Package 'metamisc'

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Title Diagnostic and prognostic meta analysis (metamisc)

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Description This package provides functions for diagnostic and prognostic meta-analyses. It estimates univariate, bivariate and multivariate models, and allows the aggregation of previously published prediction models with new data.

Depends stats, mvtnorm, ellipse, bbmle, rjags, coda

License GPL-2

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`metamisc-package` *Diagnostic and prognostic meta-analysis*

Description

This package provides functions for diagnostic and prognostic meta-analyses. It estimates univariate, bivariate and multivariate models, and allows the aggregation of previously published prediction models with new data.

Details

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License:	GPL-2

The package provides tools for the meta-analysis of individual participant (IPD) and/or aggregate data (AD). At this stage, it is possible to pool univariate (with `uvmeta`) and bivariate (with `riley`) summary data using frequentist and Bayesian approaches.

Author(s)

Thomas Debray <thomas.debray@gmail.com>

References

DerSimonian R, Laird N. Meta-analysis in clinical trials. *Controlled Clinical Trials* 1986; **7**: 177–188.

Reitsma J, Glas A, Rutjes A, Scholten R, Bossuyt P, Zwinderman A. Bivariate analysis of sensitivity and specificity produces informative summary measures in diagnostic reviews. *Journal of Clinical Epidemiology* 2005; **58**: 982–990.

Riley RD, Thompson JR, Abrams KR. An alternative model for bivariate random-effects meta-analysis when the within-study correlations are unknown. *Biostatistics* 2008; **9**: 172–186.

See Also

`Daniels`, `Kertai`, `riley`, `Scheidler`, `uvmeta`

`Collins` *Collins data*

Description

A meta-analysis of nine clinical trials investigating the effect of taking diuretics during pregnancy on the risk of pre-eclampsia.

Usage

```
data(Collins)
```

Format

A data frame with 9 observations on the following 2 variables.

`logOR` a numeric vector with treatment effect sizes (log odds ratio)

`SE` a numeric vector with the standard error of the treatment effect sizes

Source

Collins, R., Yusuf, S., Peto, R. Overview of randomised trials of diuretics in pregnancy. *British Medical Journal* 1985, **290**, 17–23.

Hardy, R.J. Thompson, S.G. A likelihood approach to meta-analysis with random effects. *Statistics in Medicine* 1996; **15**:619–629.

Examples

```
data(Collins)
```

Daniels *Daniels and Hughes data*

Description

Data frame with treatment differences in CD4 cell count.

Usage

```
data("Daniels")
```

Format

A data frame with 15 observations on the following 2 variables.

`Y1` Treatment differences for the log hazard ratio for the development of AIDS or death over 2 years.

`vars1` Error variances of Y1.

`Y2` Difference in mean change in CD4 cell count between baseline and 6 month for studies of the AIDS Clinical Trial Group

`vars2` Error variances of Y2.

Details

The `Daniels` data comprises 15 phase II/III randomized clinical trials of the HIV Disease Section of the Adult AIDS Clinical Trials Group of the National Institutes of Health, which had data available as of May 1996, which had at least six months of follow-up on some patients and in which at least one patient developed AIDS or died.

Source

Daniels MJ, Hughes MD. Meta-analysis for the evaluation of potential surrogate markers. *Statistics in Medicine* 1997; **16**: 1965–1982.

Riley RD, Thompson JR, Abrams KR. An alternative model for bivariate random-effects meta-analysis when the within-study correlations are unknown. *Biostatistics* 2008; **9**: 172–186.

inv.logit *Apply the inverse logit tranformation*

Description

Transforms a linear predictor into a probability.

Usage

```
inv.logit(x)
```

Arguments

x	A vector of numerics (between -Inf and Inf)

Value

A vector of numerics between 0 and 1.

Author(s)

Thomas Debray <thomas.debray@gmail.com>

See Also

logit

Kertai *Kertai data*

Description

Data frame with diagnostic accuracy data from exercise electrocardiography.

Usage

```
data("Kertai")
```

Format

One data frame with 4 variables.

