NNT)

## **Description**

Calculate the number needed to treat (NNT) from estimated risk difference, risk ratio, or odds ratio, and a baseline risk.

nnt 195

## Usage

```
nnt(x, ...)
## S3 method for class 'meta'
nnt(x, p.c, common = x$common, random = x$random, ...)
## Default S3 method:
nnt(x, p.c, sm, lower, upper, ...)
## S3 method for class 'nnt.meta'
print(
    x,
    common = x$common,
    random = x$random,
    digits = gs("digits"),
    digits.prop = gs("digits.prop"),
    big.mark = gs("big.mark"),
    ...
)
```

### **Arguments**

X	An object of class meta, or estimated treatment effect, i.e., risk difference(s), risk ratio(s), or odds ratio(s).
	Additional arguments (to catch deprecated arguments).
p.c	Baseline risk (control group event probability).
common	A logical indicating whether NNTs should be calculated based on common effect estimate.
random	A logical indicating whether NNTs should be calculated based on random effects estimate.
sm	Summary measure.
lower	Lower confidence interval limit.
upper	Upper confidence interval limit.
digits	Minimal number of significant digits, see print.default.
digits.prop	Minimal number of significant digits for proportions, see print.default.
big.mark	A character used as thousands separator.

## **Details**

The number needed to treat (NNT) can be easily computed from an estimated risk difference (RD), risk ratio (RR), or odds ratio (OR) and a given baseline risk (Higgins & Green, 2011, section 12.5).

Accordlingly, this function can be used to calculate NNTs for meta-analyses generated with metabin or metagen if argument sm was equal to "RD", "RR", or "OR". It is also possible to directly provide estimated treatment effects without conducting a meta-analysis (see Examples).

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The baseline risk can be specified using argument p.c. If this argument is missing, the minimum, mean, and maximum of the control event probabilities in the meta-analysis are used for metabin; otherwise the control event probabilities 0.1, 0.2, ..., 0.9 are used.

#### Author(s)

Guido Schwarzer <sc@imbi.uni-freiburg.de>

#### References

Higgins, J.P.T and S. Green (2011): Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [Updated March 2011]. The Cochrane Library: http://www.cochrane-handbook.org

### See Also

```
metabin, metagen
```

### **Examples**

01kin1995

Thrombolytic Therapy after Acute Myocardial Infarction

## Description

Meta-analysis on Thrombolytic Therapy after Acute Myocardial Infarction

or2smd

### **Format**

A data frame with the following columns:

```
    author first author
    year year of publication
    ev.exp number of events in experimental group
    n.exp number of observations in experimental group
    ev.cont number of events in control group
    n.cont number of observations in control group
```

## Source

Olkin I (1995): Statistical and theoretical considerations in meta-analysis. *Journal of Clinical Epidemiology*, **48**, 133–46

## **Examples**

```
data(Olkin1995)
metabin(ev.exp, n.exp, ev.cont, n.cont, data = Olkin1995)
```

or2smd

Conversion from log odds ratio to standardised mean difference

## **Description**

Conversion from log odds ratio to standardised mean difference using method by Hasselblad & Hedges (1995) or Cox (1970).

## Usage

```
or2smd(
    lnOR,
    selnOR,
    studlab,
    data = NULL,
    subset = NULL,
    exclude = NULL,
    method = "HH",
    ...
)
```

## **Arguments**

1nOR Log odds ratio(s) or meta-analysis object.

selnOR Standard error(s) of log odds ratio(s) (ignored if argument lnOR is a meta-

analysis object).

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studlab	An optional vector with study labels (ignored if argument 1nOR is a meta-analysis object).
data	An optional data frame containing the study information (ignored if argument 1nOR is a meta-analysis object).
subset	An optional vector specifying a subset of studies to be used (ignored if argument 1nOR is a meta-analysis object).
exclude	An optional vector specifying studies to exclude from meta-analysis, however, to include in printouts and forest plots (ignored if argument 1nOR is a meta-analysis object).
method	A character string indicating which method is used to convert log odds ratios to standardised mean differences. Either "HH" or "CS", can be abbreviated.
• • •	Additional arguments passed on to metagen (ignored if argument 1nOR is a meta-analysis object).

## **Details**

This function implements the following methods for the conversion from log odds ratios to standardised mean difference:

- Hasselblad & Hedges (1995) assuming logistic distributions (method == "HH")
- Cox (1970) and Cox & Snell (1989) assuming normal distributions (method == "CS")

Internally, metagen is used to conduct a meta-analysis with the standardised mean difference as summary measure.

Argument 1nOR can be either a vector of log odds ratios or a meta-analysis object created with metabin or metagen and the odds ratio as summary measure.

Argument selnOR is mandatory if argument lnOR is a vector and ignored otherwise. Additional arguments in . . . are only passed on to metagen if argument lnOR is a vector.

#### Value

An object of class "meta" and "metagen"; see metagen.

# Author(s)

Guido Schwarzer <sc@imbi.uni-freiburg.de>

#### References

Borenstein M, Hedges LV, Higgins JPT, Rothstein HR (2009): *Introduction to Meta-Analysis*. Chichester: Wiley

Cox DR (1970): Analysis of Binary Data. London: Chapman and Hall / CRC

Cox DR, Snell EJ (1989): Analysis of Binary Data (2nd edition). London: Chapman and Hall / CRC

Hasselblad V, Hedges LV (1995): Meta-analysis of screening and diagnostic tests. *Psychological Bulletin*, **117**, 167–78

Pagliaro 1992 199

### See Also

```
smd2or, metabin, metagen, metacont
```

### **Examples**

```
# Example from Borenstein et al. (2009), Chapter 7
#
mb <- or2smd(0.9069, sqrt(0.0676))
# TE = standardised mean difference (SMD); seTE = standard error of SMD
data.frame(SMD = round(mb$TE, 4), varSMD = round(mb$seTE^2, 4))
# Use dataset from Fleiss (1993)
# data(Fleiss1993bin)
m1 <- metabin(d.asp, n.asp, d.plac, n.plac,
    data = Fleiss1993bin, studlab = paste(study, year),
    sm = "OR", random = FALSE)
or2smd(m1)</pre>
```

Pagliaro1992

Meta-analysis on Prevention of First Bleeding in Cirrhosis

### **Description**

Meta-analysis on Prevention of First Bleeding in Cirrhosis comparing beta-blocker or sclerotherapy with placebo.

### **Format**

A data frame with the following columns:

```
study id
       id
 treat.exp
            treatment in experimental group
   logOR
            log odds ratio
 selogOR
            standard error of log odds ratio
            number of bleedings in experimental group
bleed.exp
            number of observations in experimental group
   n.cont
bleed.plac
            number of bleedings in placebo group
   n.plac
            number of observations in placebo group
```

### **Source**

Pagliaro L, D'Amico G et al. (1992): Prevention of first bleeding in cirrhosis. *Annals in Internal Medicine*, **117**, 59–70

### **Examples**

```
data(Pagliaro1992)
sclero <- subset(Pagliaro1992, treat.exp == "Sclerotherapy")
m <- metagen(logOR, selogOR, data = sclero, sm = "OR")
m
# Thompson & Sharp (1999), Table IV, method (2)
metabias(m, method = "Egger")
# Thompson & Sharp (1999), Table IV, method (3a)
metabias(m, method = "Thompson")
# Thompson & Sharp (1999), Table IV, method (3b)
update(m, method.tau = "ML")
metabias(update(m, method.tau = "ML"), method = "Thompson")</pre>
```

print.meta

Print meta-analysis results

## **Description**

Print method for objects of class meta.

R function cilayout can be utilised to change the layout to print confidence intervals (both in printout from print.meta and print.summary.meta function as well as in forest plots). The default layout is "[lower; upper]". Another popular layout is "(lower - upper)" which is used throughout an R session by using R command cilayout("(", " - ").

Argument pscale can be used to rescale single proportions or risk differences, e.g. pscale = 1000 means that proportions are expressed as events per 1000 observations. This is useful in situations with (very) low event probabilities.

Argument irscale can be used to rescale single rates or rate differences, e.g. irscale = 1000 means that rates are expressed as events per 1000 time units, e.g. person-years. This is useful in situations with (very) low rates. Argument irunit can be used to specify the time unit used in individual studies (default: "person-years"). This information is printed in summaries and forest plots if argument irscale is not equal to 1.

# Usage

```
## $3 method for class 'meta'
print(
    x,
    common = x$common,
    random = x$random,
    prediction = x$prediction,
    overall = x$overall,
    overall.hetstat = x$overall.hetstat,
```

```
test.subgroup = x$test.subgroup,
  test.subgroup.common = test.subgroup & common,
  test.subgroup.random = test.subgroup & random,
  prediction.subgroup = x$prediction.subgroup,
  backtransf = x$backtransf,
  pscale = x$pscale,
  irscale = x$irscale,
  irunit = x$irunit,
  subgroup.name = x$subgroup.name,
  print.subgroup.name = x$print.subgroup.name,
  sep.subgroup = x$sep.subgroup,
  nchar.subgroup = 35,
  header = TRUE,
  print.CMH = x*print.CMH,
  digits = gs("digits"),
  digits.stat = gs("digits.stat"),
  digits.pval = max(gs("digits.pval"), 2),
  digits.pval.Q = max(gs("digits.pval.Q"), 2),
  digits.Q = gs("digits.Q"),
  digits.tau2 = gs("digits.tau2"),
  digits.tau = gs("digits.tau"),
  digits.H = gs("digits.H"),
  digits.I2 = gs("digits.I2"),
  scientific.pval = gs("scientific.pval"),
  big.mark = gs("big.mark"),
  zero.pval = gs("zero.pval"),
  JAMA.pval = gs("JAMA.pval"),
  print.tau2 = TRUE,
  print.tau = TRUE,
  print.I2 = gs("print.I2"),
  print.H = gs("print.H"),
  print.Rb = gs("print.Rb"),
  text.tau2 = gs("text.tau2"),
  text.tau = gs("text.tau"),
  text.I2 = gs("text.I2"),
  text.Rb = gs("text.Rb"),
  details.methods = TRUE,
  warn.backtransf = FALSE,
  warn.deprecated = gs("warn.deprecated"),
)
cilayout(
  bracket = gs("CIbracket"),
  separator = gs("CIseparator"),
  lower.blank = gs("CIlower.blank"),
  upper.blank = gs("CIupper.blank")
)
```