TP integer. number of true positives

FN integer. number of false negatives

FP integer. number of false positives

TN integer. number of true negatives

Details

The `Kertai` data set is a meta-analysis of prognostic test studies and comprises 7 studies where the diagnostic test accuracy of exercise electrocardiography for predicting cardiac events in patients undergoing major vascular surgery was measured.

Source

Kertai MD, Boersma E, Bax JJ, Heijenbrok-Kal MH, Hunink MGM, L'talien GJ, Roelandt JRTC, van Urk H, Poldermans D. A meta-analysis comparing the prognostic accuracy of six diagnostic tests for predicting perioperative cardiac risk in patients undergoing major vascular surgery. *Heart* 2003; **89**: 1327–1334.

Jackson D, Riley RD, & White IW. Multivariate meta-analysis: Potential and promise. *Statistics in Medicine* 2010; **30**: 2481–2498.

`logit` *Apply logit tranformation*

Description

Transforms values between 0 and 1 to values between -Inf and Inf.

Usage

```
logit(x)
```

Arguments

`x`	A vector of numerics (between 0 and 1)

Value

A vector of numerics (between -Inf and Inf).

Author(s)

Thomas Debray <thomas.debray@gmail.com>

See Also

`inv.logit`

`logLik.riley` *Print the log-likelihood*

Description

This function provides the (restricted) log-likelihood of a fitted model.

Usage

```
## S3 method for class 'riley'
logLik(object, ...)
```

Arguments

`object`	a `riley` object, representing a fitted alternative model for bivariate random-effects meta-analysis when the within-study correlations are unknown.
`...`	arguments to be passed on to other functions, currently ignored

Value

Returns an object of class `logLik`. This is the (restricted) log-likelihood of the model represented by `object` evaluated at the estimated coefficients. It contains at least one attribute, "`df`" (degrees of freedom), giving the number of (estimated) parameters in the model.

Author(s)

Thomas Debray <thomas.debray@gmail.com>

References

Riley RD, Thompson JR, Abrams KR. An alternative model for bivariate random-effects meta-analysis when the within-study correlations are unknown. *Biostatistics* 2008; **9**: 172–186.

See Also

`plot.riley`, `predict.riley`, `summary.riley`, `riley`, `rileyDA`, `rileyES`

Examples

```
data(Scheidler)
ds <- Scheidler[which(Scheidler$modality==1),]
fit <- riley(ds, type="test.accuracy")
logLik(fit)
```

plot.riley *Plot the summary of the bivariate model from Riley et al. (2008).*

Description

This function plots the summary sensitivity and false positive rate with their corresponding confidence regions.

Usage

```
## S3 method for class 'riley'
plot(x, plotsumm = TRUE, plotnumerics = TRUE, level = 0.95,
main="", ylim = c(0,1), xlim = c(0,1), pch = 1, lty = 1, lwd = 1,
cex.numerics=0.45, add=FALSE, ...)
```

Arguments

x	a riley object.
plotsumm	logical, should the plot draw the summary pair of sensitivity and false positive rate?
plotnumerics	logical, should the plot contain a summary table of sensitivity and false positive rate?
level	numeric, the level for calculations of confidence intervals
main	string, title of the plot
ylim	numeric of length 2, which section of the sensitivities to plot?
xlim	numeric of length 2, which section of the false positive rates to plot?
pch	integer, symbol for the pair of mean sensitivity and false positive rate
lty	integer, line type of confidence curve
lwd	integer, line width of the confidence curve
cex.numerics	numeric, text size
add	logical, should the confidence region be added to the current plot?
...	arguments to be passed on to other functions

Author(s)

Thomas Debray <thomas.debray@gmail.com>

References

Riley RD, Thompson JR, Abrams KR. An alternative model for bivariate random-effects meta-analysis when the within-study correlations are unknown. *Biostatistics* 2008; **9**: 172–186.

See Also

riley

Examples

```
data(Scheidler)

ds1 <- Scheidler[which(Scheidler$modality==1),]
ds2 <- Scheidler[which(Scheidler$modality==2),]
ds3 <- Scheidler[which(Scheidler$modality==3),]

#Perform the analyses
fit1 <- riley(ds1, type="test.accuracy")
fit2 <- riley(ds2, type="test.accuracy")
fit3 <- riley(ds3, type="test.accuracy")

plot(fit1,plotnumerics=FALSE,pch=0) #CT
plot(fit2,plotnumerics=FALSE,add=TRUE,pch=1) #LAG
plot(fit3,plotnumerics=FALSE,add=TRUE,pch=2) #MRI
```

---

predict.riley *Prediction Interval*

Description

Calculates a prediction interval for the summary parameters of Riley's alternative model for bivariate random-effects meta-analysis. This interval predicts in what range future observations will fall given what has already been observed.

Usage

```
## S3 method for class 'riley'
predict(object, level = 0.95, ...)
```

Arguments

`object`	a `riley` object.
`level`	numeric, the level for calculations of confidence intervals
`...`	arguments to be passed on to other functions

Details

Prediction intervals are based on Student's t-distribution with (numstudies - 5) degrees of freedom.

Value

Array containing prediction intervals for the summary estimates `beta1` and `beta2` (for effect size data), or for the mean sensitivity and false positive rate (diagnostic test accuracy data).

Author(s)

Thomas Debray <thomas.debray@gmail.com>

See Also

riley

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riley *Fit the alternative model for bivariate random-effects meta-analysis (Riley)*

Description

This function fits the alternative model for bivariate random-effects meta-analysis when the within-study correlations are unknown. This bivariate model was proposed by Riley et al. (2008) and is similar to the general bivariate random-effects model (van Houwelingen et al. 2002), but includes an overall correlation parameter rather than separating the (usually unknown) within- and between-study correlation. As a consequence, the alternative model is not fully hierarchical, and estimates of additional variation beyond sampling error (psi) are not directly equivalent to the between-study variation (tau) from the general model. This model is particularly useful when there is large within-study variability, few primary studies are available or the general model estimates the between-study correlation as 1 or -1. Although the model can also be used for diagnostic test accuracy data when substantial within-study correlations are expected, assuming zero within-study correlations (i.e. applying Reitsma's approach) is usually justified (Reitsma et al. 2005, Daniels and Hughes 1997, Korn et al. 2005, Thompson et al. 2005, Van Houwelingen et al. 2002).

Usage

```
riley(X, type="effect.size", optimization = "Nelder-Mead", control = list(), ...)
## Default S3 method:
riley(X, type="effect.size", optimization = "Nelder-Mead", control = list(), ...)
```

Arguments

X	data frame containing integer variables TP, FN, FP and TN (for diagnostic test accuracy data, cfr. rileyDA) or numeric variables Y1, vars1, Y2 and vars2 (for effect size data, cfr. rileyES).
type	a character string defining the type of data that is being summarized. Defaults to "effect.size" for summarizing effect sizes for which the normality assumption holds (for more details see rileyES). Diagnostic test accuracy data (i.e. sensitivities and specificities) can be pooled by choosing "test.accuracy" (for more details see rileyDA).
optimization	The optimization method that should be used for minimizing the negative (restricted) log-likelihood function. The default method is an implementation of that of Nelder and Mead (1965), that uses only function values and is robust but relatively slow. Other methods are described in optim.
control	A list of control parameters to pass to optim.
...	arguments to be passed on to other functions.

Details

Parameters are estimated by iteratively maximizing the restriced log-likelihood using the Newton-Raphson procedure. Algorithms for dealing with missing data are currently not implemented, but Bayesian approaches will become available in later versions.

Value

An object of the class `riley` for which many standard methods are available.

Author(s)

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References

Nelder JA, Mead R. A simplex algorithm for function minimization. *Computer Journal* (1965); **7**: 308–313.

Daniels MJ, Hughes MD. Meta-analysis for the evaluation of potential surrogate markers. *Statistics in Medicine* 1997; **16**: 1965–1982.

van Houwelingen HC, Arends LR, Stijnen T. Advanced methods in meta-analysis: multivariate approach and meta-regression. *Statistics in Medicine* 2002; **21**: 589–624.