### **Arguments**

x An object of class meta.

common A logical indicating whether results for common effect meta-analysis should be

printed.

random A logical indicating whether results for random effects meta-analysis should be

printed.

prediction A logical indicating whether a prediction interval should be printed.

overall A logical indicating whether overall summaries should be reported. This argu-

ment is useful in a meta-analysis with subgroups if overall results should not be

reported.

overall.hetstat

A logical value indicating whether to print heterogeneity measures for overall treatment comparisons. This argument is useful in a meta-analysis with subgroups if heterogeneity statistics should only be printed on subgroup level.

test.subgroup A logical value indicating whether to print results of test for subgroup differ-

ences.

test.subgroup.common

A logical value indicating whether to print results of test for subgroup differences (based on common effect model).

test.subgroup.random

A logical value indicating whether to print results of test for subgroup differences (based on random effects model).

prediction.subgroup

A logical indicating whether prediction intervals should be printed for sub-

groups.

backtransf A logical indicating whether printed results should be back transformed. If

backtransf=TRUE, results for sm="OR" are printed as odds ratios rather than log odds ratios and results for sm="ZCOR" are printed as correlations rather than

Fisher's z transformed correlations, for example.

pscale A numeric giving scaling factor for printing of single event probabilities or risk

differences, i.e. if argument sm is equal to "PLOGIT", "PLN", "PRAW", "PAS",

"PFT", or "RD".

irscale A numeric defining a scaling factor for printing of single incidence rates or in-

cidence rate differences, i.e. if argument sm is equal to "IR", "IRLN", "IRS",

"IRFT", or "IRD".

irunit A character specifying the time unit used to calculate rates, e.g. person-years.

subgroup. name A character string with a name for the grouping variable.

print.subgroup.name

A logical indicating whether the name of the grouping variable should be printed

in front of the group labels.

sep.subgroup A character string defining the separator between label and levels of grouping

variable.

nchar.subgroup A numeric specifying the number of characters to print from subgroup labels.

header	A logical indicating whether information on title of meta-analysis, comparison and outcome should be printed at the beginning of the printout.
print.CMH	A logical indicating whether result of the Cochran-Mantel-Haenszel test for overall effect should be printed.
digits	Minimal number of significant digits, see print.default.
digits.stat	Minimal number of significant digits for z- or t-value of test for overall effect, see print.default.
digits.pval	Minimal number of significant digits for p-value of overall treatment effect, see print.default.
digits.pval.Q	Minimal number of significant digits for p-value of heterogeneity test, see print.default.
digits.Q	Minimal number of significant digits for heterogeneity statistic Q, see print.default.
digits.tau2	Minimal number of significant digits for between-study variance $\tau^2$ , see print.default.
digits.tau	Minimal number of significant digits for $\tau$ , the square root of the between-study variance $\tau^2$ .
digits.H	Minimal number of significant digits for H statistic, see print.default.
digits.I2	Minimal number of significant digits for I-squared and Rb statistic, see print.default.
scientific.pva	
	A logical specifying whether p-values should be printed in scientific notation, e.g., 1.2345e-01 instead of 0.12345.
big.mark	A character used as thousands separator.
zero.pval	A logical specifying whether p-values should be printed with a leading zero.
JAMA.pval	A logical specifying whether p-values for test of overall effect should be printed according to JAMA reporting standards.
print.tau2	A logical specifying whether between-study variance $\tau^2$ should be printed.
print.tau	A logical specifying whether $\tau$ , the square root of the between-study variance $\tau^2$ , should be printed.
print.I2	A logical specifying whether heterogeneity statistic I <sup>2</sup> should be printed.
print.H	A logical specifying whether heterogeneity statistic H should be printed.
print.Rb	A logical specifying whether heterogeneity statistic $R_b$ should be printed.
text.tau2	Text printed to identify between-study variance $\tau^2$ .
text.tau	Text printed to identify $\tau$ , the square root of the between-study variance $\tau^2$ .
text.I2	Text printed to identify heterogeneity statistic I <sup>2</sup> .
text.Rb	Text printed to identify heterogeneity statistic $R_b$ .
details.method	
	A logical specifying whether details on statistical methods should be printed.
warn.backtrans	A logical indicating whether a warning should be printed if backtransformed
	proportions and rates are below 0 and backtransformed proportions are above 1.
warn.deprecated	
	A logical indicating whether warnings should be printed if deprecated arguments

are used.

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	Additional arguments (passed on to prmatrix).
bracket	A character with bracket symbol to print lower confidence interval: "[", "(", "{", """.
separator	A character string with information on separator between lower and upper confidence interval.
lower.blank	A logical indicating whether blanks between left bracket and lower confidence limit should be printed.
upper.blank	A logical indicating whether blanks between separator and upper confidence limit should be printed.
print.rm5	Cochrane review: summary of meta-analyses

# Description

Calculate and print a summary of all meta-analyses in a Cochrane review.

## Usage

```
## S3 method for class 'rm5'
print(x, comp.no, outcome.no, ...)
```

### **Arguments**

x An object of class rm5.
 comp.no Comparison number.
 outcome.no Outcome number.
 ... Additional arguments (passed on to metacr).

### **Details**

This function can be used to redo all or selected meta-analyses of a Cochrane Review.

Review Manager 5 (RevMan 5) is the current software used for preparing and maintaining Cochrane Reviews (https://training.cochrane.org/online-learning/core-software-cochrane-reviews/revman). In RevMan 5, subgroup analyses can be defined and data from a Cochrane review can be imported to R using the function read.rm5.

The R function metacr is called internally.

### Author(s)

Guido Schwarzer <sc@imbi.uni-freiburg.de>

# References

Higgins, J.P.T and S. Green (2011): Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [Updated March 2011]. The Cochrane Library: http://www.cochrane-handbook.org

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### See Also

```
summary.meta, metacr, read.rm5, metabias.rm5
```

### **Examples**

```
# Locate export data file "Fleiss1993_CR.csv"
# in sub-directory of package "meta"
#
filename <- system.file("extdata", "Fleiss1993_CR.csv", package = "meta")
Fleiss1993_CR <- read.rm5(filename)
# Print results for all meta-analysis
#
Fleiss1993_CR
# Print results only for second outcome of first comparison
#
print(Fleiss1993_CR, comp.no = 1, outcome.no = 2)</pre>
```

print.summary.meta

Print detailed meta-analysis results

### **Description**

Print method for objects of class summary.meta.

### Usage

```
## S3 method for class 'summary.meta'
print(
  х,
  sortvar,
  common = x$x$common,
  random = x$x$random,
  details = FALSE,
 ma = TRUE,
  overall = x$overall,
  backtransf = x$backtransf,
  pscale = x*pscale,
  irscale = x$irscale,
  irunit = x$irunit,
  digits = gs("digits"),
  digits.se = gs("digits.se"),
  digits.pval = max(gs("digits.pval"), 2),
  digits.tau2 = gs("digits.tau2"),
  digits.tau = gs("digits.tau"),
  digits.I2 = gs("digits.I2"),
```