Reitsma J, Glas A, Rutjes A, Scholten R, Bossuyt P, Zwinderman A. Bivariate analysis of sensitivity and specificity produces informative summary measures in diagnostic reviews. *Journal of Clinical Epidemiology* 2005; **58**: 982–990.

Korn EL, Albert PS, McShane LM. Assessing surrogates as trial endpoints using mixed models. *Statistics in Medicine* 2005; **24**: 163–182.

Thompson JR, Minelli C, Abrams KR, Tobin MD, Riley RD. Meta-analysis of genetic studies using mendelian randomization–a multivariate approach. *Statistics in Medicine* 2005; **24**: 2241–2254.

Riley RD, Thompson JR, Abrams KR. An alternative model for bivariate random-effects meta-analysis when the within-study correlations are unknown. *Biostatistics* 2008; **9**: 172–186.

See Also

`logLik.riley`, `plot.riley`, `predict.riley`, `rileyDA`, `rileyES`, `summary.riley`, `vcov.riley`

Examples

```
data(Scheidler)
data(Daniels)
data(Kertai)

#Meta-analysis of potential surrogate markers data
fit1 <- riley(Daniels) #Maxit reached, try again with more iterations
fit1 <- riley(Daniels,control=list(maxit=10000))
summary(fit1)

#Meta-analysis of prognostic test studies
fit2 <- riley(Kertai,type="test.accuracy")
```

```
summary(fit2)

#Meta-analysis of computed tomography data
ds <- Scheidler[which(Scheidler$modality==1),]
fit3 <- riley(ds,type="test.accuracy")
summary(fit3)
```

`rileyDA` *Fit the alternative model for bivariate random-effects meta-analysis (Riley)*

Description

This function fits the alternative model for bivariate random-effects meta-analysis on diagnostic test accuracy data when the within-study correlations are unknown assumed to be different from zero. A transformation is applied to the sensitivities ans false positive rates of each study, in order to meet the normality assumptions of the model.

Usage

```
rileyDA(X = NULL, TP, FN, FP, TN, correction = 0.5,
           correction.control = "all", optimization = "Nelder-Mead",
           control = list(), ...)
```

Arguments

`X`	any object that can be converted to a data frame with integer variables `TP`, `FN`, `FP` and `TN`.
`TP`	vector of integers representing the number of true positives, ignored if `X` is not `NULL`
`FN`	vector of integers representing the number of false negatives, ignored if `X` is not `NULL`
`FP`	vector of integers representing the number of false positives, ignored if `X` is not `NULL`
`TN`	vector of integers representing the number of true negatives, ignored if `X` is not `NULL`
`correction`	numeric, continuity correction applied if zero cells
`correction.control`	character, if set to `"all"` (the default) the continuity correction is added to the whole data if only one cell in one study is zero. If set to `"single"` the correction is only applied to rows of the data which have a zero.
`optimization`	The optimization method that should be used for minimizing the negative (restricted) log-likelihood function. The default method is an implementation of that of Nelder and Mead (1965), that uses only function values and is robust but relatively slow. Other methods are described in `optim`.
`control`	A list of control parameters to pass to `optim`.
`...`	arguments to be passed on to other functions, currently ignored

Details

The following parameters are estimated using rileyES: logit of sensitivity (beta1), logit of false positive rate (beta2), additional variation of beta1 beyond sampling error (psi1), additional variation of beta2 beyond sampling error (psi2) and a transformation of the correlation between psi1 and psi2 (rhoT). The original correlation is given as inv.logit(rhoT)*2-1. The results from a univariate random-effects meta-analysis with a method-of-moments estimator are used as starting values for beta1, beta2, psi1 and psi2 in the optim command. The starting value for rhoT is 0. Standard errors for all parameters are obtained from the inverse Hessian matrix.

Value

An object of the class riley for which many standard methods are available. A warning message is casted when the Hessian matrix contains negative eigenvalues, which implies that the identified solution is a saddle point and thus not optimal.

Author(s)

Thomas Debray <thomas.debray@gmail.com>

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rileyES *Fit the alternative model for bivariate random-effects meta-analysis (Riley)*

Description

This function fits the alternative model for bivariate random-effects meta-analysis on effect size data when the within-study correlations are unknown. This bivariate model was proposed by Riley et al. (2008) and is similar to the bivariate random-effects model from Reitsma et al. (2005), but includes an overall correlation parameter rather than separating the (usually unknown) within- and between-study correlation. As a consequence, the alternative model is not fully hierarchical, and estimates of additional variation beyond sampling error (psi) are not directly equivalent to the between-study variation (tau) from the general model. Furthermore, it has been argumented that assuming zero within-study correlations (i.e. applying Reitsma's approach) is reasonable when summarizing the sensitivities and false positive rates of a diagnostic test (Reitsma et al. 2005, Daniels and Hughes 1997, Korn et al. 2005, Thompson et al. 2005, Van Houwelingen et al. 2002). The alternative model for bivariate random-effects meta-analysis may, however, be useful when there is large within-study variability, few primary studies are available or the general model estimates the between-study correlation as 1 or -1.

Usage

```
rileyES(X = NULL, Y1, Y2, vars1, vars2, optimization = "Nelder-Mead",
           control = list(),...)
```

Arguments

X	any object that can be converted to a data frame with integer variables Y1, vars1, Y2 and vars2.
Y1	vector of numerics representing the effect sizes of outcome 1, ignored if X is not NULL
vars1	vector of numerics representing the error variances of Y1, ignored if X is not NULL
Y2	vector of numerics representing the effect sizes of outcome 2, ignored if X is not NULL
vars2	vector of numerics representing the error variances of Y2, ignored if X is not NULL
optimization	The optimization method that should be used for minimizing the negative (restricted) log-likelihood function. The default method is an implementation of that of Nelder and Mead (1965), that uses only function values and is robust but relatively slow. Other methods are described in optim.
control	A list of control parameters to pass to optim.
...	arguments to be passed on to other functions, currently ignored

Details

The following parameters are estimated by iteratively maximizing the restriced log-likelihood using the Newton-Raphson procedure: pooled effect size for outcome 1 (beta1), pooled effect size for outcome 2 (beta2), additional variation of beta1 beyond sampling error (psi1), additional variation of beta2 beyond sampling error (psi2) and a transformation of the correlation between psi1 and psi2 (rhoT). The original correlation is given as inv.logit(rhoT)*2-1. The results from a univariate random-effects meta-analysis with a method-of-moments estimator are used as starting values for beta1, beta2, psi1 and psi2 in the optim command. The starting value for rhoT is 0. Standard errors for all parameters are obtained from the inverse Hessian matrix.

Value

An object of the class riley for which many standard methods are available. A warning message is casted when the Hessian matrix contains negative eigenvalues, which implies that the identified solution is a saddle point and thus not optimal.

Author(s)

Thomas Debray <thomas.debray@gmail.com>

References

Nelder JA, Mead R. A simplex algorithm for function minimization. *Computer Journal* (1965); **7**: 308–313.

Daniels MJ, Hughes MD. Meta-analysis for the evaluation of potential surrogate markers. *Statistics in Medicine* 1997; **16**: 1965–1982.

van Houwelingen HC, Arends LR, Stijnen T. Advanced methods in meta-analysis: multivariate approach and meta-regression. *Statistics in Medicine* 2002; **21**: 589–624.

Reitsma J, Glas A, Rutjes A, Scholten R, Bossuyt P, Zwinderman A. Bivariate analysis of sensitivity and specificity produces informative summary measures in diagnostic reviews. *Journal of Clinical Epidemiology* 2005; **58**: 982–990.

Korn EL, Albert PS, McShane LM. Assessing surrogates as trial endpoints using mixed models. *Statistics in Medicine* 2005; **24**: 163–182.

Thompson JR, Minelli C, Abrams KR, Tobin MD, Riley RD. Meta-analysis of genetic studies using mendelian randomization–a multivariate approach. *Statistics in Medicine* 2005; **24**: 2241–2254.

Riley RD, Thompson JR, Abrams KR. An alternative model for bivariate random-effects meta-analysis when the within-study correlations are unknown. *Biostatistics* 2008; **9**: 172–186.