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```
digits.prop = gs("digits.prop"),
digits.weight = gs("digits.weight"),
scientific.pval = gs("scientific.pval"),
zero.pval = gs("zero.pval"),
JAMA.pval = gs("JAMA.pval"),
big.mark = gs("big.mark"),
text.tau2 = gs("text.tau2"),
text.tau = gs("text.tau"),
text.I2 = gs("text.I2"),
truncate,
text.truncate = "*** Output truncated ***",
details.methods = TRUE,
warn.backtransf = FALSE,
...
```

# Arguments

x	An object of class summary.meta
sortvar	An optional vector used to sort the individual studies (must be of same length as $x$ \$TE).
common	A logical indicating whether a common effect meta-analysis should be conducted.
random	A logical indicating whether a random effects meta-analysis should be conducted.
details	A logical indicating whether further details of individual studies should be printed.
ma	A logical indicating whether the summary results of the meta-analysis should be printed.
overall	A logical indicating whether overall summaries should be reported. This argument is useful in a meta-analysis with subgroups if overall results should not be reported.
backtransf	A logical indicating whether printed results should be back transformed. If backtransf = TRUE, results for sm = "OR" are printed as odds ratios rather than log odds ratios and results for sm = "ZCOR" are printed as correlations rather than Fisher's z transformed correlations, for example.
pscale	A numeric giving scaling factor for printing of single event probabilities or risk differences, i.e. if argument sm is equal to "PLOGIT", "PLN", "PRAW", "PAS", "PFT", or "RD".
irscale	A numeric defining a scaling factor for printing of single incidence rates or incidence rate differences, i.e. if argument sm is equal to "IR", "IRLN", "IRS", "IRFT", or "IRD".
irunit	A character specifying the time unit used to calculate rates, e.g. person-years.
digits	Minimal number of significant digits, see print.default.
digits.se	Minimal number of significant digits for standard deviations and standard errors, see print.default.

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digits.pval	Minimal number of significant digits for p-value of test of treatment effect, see print.default.
digits.tau2	Minimal number of significant digits for between-study variance, see print.default.
digits.tau	Minimal number of significant digits for square root of between-study variance, see print.default.
digits.I2	$Minimal\ number\ of\ significant\ digits\ for\ I-squared\ and\ Rb\ statistic,\ see\ \verb"print.default".$
digits.prop	Minimal number of significant digits for proportions, see print.default.
digits.weight	Minimal number of significant digits for weights, see print.default.
scientific.pval	
	A logical specifying whether p-values should be printed in scientific notation, e.g., 1.2345e-01 instead of 0.12345.
zero.pval	A logical specifying whether p-values should be printed with a leading zero.
JAMA.pval	A logical specifying whether p-values for test of overall effect should be printed according to JAMA reporting standards.
big.mark	A character used as thousands separator.
text.tau2	Text printed to identify between-study variance $\tau^2$ .
text.tau	Text printed to identify $\tau$ , the square root of the between-study variance $\tau^2$ .
text.I2	Text printed to identify heterogeneity statistic $I^2$ .
truncate	An optional vector used to truncate the printout of results for individual studies (must be a logical vector of same length as x\$TE or contain numerical values).
text.truncate	A character string printed if study results were truncated from the printout.
details.methods	
	A logical specifying whether details on statistical methods should be printed.
warn.backtransf	
	A logical indicating whether a warning should be printed if backtransformed proportions and rates are below 0 and backtransformed proportions are above 1.
	Additional arguments (passed on to print.meta called internally).

### **Details**

Print method for objects of class summary.meta giving detailed information on the meta-analysis.

Argument pscale can be used to rescale single proportions or risk differences, e.g. pscale = 1000 means that proportions are expressed as events per 1000 observations. This is useful in situations with (very) low event probabilities.

Argument irscale can be used to rescale single rates or rate differences, e.g. irscale = 1000 means that rates are expressed as events per 1000 time units, e.g. person-years. This is useful in situations with (very) low rates. Argument irunit can be used to specify the time unit used in individual studies (default: "person-years"). This information is printed in summaries and forest plots if argument irscale is not equal to 1.

### Author(s)

Guido Schwarzer <sc@imbi.uni-freiburg.de>

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### References

Cooper H & Hedges LV (1994), *The Handbook of Research Synthesis*. Newbury Park, CA: Russell Sage Foundation.

Crippa A, Khudyakov P, Wang M, Orsini N, Spiegelman D (2016), A new measure of between-studies heterogeneity in meta-analysis. *Statistics in Medicine*, **35**, 3661–75.

Higgins JPT & Thompson SG (2002), Quantifying heterogeneity in a meta-analysis. *Statistics in Medicine*, **21**, 1539–58.

#### See Also

```
summary.meta, update.meta, metabin, metacont, metagen
```

### **Examples**

```
data(Fleiss1993cont)
m1 <- metacont(n.psyc, mean.psyc, sd.psyc, n.cont, mean.cont, sd.cont,
   data = Fleiss1993cont, sm = "SMD", studlab = paste(study, year))
sm1 <- summary(m1)
sm1

print(sm1, digits = 2)

## Not run:
# Use unicode characters to print tau^2, tau, and I^2
print(sm1,
   text.tau2 = "\u03c4\u00b2",
   text.tau = "\u03c4\u00b2", text.I2 = "I\u00b2")

## End(Not run)</pre>
```

radial.meta

Radial plot

# Description

Draw a radial plot (also called Galbraith plot) which can be used to assess bias in meta-analysis.

## Usage

```
## S3 method for class 'meta'
radial(
    x,
    xlim = NULL,
    ylim = NULL,
    xlab = "Inverse of standard error",
    ylab = "Standardised treatment effect (z-score)",
```

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```
common = TRUE,
  axes = TRUE,
 pch = 1,
 text = NULL,
  cex = 1,
  col = NULL,
 level = NULL,
 warn.deprecated = gs("warn.deprecated"),
 fixed,
)
## Default S3 method:
radial(
 Х,
 у,
 xlim = NULL,
 ylim = NULL,
 xlab = "Inverse of standard error",
 ylab = "Standardised treatment effect (z-score)",
 common = TRUE,
  axes = TRUE,
 pch = 1,
  text = NULL,
 cex = 1,
 col = NULL,
 level = NULL,
)
```

## **Arguments**

X	An object of class meta, or estimated treatment effect in individual studies.
xlim	The x limits (min, max) of the plot.
ylim	The y limits (min, max) of the plot.
xlab	A label for the x-axis.
ylab	A label for the y-axis.
common	A logical indicating whether the pooled common effect estimate should be plotted.
axes	A logical indicating whether axes should be drawn on the plot.
pch	The plotting symbol used for individual studies.
text	A character vector specifying the text to be used instead of plotting symbol.
cex	The magnification to be used for plotting symbol.
col	A vector with colour of plotting symbols.
level	The confidence level utilised in the plot.

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warn.deprecated

A logical indicating whether warnings should be printed if deprecated arguments

are used.

fixed Deprecated argument (replaced by 'common').

. . . Graphical arguments as in par may also be passed as arguments.

y Standard error of estimated treatment effect.

#### **Details**

A radial plot (Galbraith 1988a,b), also called Galbraith plot, is drawn in the active graphics window. If common is TRUE, the pooled estimate of the common effect model is plotted. If level is not NULL, the corresponding confidence limits are drawn.

## Author(s)

Guido Schwarzer <sc@imbi.uni-freiburg.de>

#### References

Galbraith RF (1988a): Graphical display of estimates having differing standard errors. *Technometrics*, **30**, 271–81

Galbraith RF (1988b): A note on graphical presentation of estimated odds ratios from several clinical trials. *Statistics in Medicine*, **7**, 889–94

#### See Also

```
metabias, metabin, metagen, funnel
```

## **Examples**

```
data(Olkin1995)
m1 <- metabin(ev.exp, n.exp, ev.cont, n.cont,
   data = Olkin1995, subset = c(41, 47, 51, 59),
   studlab = paste(author, year), sm = "RR", method = "I")
# Radial plot
#
radial(m1, level = 0.95)</pre>
```

read.mtv

Import RevMan 4 data files (.mtv)

## **Description**

Reads a file created with RevMan 4 and creates a data frame from it.

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### Usage

```
read.mtv(file)
```

### **Arguments**

file The name of a file to read data values from.

#### **Details**

Reads a file created with RevMan 4 (Menu: "File" - "Export" - "Analysis data file...") and creates a data frame from it.

#### Value

A data frame containing the following components:

comp.no Comparison number.
outcome.no Outcome number.
group.no Group number.
studlab Study label.

year Year of publication.

event.e Number of events in experimental group.

n.e Number of observations in experimental group.

event.c Number of events in control group.

n.c Number of observations in control group.mean.e Estimated mean in experimental group.sd.e Standard deviation in experimental group.

mean.c Estimated mean in control group.

sd.c Standard deviation in control group.

0.E Observed minus expected (IPD analysis).

V Variance of 0.E (IPD analysis).

order Ordering of studies.

conceal Concealment of treatment allocation.

grplab Group label.

type Type of outcome. D = dichotomous, C = continuous, P = IPD.

outclab Outcome label.

graph.exp Graph label for experimental group.

graph.cont Graph label for control group.

label.exp Label for experimental group.

Label for control group.

complab Comparison label.

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### Author(s)

Guido Schwarzer <sc@imbi.uni-freiburg.de>

#### References

*Review Manager (RevMan)* [Computer program]. Version 4.2. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2003

### See Also

```
metabin, metacont, metagen
```

### **Examples**

```
# Locate MTV-data file "FLEISS1993.MTV" in sub-directory of R package
# meta
#
filename <- system.file("extdata/FLEISS1993.MTV", package = "meta")
fleiss1933.cc <- read.mtv(filename)

# Same result as R Command example(Fleiss1993bin):
#
metabin(event.e, n.e, event.c, n.c,
    data = fleiss1933.cc, subset = type == "D",
    studlab = paste(studlab, year))

# Same result: example(Fleiss1993cont)
#
metacont(n.e, mean.e, sd.e, n.c, mean.c, sd.c,
    data = fleiss1933.cc, subset = type == "C",
    studlab = paste(studlab, year))</pre>
```

read.rm5

Import RevMan 5 analysis data

## **Description**

Reads analysis data from Cochrane intervention review created with RevMan 5 and creates a data frame from it.

# Usage

```
read.rm5(
    file,
    sep = ",",
    quote = "\"",
    title,
```

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```
numbers.in.labels = TRUE,
debug = 0
)
```

#### **Arguments**

file The name of a file to read data values from.

sep The field separator character (only considered for CSV-files). Values on each

line of the file are separated by this character. The comma is the default field

separator character in RevMan 5.

quote The set of quoting characters (only considered for CSV-files). In RevMan 5 a

"\"" is the default quoting character.

title Title of Cochrane review.

numbers.in.labels

A logical indicating whether comparision number and outcome number should be printed at the beginning of the comparison (argument complab) and outcome

label (argument outclab); this is the default in RevMan 5.

debug An integer between 0 and 3 indicating whether to print debug messages (only

considered for RM5-files).

#### **Details**

Review Manager 5 (RevMan 5) was the software used for preparing and maintaining Cochrane reviews (https://training.cochrane.org/online-learning/core-software-cochrane-reviews/revman). RevMan 5 includes the ability to write systematic reviews of interventions, diagnostic test accuracy reviews, methodology reviews and overviews of reviews.

This function provides the ability to read the analysis data from a Cochrane intervention review created with RevMan 5; a data frame is created from it. Cochrane intervention reviews are based on comparisons of two interventions.

By default in RevMan 5, the name of the exported CSV data file is the title of the Cochrane review. Furthermore, the title is part of the RM5-file. Argument title can be used to overwrite the title of the Cochrane review.

### **Import RM5-file:**

A RM5-file (which is in a specific XML format) can be used directly to import the analysis dataset. If the import fails, use argument debug = 3 for more details.

### **Import CSV-file:**

In the past, the following (rather complicated) procedure based on a CSV-file generated within RevMan 5 was necessary - which is only described here for backward compatibility.

In order to generate a data analysis file in RevMan 5 use the following Menu points: "File" - "Export" - "Data and analyses". It is mandatory to include the following fields in the exported data file by selecting them with the mouse cursor in the Export Analysis Data Wizard: (i) Comparison Number, (ii) Outcome Number, (iii) Subgroup Number. When these fields are not selected a corresponding error message will be printed in R. It is recommended to include all fields in the exported data file except for the last field "Risk of bias tables". For example, in order to redo the meta-analysis in R for the RevMan 5 data type "0-E and Variance" the fields "0-E" and

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"Variance" have to be selected in the Export Analysis Data Wizard. If the last field "Risk of bias tables" is selected the import in R fails with an error message "line X did not have Y elements".

### Value

A data frame containing the following components:

comp.no Comparison number.
outcome.no Outcome number.
group.no Group number.
studlab Study label.

year Year of publication.

event.e Number of events in experimental group.

n.e Number of observations in experimental group.

event.c Number of events in control group.

n.c Number of observations in control group.mean.e Estimated mean in experimental group.sd.e Standard deviation in experimental group.

mean.c Estimated mean in control group.

sd.c Standard deviation in control group.

O.E Observed minus expected (IPD analysis).

V Variance of 0.E (IPD analysis).

TE, seTE Estimated treatment effect and standard error of individual studies.

lower, upper Lower and upper limit of 95% confidence interval for treatment effect in indi-

vidual studies.

weight Weight of individual studies (according to meta-analytical method used in re-

spective meta-analysis - see details).

order Ordering of studies.

grplab Group label.

type Type of outcome. D = dichotomous, C = continuous, P = IPD.

method A character string indicating which method has been used for pooling of studies.

One of "Inverse", "MH", or "Peto".

sm A character string indicating which summary measure has been used for pooling

of studies.

model A character string indicating which meta-analytical model has been used (either

"Fixed" or "Random").

common A logical indicating whether common effect meta-analysis has been used in re-

spective meta-analysis (see details).

random A logical indicating whether random effects meta-analysis has been used in re-

spective meta-analysis (see details).

outclab Outcome label.

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k	Total number of studies combined in respective meta-analysis).
event.e.pooled	Number of events in experimental group in respective meta-analysis (see details).
n.e.pooled	Number of observations in experimental group in respective meta-analysis (see details).
${\tt event.c.pooled}$	Number of events in control group in respective meta-analysis (see details).
n.c.pooled	Number of observations in control group in respective meta-analysis (see details).
TE.pooled	Estimated treatment effect in respective meta-analysis (see details).
lower, upper	Lower and upper limit of $95\%$ confidence interval for treatment effect in respective meta-analysis (see details).
weight.pooled	Total weight in respective meta-analysis (see details).
Z.pooled	Z-score for test of overall treatment effect in respective meta-analysis (see details).
pval.pooled	P-value for test of overall treatment effect in respective meta-analysis (see details).
Q	Heterogeneity statistic Q in respective meta-analysis (see details).
pval.Q	P-value of heterogeneity statistic Q in respective meta-analysis (see details).
12	Heterogeneity statistic $I^2$ in respective meta-analysis (see details).
tau2	Between-study variance (moment estimator of DerSimonian-Laird) in respective meta-analysis.
Q.w	Heterogeneity statistic Q within groups in respective meta-analysis (see details).
pval.Q.w	P-value of heterogeneity statistic Q within groups in respective meta-analysis (see details).
I2.w	Heterogeneity statistic ${\rm I}^2$ within groups in respective meta-analysis (see details).
label.e	Label for experimental group.
label.c	Label for control group.
label.left	Graph label on left side of forest plot.
label.right	Graph label on right side of forest plot.
complab	Comparison label.

# Author(s)

Guido Schwarzer <sc@imbi.uni-freiburg.de>

### References

Review Manager (RevMan) [Computer program]. Version 5.4. The Cochrane Collaboration, 2020

# See Also

summary.rm5, metabias.rm5, metabin, metacont, metagen, metacr, print.rm5

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### **Examples**

```
# Locate export data file "Fleiss1993_CR.csv"
# in sub-directory of package "meta"
#
filename <- system.file("extdata", "Fleiss1993_CR.csv", package = "meta")
Fleiss1993_CR <- read.rm5(filename)
# Same result as R command example(Fleiss1993bin):
# metacr(Fleiss1993_CR)
# Same result as R command example(Fleiss1993cont):
# metacr(Fleiss1993_CR, 1, 2)</pre>
```

settings.meta

Print and change default settings to conduct and print or plot metaanalyses in R package meta.

### Description

Print and change default settings to conduct and print or plot meta-analyses in R package **meta**. The following general settings are available: *Review Manager 5*, *Journal of the American Medical Association*.

### Usage

```
settings.meta(..., quietly = TRUE)
```

### Arguments

... Arguments to change default settings.

quietly A logical indicating whether information on settings should be printed.

### **Details**

This function can be used to define defaults for several arguments (i.e., assignments using gs) of the following R functions: metabin, metacont, metacor, metacr, metagen, metainc, metaprop, metarate

Furthermore, some of these settings are considered to print meta-analysis results and to produce forest plots.

The function can be used to either change individual settings (see Examples) or use one of the following general settings:

```
• settings.meta("revman5")
```

```
• settings.meta("jama")
```

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- settings.meta("iqwig5")
- settings.meta("iqwig6")
- settings.meta("geneexpr")
- settings.meta("meta4")

The first command can be used to reproduce meta-analyses from Cochrane reviews conducted with Review Manager 5 (RevMan 5, https://training.cochrane.org/online-learning/core-software-cochrane-reviewman) and specifies to use a RevMan 5 layout in forest plots.

The second command can be used to generate forest plots following instructions for authors of the *Journal of the American Medical Association* (https://jamanetwork.com/journals/jama/pages/instructions-for-authors/).Study labels according to JAMA guidelines can be generated using labels.meta.

The next commands implement the recommendations of the Institute for Quality and Efficiency in Health Care, Germany (IQWiG) accordinging to General Methods 5 and 6, respectively (https://www.iqwig.de/en/about-us/methods/methods-paper/).

The setting "geneexpr" can be used to print p-values in scientific notation and to suppress the calculation of confidence intervals for the between-study variance.

The last setting uses the default settings of R package **meta**, version 4 or below.

RevMan 5 settings, in detail:

Argument	Value	Comment
hakn	FALSE	method not available in RevMan 5
method.tau	"DL"	only available method in RevMan 5
tau.common	FALSE	common between-study variance in subgroups
MH.exact	FALSE	exact Mantel-Haenszel method
RR.Cochrane	TRUE	calculation of risk ratios
Q.Cochrane	TRUE	calculation of heterogeneity statistic
layout	"RevMan5"	layout for forest plots
test.overall	TRUE	print information on test of overall effect
digits.I2	0	number of digits for I-squared measure
digits.tau2	2	number of digits for tau-squared
digits.tau	4	number of digits for square root of tau-squared
CIbracket,	"["	
CIseparator	", "	print confidence intervals as "[., .]"

# JAMA settings:

Argument	Value	Comment
layout	"JAMA"	layout for forest plots
test.overall	TRUE	print information on test of overall effect
digits.I2	0	number of digits for I-squared measure
CIbracket,	"("	
CIseparator	"_"	print confidence intervals as "()"
zero.pval,	TRUE	print p-values with leading zero
JAMA.pval,	TRUE	round p-values to three digits (for $0.001 ) or two digits (p > 0.01)$

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# IQWiG, General Methods 5 settings:

Argument	Value	Comment
hakn	TRUE	Hartung-Knapp method
prediction	TRUE	Prediction interval

# IQWiG, General Methods 6 settings:

Argument	Value	Comment
hakn	TRUE	Hartung-Knapp method
adhoc.hakn	"ci"	ad hoc variance correction
method.tau	"PM"	Paule-Mandel estimator for between-study variance
prediction	TRUE	Prediction interval

# Settings for gene expression data:

Argument	Value	Comment
scientific.pval	TRUE	Scientific notation for p-values
method.tau.ci	FALSE	no confidence interval for
	between-study heterogeneity variance	

Settings for **meta**, version 4 or below:

Argument	Value	Comment
method tall	"DI "	DerSimonian-Laird estimator

A list of all arguments with current settings is printed using the command settings.meta("print").

In order to reset all settings of R package **meta** the command settings.meta("reset") or settings.meta(reset = TRUE) can be used.

# Author(s)

```
Guido Schwarzer <sc@imbi.uni-freiburg.de>
```

# See Also

```
gs, forest.meta, print.meta, labels.meta
```

# Examples

```
# Get listing of current settings
#
settings.meta()
```

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```
# Meta-analyses using default settings
metabin(10, 20, 15, 20)
metaprop(4, 20)
metabin(10, 20, 15, 20, sm = "RD")
metaprop(4, 20, sm = "PLN")
# Change summary measure for R functions metabin and metaprop
# and store old settings
oldset <- settings.meta(smbin = "RD", smprop = "PLN")</pre>
metabin(10, 20, 15, 20)
metaprop(4, 20)
# Use old settings
settings.meta(oldset)
# Change level used to calculate confidence intervals
# (99%-CI for studies, 99.9%-CI for pooled effects)
metagen(1:3, 2:4 / 10, sm = "MD")
settings.meta(level = 0.99, level.ma = 0.999)
metagen(1:3, 2:4 / 10, sm = "MD")
# Always print a prediction interval
settings.meta(prediction = TRUE)
metagen(1:3, 2:4 / 10, sm = "MD")
metagen(4:6, 4:2 / 10, sm = "MD")
# Try to set unknown argument results in a warning
try(settings.meta(unknownarg = TRUE))
# Reset to default settings of R package meta
settings.meta("reset")
metabin(10, 20, 15, 20)
metaprop(4, 20)
metagen(1:3, 2:4 / 10, sm = "MD")
\# Do not back transform results (e.g. print log odds ratios instead
# of odds ratios, print transformed correlations / proportions
# instead of correlations / proportions)
settings.meta(backtransf = FALSE)
metabin(10, 20, 15, 20)
metaprop(4, 20)
metacor(c(0.85, 0.7, 0.95), c(20, 40, 10))
# Forest plot using RevMan 5 style
```

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```
settings.meta("revman5")
forest(metagen(1:3, 2:4 / 10, sm = "MD", common = FALSE),
 label.left = "Favours A", label.right = "Favours B",
 colgap.studlab = "2cm", colgap.forest.left = "0.2cm")
# Forest plot using JAMA style
settings.meta("jama")
forest(metagen(1:3, 2:4 / 10, sm = "MD", common = FALSE),
 label.left = "Favours A", label.right = "Favours B",
 colgap.studlab = "2cm", colgap.forest.left = "0.2cm")
# Use slightly different layout for confidence intervals
# (especially useful if upper confidence limit can be negative)
settings.meta(CIseparator = " - ")
forest(metagen(-(1:3), 2:4 / 10, sm = "MD", common = FALSE),
 label.left = "Favours A", label.right = "Favours B",
 colgap.studlab = "2cm", colgap.forest.left = "0.2cm")
# Use old settings
settings.meta(oldset)
```

smd2or

Conversion from standardised mean difference to log odds ratio

# Description

Conversion from standardised mean difference to log odds ratio using method by Hasselblad & Hedges (1995) or Cox (1970).

# Usage

```
smd2or(
  smd,
  se.smd,
  studlab,
  data = NULL,
  subset = NULL,
  exclude = NULL,
  method = "HH",
  backtransf = gs("backtransf"),
  ...
)
```

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## **Arguments**

smd	Standardised mean difference(s) (SMD) or meta-analysis object.
se.smd	Standard error(s) of SMD (ignored if argument smd is a meta-analysis object).
studlab	An optional vector with study labels (ignored if argument smd is a meta-analysis object).
data	An optional data frame containing the study information (ignored if argument smd is a meta-analysis object).
subset	An optional vector specifying a subset of studies to be used (ignored if argument smd is a meta-analysis object).
exclude	An optional vector specifying studies to exclude from meta-analysis, however, to include in printouts and forest plots (ignored if argument smd is a meta-analysis object).
method	A character string indicating which method is used to convert SMDs to log odds ratios. Either "HH" or "CS", can be abbreviated.
backtransf	A logical indicating whether odds ratios (if TRUE) or log odds ratios (if FALSE) should be shown in printouts and plots.
• • •	Additional arguments passed on to metagen (ignored if argument smd is a meta-analysis object).

#### **Details**

This function implements the following methods for the conversion from standardised mean difference to log odds ratio:

- Hasselblad & Hedges (1995) assuming logistic distributions (method == "HH")
- Cox (1970) and Cox & Snell (1989) assuming normal distributions (method == "CS")

Internally, metagen is used to conduct a meta-analysis with the odds ratio as summary measure.

Argument smd can be either a vector of standardised mean differences or a meta-analysis object created with metacont or metagen and the standardised mean difference as summary measure.

Argument se.smd is mandatory if argument smd is a vector and ignored otherwise. Additional arguments in  $\dots$  are only passed on to metagen if argument smd is a vector.

## Value

An object of class "meta" and "metagen"; see metagen.

## Author(s)

Guido Schwarzer <sc@imbi.uni-freiburg.de>

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## References

Borenstein M, Hedges LV, Higgins JPT, Rothstein HR (2009): *Introduction to Meta-Analysis*. Chichester: Wiley

Cox DR (1970): Analysis of Binary Data. London: Chapman and Hall / CRC

Cox DR, Snell EJ (1989): Analysis of Binary Data (2nd edition). London: Chapman and Hall / CRC

Hasselblad V, Hedges LV (1995): Meta-analysis of screening and diagnostic tests. *Psychological Bulletin*, **117**, 167–78

#### See Also

```
or2smd, metacont, metagen, metabin
```

# **Examples**

smoking

Smoking example

# **Description**

Meta-analyses on the effect of smoking on mortality risk.

#### **Format**

A data frame with the following columns:

 study
 study label

 participants
 total number of participants

 d.smokers
 number of deaths in smokers' group

 py.smokers
 person years at risk in smokers' group

 d.nonsmokers
 number of deaths in non-smokers' group

 py.nonsmokers
 person years at risk in non-smokers' group

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#### **Details**

Data have been reconstructed based on the famous Smoking and Health Report to the Surgeon General (Bayne-Jones S et al., 1964). Data sets can be used to evaluate the risk of smoking on overall mortality (dataset smoking) and lung-cancer deaths (dataset lungcancer), respectively.

The person time is attributed such that the rate ratios are equal to the reported mortality ratios implicitly assuming that the data have arisen from a homogeneous age group; more detailed information by age is not available from the report. Note, the group of "non-smokers" actually consists of all participants except those who are smokers of cigarettes only. Information on real non-smokers is not available from the published Smoking and Health Report.

#### Source

Bayne-Jones S et al. (1964): Smoking and Health: Report of the Advisory Committee to the Surgeon General of the United States. U-23 Department of Health, Education, and Welfare. Public Health Service Publication No. 1103.

#### See Also

metainc

# **Examples**

```
data(smoking)
m1 <- metainc(d.smokers, py.smokers, d.nonsmokers, py.nonsmokers,
  data = smoking, studlab = study)
print(m1, digits = 2)

data(lungcancer)

m2 <- metainc(d.smokers, py.smokers, d.nonsmokers, py.nonsmokers,
  data = lungcancer, studlab = study)
print(m2, digits = 2)</pre>
```

subset.longarm

Return subset of longarm object

# **Description**

The subset method returns a subset of a longarm object.

# Usage

```
## S3 method for class 'longarm'
subset(x, subset, ...)
```

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# **Arguments**

x An object of class longarm.

subset A logical expression indicating elements or rows to keep: missing values are

taken as false.

... Additional arguments.

#### Value

A longarm object is returned.

## Author(s)

```
Guido Schwarzer <sc@imbi.uni-freiburg.de>
```

## See Also

longarm

# **Examples**

```
# Artificial example with three studies
m <- metabin(1:3, 100:102, 4:6, 200:202, studlab = LETTERS[1:3])
# Transform data to long arm-based format
11 <- longarm(m)
11
# Subset without Study B
subset(11, studlab != "B")</pre>
```

summary.meta

Summary of meta-analysis results

# Description

Summary method for objects of class meta.

# Usage

```
## S3 method for class 'meta'
summary(object, ...)
```

# Arguments

```
object An object of class meta.
... Additional arguments (ignored).
```

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#### **Details**

Review Manager 5 (RevMan 5) is the current software used for preparing and maintaining Cochrane Reviews (https://training.cochrane.org/online-learning/core-software-cochrane-reviews/revman). In RevMan 5, subgroup analyses can be defined and data from a Cochrane review can be imported to Rusing the function read.rm5. If a meta-analysis is then conducted using function metacr, information on subgroups is available in R (components subgroup, subgroup.name, and print.subgroup.name, subgroup in an object of class "meta"). Accordingly, by using function metacr there is no need to define subgroups in order to redo the statistical analysis conducted in the Cochrane review.

Note, for an object of type metaprop, starting with version 3.7-0 of meta, list elements TE, lower and upper in element study correspond to transformed proportions and confidence limits (regardless whether exact confidence limits are calculated; argument ciexact=TRUE in metaprop function). Accordingly, the following results are based on the same transformation defined by argument sm: list elements TE, lower and upper in elements study, common, random, within.common and within.random.

R function cilayout can be utilised to change the layout to print confidence intervals (both in printout from print.meta and print.summary.meta function as well as in forest plots). The default layout is "[lower; upper]". Another popular layout is "(lower - upper)" which is used throughout an R session by using R command cilayout("(", " - ").

Argument pscale can be used to rescale single proportions or risk differences, e.g. pscale=1000 means that proportions are expressed as events per 1000 observations. This is useful in situations with (very) low event probabilities.

Argument irscale can be used to rescale single rates or rate differences, e.g. irscale=1000 means that rates are expressed as events per 1000 time units, e.g. person-years. This is useful in situations with (very) low rates. Argument irunit can be used to specify the time unit used in individual studies (default: "person-years"). This information is printed in summaries and forest plots if argument irscale is not equal to 1.

#### Value

An object of classes summary. meta and meta.

## Author(s)

Guido Schwarzer <sc@imbi.uni-freiburg.de>

#### References

Cooper H & Hedges LV (1994): *The Handbook of Research Synthesis*. Newbury Park, CA: Russell Sage Foundation

Crippa A, Khudyakov P, Wang M, Orsini N, Spiegelman D (2016): A new measure of between-studies heterogeneity in meta-analysis. *Statistics in Medicine*, **35**, 3661–75

Higgins JPT & Thompson SG (2002): Quantifying heterogeneity in a meta-analysis. *Statistics in Medicine*, **21**, 1539–58

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## See Also

```
print.summary.meta, metabin, metacont, metagen
```

# **Examples**

```
data(Fleiss1993cont)
m1 <- metacont(n.psyc, mean.psyc, sd.psyc, n.cont, mean.cont, sd.cont,
   data = Fleiss1993cont, studlab = paste(study, year), sm = "SMD")
summary(m1)

summary(update(m1, subgroup = c(1, 2, 1, 1, 2), subgroup.name = "group"))
forest(update(m1, subgroup = c(1, 2, 1, 1, 2), subgroup.name = "group"))

## Not run:
# Use unicode characters to print tau^2, tau, and I^2
print(summary(m1),
   text.tau2 = "\u03c4\u00b2", text.tau = "\u03c4", text.I2 = "I\u00b2")

## End(Not run)</pre>
```

summary.rm5

Cochrane review: detailed summary of meta-analyses

# Description

Calculate and print a detailed summary of all meta-analyses in a Cochrane review.

# Usage

```
## $3 method for class 'rm5'
summary(object, comp.no, outcome.no, ...)
## $3 method for class 'summary.rm5'
print(x, ...)
```

# **Arguments**

```
object An object of class rm5.

comp.no Comparison number.

outcome.no Outcome number.

... Additional arguments (passed on to metacr).

x An object of class summary.rm5.
```

#### **Details**

This function can be used to redo all or selected meta-analyses of a Cochrane Review.

Review Manager 5 (RevMan 5) is the current software used for preparing and maintaining Cochrane Reviews (https://training.cochrane.org/online-learning/core-software-cochrane-reviews/revman). In RevMan 5, subgroup analyses can be defined and data from a Cochrane review can be imported to R using the function read.rm5.

The R function metacr is called internally.

## Author(s)

Guido Schwarzer <sc@imbi.uni-freiburg.de>

#### References

Higgins, J.P.T and S. Green (2011): Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [Updated March 2011]. The Cochrane Library: http://www.cochrane-handbook.org

#### See Also

```
summary.meta, metacr, read.rm5, metabias.rm5
```

#### **Examples**

```
# Locate export data file "Fleiss1993_CR.csv"
# in sub-directory of package "meta"
#
filename <- system.file("extdata", "Fleiss1993_CR.csv", package = "meta")
Fleiss1993_CR <- read.rm5(filename)
# Print summary results for all meta-analysis
# summary(Fleiss1993_CR)
# Print summary results only for second outcome of first comparison
# summary(Fleiss1993_CR, comp.no = 1, outcome.no = 2)</pre>
```

trimfill.meta

Trim-and-fill method to adjust for bias in meta-analysis

# Description

Trim-and-fill method for estimating and adjusting for the number and outcomes of missing studies in a meta-analysis.

# Usage

```
## S3 method for class 'meta'
trimfill(
  х,
  left = NULL,
 ma.common = TRUE,
  type = "L",
  n.iter.max = 50,
  level = x$level,
  level.ma = x$level.ma,
  common = FALSE,
  random = TRUE,
  hakn = x hakn,
 method.tau = x$method.tau,
 method.tau.ci = x$method.tau.ci,
  prediction = x$prediction,
  level.predict = x$level.predict,
  backtransf = x$backtransf,
  pscale = x$pscale,
  irscale = x$irscale,
  irunit = x$irunit,
  silent = TRUE,
 warn.deprecated = gs("warn.deprecated"),
)
## Default S3 method:
trimfill(
 х,
  seTE,
  left = NULL,
 ma.common = TRUE,
  type = L'',
  n.iter.max = 50,
  sm = "",
  studlab = NULL,
  level = 0.95,
  level.ma = level,
  common = FALSE,
  random = TRUE,
  hakn = FALSE,
  method.tau = "DL",
  method.tau.ci = if (method.tau == "DL") "J" else "QP",
  prediction = FALSE,
  level.predict = level,
  backtransf = TRUE,
  pscale = 1,
  irscale = 1,
```

```
irunit = "person-years",
silent = TRUE,
...
)
```

#### **Arguments**

x An object of class meta, or estimated treatment effect in individual studies.

left A logical indicating whether studies are supposed to be missing on the left or

right side of the funnel plot. If NULL, the linear regression test for funnel plot symmetry (i.e., function metabias(..., method="Egger")) is used to deter-

mine whether studies are missing on the left or right side.

ma.common A logical indicating whether a common effect or random effects model is used

to estimate the number of missing studies.

type A character indicating which method is used to estimate the number of missing

studies. Either "L" or "R".

n.iter.max Maximum number of iterations to estimate number of missing studies.

level The level used to calculate confidence intervals for individual studies. If exist-

ing, x\$level is used as value for level; otherwise 0.95 is used.

level.ma The level used to calculate confidence interval for the pooled estimate. If exist-

ing, x\$level.ma is used as value for level.ma; otherwise 0.95 is used.

common A logical indicating whether a common effect meta-analysis should be con-

ducted.

random A logical indicating whether a random effects meta-analysis should be con-

ducted.

hakn A logical indicating whether the method by Hartung and Knapp should be used

to adjust test statistics and confidence intervals.

method.tau A character string indicating which method is used to estimate the between-

study variance  $\tau^2$  and its square root  $\tau$ . Either "DL", "PM", "REML", "ML", "HS",

"SJ", "HE", or "EB", can be abbreviated.

method.tau.ci A character string indicating which method is used to estimate the confidence

interval of  $\tau^2$  and  $\tau$ . Either "OP", "BJ", or "J", or "J", can be abbreviated.

prediction A logical indicating whether a prediction interval should be printed.

level.predict The level used to calculate prediction interval for a new study.

backtransf A logical indicating whether results should be back transformed in printouts and

plots. If backtransf=TRUE, results for sm="OR" are printed as odds ratios rather than log odds ratios and results for sm="ZCOR" are printed as correlations rather

than Fisher's z transformed correlations, for example.

pscale A numeric giving scaling factor for printing of single event probabilities or risk

differences, i.e. if argument sm is equal to "PLOGIT", "PLN", "PRAW", "PAS",

"PFT", or "RD".

irscale A numeric defining a scaling factor for printing of single incidence rates or in-

cidence rate differences, i.e. if argument sm is equal to "IR", "IRLN", "IRS",

"IRFT", or "IRD".

irunit A character specifying the time unit used to calculate rates, e.g. person-years.

silent A logical indicating whether basic information on iterations shown.

warn.deprecated

A logical indicating whether warnings should be printed if deprecated arguments

are used.

... Additional arguments (to catch deprecated arguments).

seTE Standard error of estimated treatment effect.

sm An optional character string indicating underlying summary measure, e.g., "RD",

"RR", "OR", "ASD", "HR", "MD", "SMD", or "ROM"; ignored if x is of class meta.

studlab An optional vector with study labels; ignored if x is of class meta.

#### **Details**

The trim-and-fill method (Duval, Tweedie 2000a, 2000b) can be used for estimating and adjusting for the number and outcomes of missing studies in a meta-analysis. The method relies on scrutiny of one side of a funnel plot for asymmetry assumed due to publication bias.

Three different methods have been proposed originally to estimate the number of missing studies. Two of these methods (L- and R-estimator) have been shown to perform better in simulations, and are available in this R function (argument type).

A common effect or random effects model can be used to estimate the number of missing studies (argument ma. common). Furthermore, a common effect and/or random effects model can be used to summaries study results (arguments common and random). Simulation results (Peters et al. 2007) indicate that the common-random model, i.e. using a common effect model to estimate the number of missing studies and a random effects model to summaries results, (i) performs better than the common-common model, and (ii) performs no worse than and marginally better in certain situations than the random-random model. Accordingly, the common-random model is the default.

An empirical comparison of the trim-and-fill method and the Copas selection model (Schwarzer et al. 2010) indicates that the trim-and-fill method leads to excessively conservative inference in practice. The Copas selection model is available in R package **metasens**.

The function metagen is called internally.

#### Value

An object of class c("metagen", "meta", "trimfill"). The object is a list containing the following components:

studlab, sm, left, ma.common, type, n.iter.max

As defined above.

level, level.ma, level.predict

As defined above.

common, random, prediction

As defined above.

hakn, method.tau, method.tau.ci,

As defined above.

TE, seTE Estimated treatment effect and standard error of individual studies.

lower, upper Lower and upper confidence interval limits for individual studies.

statistic, pval

Statistic and p-value for test of treatment effect for individual studies.

w.common, w.random

Weight of individual studies (in common effect and random effects model).

TE.common, seTE.common

Estimated overall treatment effect and standard error (common effect model).

TE.random, seTE.random

Estimated overall treatment effect and standard error (random effects model).

seTE.predict Standard error utilised for prediction interval.

lower.predict, upper.predict

Lower and upper limits of prediction interval.

k Number of studies combined in meta-analysis.

Q Heterogeneity statistic Q.

tau Square-root of between-study variance.

method Pooling method: "Inverse".

call Function call.

n.iter Actual number of iterations to estimate number of missing studies.

trimfill A logical vector indicating studies that have been added by trim-and-fill method.

df.hakn Degrees of freedom for test of treatment effect for Hartung-Knapp method (only

if hakn=TRUE).

title Title of meta-analysis / systematic review.

complab Comparison label.
outclab Outcome label.

label.e Label for experimental group. label.c Label for control group.

label.left Graph label on left side of forest plot.label.right Graph label on right side of forest plot.k0 Number of studies added by trim-and-fill.

n.e Number of observations in experimental group (only for object x of class metabin

or metacont).

n.c Number of observations in control group (only for object x of class metabin or

metacont).

event.e Number of events in experimental group (only for object x of class metabin).

event.c Number of events in control group (only for object x of class metabin).

mean.e Estimated mean in experimental group (only for object x of class metacont).

sd.e Standard deviation in experimental group (only for object x of class metacont).

mean.c Estimated mean in control group (only for object x of class metacont).

sd.c Standard deviation in control group (only for object x of class metacont).

n Number of observations (only for object x of class metaprop).

event Number of events (only for object x of class metaprop).

cor Corelation (only for object x of class metacor).

class.x Main class of object x (e.g. 'metabin' or 'metacont').

version Version of R package **meta** used to create object.

#### Author(s)

Guido Schwarzer <sc@imbi.uni-freiburg.de>

#### References

Duval S & Tweedie R (2000a): A nonparametric "Trim and Fill" method of accounting for publication bias in meta-analysis. *Journal of the American Statistical Association*, **95**, 89–98

Duval S & Tweedie R (2000b): Trim and Fill: A simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis. *Biometrics*, **56**, 455–63

Peters JL, Sutton AJ, Jones DR, Abrams KR, Rushton L (2007): Performance of the trim and fill method in the presence of publication bias and between-study heterogeneity. *Statistics in Medicine*, **10**, 4544–62

Schwarzer G, Carpenter J, Rücker G (2010): Empirical evaluation suggests Copas selection model preferable to trim-and-fill method for selection bias in meta-analysis *Journal of Clinical Epidemiology*, **63**, 282–8

#### See Also

```
metagen, metabias, funnel
```

# **Examples**

```
data(Fleiss1993bin)
m1 <- metabin(d.asp, n.asp, d.plac, n.plac, data = Fleiss1993bin, sm = "OR")
tf1 <- trimfill(m1)
tf1
funnel(tf1)
funnel(tf1, pch = ifelse(tf1$trimfill, 1, 16), level = 0.9, random = FALSE)
#
# Use log odds ratios on x-axis
#
funnel(tf1, backtransf = FALSE)
funnel(tf1, pch = ifelse(tf1$trimfill, 1, 16), level = 0.9, random = FALSE,
    backtransf = FALSE)
trimfill(m1$TE, m1$seTE, sm = m1$sm)</pre>
```

update.meta

Update a meta-analysis object

## Description

Update an existing meta-analysis object.

# Usage

```
## S3 method for class 'meta'
update(
  object,
  data = object$data,
  subset,
  studlab,
  exclude,
  cluster.
 method = object$method,
  sm = object$sm,
  incr,
  method.incr = object$method.incr,
  allstudies = object$allstudies,
 MH.exact = object$MH.exact,
  RR.Cochrane = object$RR.Cochrane,
  Q.Cochrane = object$Q.Cochrane,
 model.glmm = object$model.glmm,
  level = object$level,
  level.ma = object$level.ma,
  common = object$common,
  random = object$random,
  overall = object$overall,
  overall.hetstat = object$overall.hetstat,
  hakn = object$hakn,
  adhoc.hakn = object$adhoc.hakn,
  method.tau = object$method.tau,
 method.tau.ci = object$method.tau.ci,
  tau.preset = object$tau.preset,
  TE.tau = object$TE.tau,
  tau.common = object$tau.common,
  prediction = object$prediction,
  level.predict = object$level.predict,
  null.effect = object$null.effect,
 method.bias = object$method.bias,
  backtransf = object$backtransf,
  pscale = object$pscale,
  irscale = object$irscale,
  irunit = object$irunit,
  text.common = object$text.common,
  text.random = object$text.random,
  text.predict = object$text.predict,
  text.w.common = object$text.w.common,
  text.w.random = object$text.w.random,
  title = object$title,
  complab = object$complab,
  outclab = object$outclab,
  label.e = object$label.e,
```

```
label.c = object$label.c,
  label.left = object$label.left,
  label.right = object$label.right,
  n.e = object$n.e,
  n.c = object$n.c,
  pooledvar = object$pooledvar,
  method.smd = object$method.smd,
  sd.glass = object$sd.glass,
  exact.smd = object$exact.smd,
 method.ci = object$method.ci,
  subgroup,
  subgroup.name = object$subgroup.name,
  print.subgroup.name = object$print.subgroup.name,
  sep.subgroup = object$sep.subgroup,
  test.subgroup = object$test.subgroup,
  prediction.subgroup = object$prediction.subgroup,
  byvar,
  id,
  print.CMH = object$print.CMH,
  keepdata = TRUE,
  left = object$left,
  ma.common = object$ma.common,
  type = object$type,
  n.iter.max = object$n.iter.max,
 warn = FALSE,
 warn.deprecated = gs("warn.deprecated"),
  verbose = FALSE,
  control = object$control,
)
```

# **Arguments**

object An object of class meta.

data Dataset.
subset Subset.
studlab Study label.

exclude An optional vector specifying studies to exclude from meta-analysis, however,

to include in printouts and forest plots.

cluster An optional vector specifying which estimates come from the same cluster re-

sulting in the use of a three-level meta-analysis model.

method A character string indicating which method is to be used for pooling of studies;

see metabin and metainc function for admissible values.

sm A character string indicating which summary measure is used for pooling.

incr Either a numerical value or vector which can be added to each cell frequency

for studies with a zero cell count or the character string "TA" which stands for

treatment arm continuity correction.

method.incr	A character string indicating which continuity correction method should be used ("only0", "if0all", or "all").
allstudies	A logical indicating if studies with zero or all events in both groups are to be included in the meta-analysis (applies only if sm is equal to "RR" or "OR").
MH.exact	A logical indicating if incr is not to be added to all cell frequencies for studies with a zero cell count to calculate the pooled estimate based on the Mantel-Haenszel method.
RR.Cochrane	A logical indicating if 2*incr instead of 1*incr is to be added to n.e and n.c in the calculation of the risk ratio (i.e., sm="RR") for studies with a zero cell. This is used in RevMan 5, the program for preparing and maintaining Cochrane reviews.
Q.Cochrane	A logical indicating if the Mantel-Haenszel estimate is used in the calculation of the heterogeneity statistic Q which is implemented in RevMan 5, the program for preparing and maintaining Cochrane reviews.
model.glmm	A character string indicating which GLMM model should be used.
level	The level used to calculate confidence intervals for individual studies.
level.ma	The level used to calculate confidence intervals for pooled estimates.
common	A logical indicating whether a common effect meta-analysis should be conducted.
random	A logical indicating whether a random effects meta-analysis should be conducted.
overall	A logical indicating whether overall summaries should be reported. This argument is useful in a meta-analysis with subgroups if overall results should not be
	reported.
overall.hetsta	reported. t
overall.hetsta	_
overall.hetsta	A logical value indicating whether to print heterogeneity measures for overall treatment comparisons. This argument is useful in a meta-analysis with sub-
	A logical value indicating whether to print heterogeneity measures for overall treatment comparisons. This argument is useful in a meta-analysis with subgroups if heterogeneity statistics should only be printed on subgroup level.  A logical indicating whether the method by Hartung and Knapp should be used
hakn	A logical value indicating whether to print heterogeneity measures for overall treatment comparisons. This argument is useful in a meta-analysis with subgroups if heterogeneity statistics should only be printed on subgroup level.  A logical indicating whether the method by Hartung and Knapp should be used to adjust test statistics and confidence intervals.  A character string indicating whether an <i>ad hoc</i> variance correction should be
hakn adhoc.hakn	A logical value indicating whether to print heterogeneity measures for overall treatment comparisons. This argument is useful in a meta-analysis with subgroups if heterogeneity statistics should only be printed on subgroup level. A logical indicating whether the method by Hartung and Knapp should be used to adjust test statistics and confidence intervals. A character string indicating whether an <i>ad hoc</i> variance correction should be applied in the case of an arbitrarily small Hartung-Knapp variance estimate. A character string indicating which method is used to estimate the between-study variance $\tau^2$ and its square root $\tau$ . Either "DL", "PM", "REML", "ML", "HS",
hakn adhoc.hakn method.tau	A logical value indicating whether to print heterogeneity measures for overall treatment comparisons. This argument is useful in a meta-analysis with subgroups if heterogeneity statistics should only be printed on subgroup level. A logical indicating whether the method by Hartung and Knapp should be used to adjust test statistics and confidence intervals. A character string indicating whether an <i>ad hoc</i> variance correction should be applied in the case of an arbitrarily small Hartung-Knapp variance estimate. A character string indicating which method is used to estimate the between-study variance $\tau^2$ and its square root $\tau$ . Either "DL", "PM", "REML", "ML", "HS", "SJ", "HE", or "EB", can be abbreviated. See function metagen. A character string indicating which method is used to estimate the confidence
hakn adhoc.hakn method.tau method.tau.ci	A logical value indicating whether to print heterogeneity measures for overall treatment comparisons. This argument is useful in a meta-analysis with subgroups if heterogeneity statistics should only be printed on subgroup level. A logical indicating whether the method by Hartung and Knapp should be used to adjust test statistics and confidence intervals. A character string indicating whether an <i>ad hoc</i> variance correction should be applied in the case of an arbitrarily small Hartung-Knapp variance estimate. A character string indicating which method is used to estimate the between-study variance $\tau^2$ and its square root $\tau$ . Either "DL", "PM", "REML", "ML", "HS", "SJ", "HE", or "EB", can be abbreviated. See function metagen. A character string indicating which method is used to estimate the confidence interval of $\tau^2$ and $\tau$ . Either "QP", "BJ", or "J", can be abbreviated.
hakn adhoc.hakn method.tau method.tau.ci tau.preset	A logical value indicating whether to print heterogeneity measures for overall treatment comparisons. This argument is useful in a meta-analysis with subgroups if heterogeneity statistics should only be printed on subgroup level. A logical indicating whether the method by Hartung and Knapp should be used to adjust test statistics and confidence intervals. A character string indicating whether an <i>ad hoc</i> variance correction should be applied in the case of an arbitrarily small Hartung-Knapp variance estimate. A character string indicating which method is used to estimate the between-study variance $\tau^2$ and its square root $\tau$ . Either "DL", "PM", "REML", "ML", "HS", "SJ", "HE", or "EB", can be abbreviated. See function metagen. A character string indicating which method is used to estimate the confidence interval of $\tau^2$ and $\tau$ . Either "QP", "BJ", or "J", can be abbreviated. Prespecified value for the square root of the between-study variance $\tau^2$ .
hakn adhoc.hakn method.tau method.tau.ci tau.preset TE.tau	A logical value indicating whether to print heterogeneity measures for overall treatment comparisons. This argument is useful in a meta-analysis with subgroups if heterogeneity statistics should only be printed on subgroup level. A logical indicating whether the method by Hartung and Knapp should be used to adjust test statistics and confidence intervals. A character string indicating whether an <i>ad hoc</i> variance correction should be applied in the case of an arbitrarily small Hartung-Knapp variance estimate. A character string indicating which method is used to estimate the between-study variance $\tau^2$ and its square root $\tau$ . Either "DL", "PM", "REML", "ML", "HS", "SJ", "HE", or "EB", can be abbreviated. See function metagen. A character string indicating which method is used to estimate the confidence interval of $\tau^2$ and $\tau$ . Either "QP", "BJ", or "J", can be abbreviated. Prespecified value for the square root of the between-study variance $\tau^2$ . Overall treatment effect used to estimate the between-study variance $\tau^2$ .

null.effect A numeric value specifying the effect under the null hypothesis. method.bias A character string indicating which test for funnel plot asymmetry is to be used, can be abbreviated. See function metabias. backtransf A logical indicating whether results should be back transformed in printouts and plots. If backtransf = TRUE, results for sm = "OR" are printed as odds ratios rather than log odds ratios and results for sm = "ZCOR" are printed as correlations rather than Fisher's z transformed correlations, for example. A numeric giving scaling factor for printing of single event probabilities or risk pscale differences, i.e. if argument sm is equal to "PLOGIT", "PLN", "PRAW", "PAS", "PFT", or "RD". irscale A numeric defining a scaling factor for printing of single incidence rates or incidence rate differences, i.e. if argument sm is equal to "IR", "IRLN", "IRS", "IRFT", or "IRD". A character specifying the time unit used to calculate rates, e.g. person-years. irunit text.common A character string used in printouts and forest plot to label the pooled common effect estimate. A character string used in printouts and forest plot to label the pooled random text.random effects estimate. text.predict A character string used in printouts and forest plot to label the prediction interval. text.w.common A character string used to label weights of common effect model. A character string used to label weights of random effects model. text.w.random title Title of meta-analysis / systematic review. complab Comparison label. outclab Outcome label. label.e Label for experimental group. label.c Label for control group. label.left Graph label on left side of forest plot. label.right Graph label on right side of forest plot. Number of observations in experimental group. (only for metagen object) n.e Number of observations in control group. (only for metagen object) n.c pooledvar A logical indicating if a pooled variance should be used for the mean difference (only for metacont object with sm = "MD"). method.smd A character string indicating which method is used to estimate the standardised mean difference (only for metacont object with sm = "SMD"). Either "Hedges" for Hedges' g (default), "Cohen" for Cohen's d, or "Glass" for Glass' delta, can be abbreviated. sd.glass A character string indicating which standard deviation is used in the denominator for Glass' method to estimate the standardised mean difference (only for

metacont object with sm = "SMD"). Either "control" using the standard deviation in the control group (sd.c) or "experimental" using the standard deviation

in the experimental group (sd.e), can be abbreviated.

exact.smd A logical indicating whether exact formulae should be used in estimation of the

standardised mean difference and its standard error.

method.ci A character string indicating which method is used to calculate confidence inter-

vals for individual studies. Either "z", "t", "WS", "WSCC", "AC", "SA", "SACC", "NAsm", or "Poisson", can be abbreviated. See functions metacont, metaprop

and metarate.

subgroup An optional vector to conduct a meta-analysis with subgroups.

subgroup.name A character string with a name for the subgroup variable.

print.subgroup.name

A logical indicating whether the name of the subgroup variable should be printed

in front of the group labels.

sep. subgroup A character string defining the separator between name of subgroup variable and

subgroup label.

test.subgroup A logical value indicating whether to print results of test for subgroup differ-

ences.

prediction.subgroup

A logical indicating whether prediction intervals should be printed for sub-

groups.

byvar Deprecated argument (replaced by 'subgroup').

id Deprecated argument (replaced by 'cluster').

print.CMH A logical indicating whether result of the Cochran-Mantel-Haenszel test for

overall effect should be printed.

keepdata A logical indicating whether original data (set) should be kept in meta object.

left A logical indicating whether studies are supposed to be missing on the left or

right side of the funnel plot. If NULL, the linear regression test for funnel plot symmetry (i.e., function metabias(..., method = "linreg")) is used to deter-

mine whether studies are missing on the left or right side.

ma.common A logical indicating whether a common effect or random effects model is used

to estimate the number of missing studies.

type A character indicating which method is used to estimate the number of missing

studies. Either "L" or "R".

n.iter.max Maximum number of iterations to estimate number of missing studies.

warn A logical indicating whether warnings should be printed (e.g., if incr is added

to studies with zero cell frequencies).

warn.deprecated

A logical indicating whether warnings should be printed if deprecated arguments

are used.

verbose A logical indicating whether to print information on updates of older meta ver-

sions.

control An optional list to control the iterative process to estimate the between-study

variance  $\tau^2$ . This argument is passed on to rma.uni or rma.glmm, respectively.

. . . Additional arguments (ignored at the moment).

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#### **Details**

Wrapper function to update an existing meta-analysis object which was created with R function metabin, metacont, metacon, metagen, metainc, metamean, metaprop, or metarate. More details on function arguments are available in help files of respective R functions.

This function can also be used for objects of class 'trimfill', 'metacum', and 'metainf'.

#### Value

```
An object of class "meta" and "metabin", "metacont", "metacor", "metainc", "metagen", "metamean", "metaprop", or "metarate".
```

## Author(s)

Guido Schwarzer <sc@imbi.uni-freiburg.de>

#### See Also

metabin, metacont, metacor, metagen, metainc, metamean, metaprop, metarate

## **Examples**

```
data(Fleiss1993cont)
m1 <- metacont(n.psyc, mean.psyc, sd.psyc, n.cont, mean.cont, sd.cont,
  data = Fleiss1993cont, studlab = paste(study, year), sm = "SMD")
m1

# Change summary measure (from 'SMD' to 'MD')
#
update(m1, sm = "MD")

# Restrict analysis to subset of studies
#
update(m1, subset = 1:2)

# Use different levels for confidence intervals
#
m2 <- update(m1, level = 0.66, level.ma = 0.99)
print(m2, digits = 2)
forest(m2)</pre>
```

weights.meta

Calculate absolute and percentage weights for meta-analysis

## **Description**

This function returns a data frame containing information on absolute and percentage weights of individual studies contributing to common effect and random effects meta-analysis.

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# Usage

```
## S3 method for class 'meta'
weights(
  object,
  common = object$common,
  random = object$random,
  warn.deprecated = gs("warn.deprecated"),
  ...
)
```

# **Arguments**

object	An object of class meta.
common	A logical indicating whether absolute and percentage weights from the common effect model should be calculated.
random	A logical indicating whether absolute and percentage weights from the random effects model should be calculated.
warn.deprecated	1
	A logical indicating whether warnings should be printed if deprecated arguments are used.
	Additional arguments (to catch deprecated arguments).

## Value

A data frame with the following variables is returned:

Variable	Definition	Condition
w.common	absolute weights in common effect model	(if common = TRUE)
p.common	percentage weights in common effect model	(if common = TRUE)
w.random	absolute weights in random effects model	(if random = TRUE)
p.random	percentage weights in random effects model	(if random = TRUE)

## Author(s)

```
Guido Schwarzer <sc@imbi.uni-freiburg.de>
```

## See Also

```
metabin, metacont, metagen
```

# **Examples**

```
data(Fleiss1993cont)
# Do meta-analysis (common effect and random effects model)
#
meta1 <- metacont(n.psyc, mean.psyc, sd.psyc, n.cont, mean.cont, sd.cont,
    data = Fleiss1993cont, studlab = paste(study, year), sm = "SMD")
# Print weights for common effect and random effects meta-analysis</pre>
```

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```
#
weights(meta1)

# Do meta-analysis (only random effects model)
#
meta2 <- update(meta1, common = FALSE)

# Print weights for random effects meta-analysis
#
weights(meta2)

# Print weights for common effect and random effects meta-analysis
#
weights(meta2, common = TRUE)</pre>
```

woodyplants

Elevated CO\_2 and total biomass of woody plants

## Description

Meta-analysis on effects of elevated CO\_2 on total biomass of woody plants

This dataset has been used as an example in Hedges et al. (1999) to describe methods for the meta-analysis of response ratios. The complete dataset with 102 observations and 26 variables is available online as a supplement. Here only a subset of 10 variables is provided and used in the examples.

# Format

A data frame with the following columns:

```
obsno
            observation number
            database paper number
    papno
     treat
            treatment code
            treatment level
     level
    n.elev
            number of observations in experimental group (elevated CO_2-level)
mean.elev
             estimated mean in experimental group
            standard deviation in experimental group
   sd.elev
   n.amb
            number of observations in control group (ambient CO_2-level)
            estimated mean in control group
mean.amb
   sd.amb
            standard deviation in control group
```

# Source

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## References

Hedges LV, Gurevitch J, Curtis PS (1999): The meta-analysis of response ratios in experimental ecology. *Ecology*, **80**, 1150–6

# **Examples**

```
data(woodyplants)

# Meta-analysis of response ratios (Hedges et al., 1999)

#
m1 <- metacont(n.elev, mean.elev, sd.elev, n.amb, mean.amb, sd.amb,
    data = woodyplants, sm = "ROM", studlab = paste(obsno, papno, sep = " / "))
print(m1, prediction = TRUE)

# Meta-analysis for plants grown with low soil fertility treatment

#
m2 <- update(m1, subset = (treat == "fert" & level == "low"))
print(m2, prediction = TRUE)

# Meta-analysis for plants grown under low light conditions

#
m3 <- update(m1, subset = (treat == "light" & level == "low"))
print(m3, prediction = TRUE)</pre>
```

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