`Roberts` *Roberts data*

Description

Data frame with summary data from 14 comparative studies.

Usage

```
data("Roberts")
```

Format

One data frame with 2 variables.

SDM Effect sizes (standardized differences in means)

SE Standard error of the effect sizes

Details

The `Roberts` data set is a meta-analysis of 14 studies comparing 'set shifting' ability (the ability to move back and forth between different tasks) in people with eating disorders and healthy controls.

Source

Roberts ME, Tchanturia K, Stahl D, Southgate L, Treasure J. A systematic review and meta-analysis of set-shifting ability in eating disorders. *Psychological Medicine* 2007, **37**: 1075–1084.

Higgins JPT, Thompson SG, Spiegelhalter DJ. A re-evaluation of random-effects meta-analysis. *Journal of the Royal Statistical Society. Series A (Statistics in Society)* 2009, **172**: 137–159.

`Scheidler` *Diagnostic accuracy data*

Description

Data frame with diagnostic accuracy data from three imaging techniques for the diagnosis of lymph node metastasis in women with cervical cancer.

Usage

```
data("Scheidler")
```

Format

One data frame with 6 variables.

author string . author of article

modality integer . type of test (1=CT, 2=LAG, 3=MRI)

TP integer. number of true positives

FN integer. number of false negatives

FP integer. number of false positives

TN integer. number of true negatives

Details

The `Scheidler` data comprises the results from a meta-analysis where three imaging techniques for the diagnosis of lymph node metastasis in women with cervical cancer are compared. Forty-four studies in total were included: 17 studies evaluated lymphangiography, another 17 studies examined computed tomography and the remaining 10 studies focused on magnetic resonance imaging. Diagnosis of metastatic disease by lymphangiography (LAG) is based on the presence of nodal-filling defects, whereas computed tomography (CT) and magnetic resonance imaging (MRI) rely on nodal enlargement.

Source

Scheidler J, Hricak H, Yu KK, Subak L, Segal MR. Radiological evaluation of lymph node metastases in patients with cervical cancer. A meta-analysis. *Journal of the American Medical Association* 1997; **278**: 1096–1101.

Reitsma J, Glas A, Rutjes A, Scholten R, Bossuyt P, Zwinderman A. Bivariate analysis of sensitivity and specificity produces informative summary measures in diagnostic reviews. *Journal of Clinical Epidemiology* 2005; **58**: 982–990.

`summary.riley` *Parameter summaries*

Description

Provides the summary estimtes of the alternative model for bivariate random-effects meta-analysis by Riley et al. (2008) with their corresponding confidence intervals. The model parameters are given as `beta1`, `beta2`, `psi1`, `psi2` and `rho`. Confidence intervals are derived from the inverse Hessian.

Usage

```
## S3 method for class 'riley'
summary(object, level = 0.95, ...)
```

Arguments

`object`	a `riley` object
`level`	numeric, the level for calculations of confidence intervals
`...`	arguments to be passed on to other functions

Details

For diagnostic test accuracy data, `beta1` equals the logit sensitivity (Sens) and `beta2` equals the logit false positive rate (FPR). The summary sensitivity and FPR are added for completeness.

Value

array with confidence intervals for the estimated model parameters. For diagnostic test accuracy data, the resulting summary sensitivity and false positive rate are included.

Author(s)

Thomas Debray <thomas.debray@gmail.com>

References

Riley RD, Thompson JR, Abrams KR. An alternative model for bivariate random-effects meta-analysis when the within-study correlations are unknown. *Biostatistics* 2008; **9**: 172–186.

See Also

`riley` `plot.riley`

summary.uvmeta *Parameter summaries*

Description

This function provides summary estimates of a univariate meta-analysis model.

Usage

```
 ## S3 method for class 'uvmeta'
summary(object, ...)
```

Arguments

object	a uvmeta object.
...	arguments to be passed on to other functions

Value

The model parameters are given as mu (overall treatment effect),tausq (between-study variance if random effects were assumed), Q (Cochran's Q statistic) and Isq (I-square index).

Note

There are no confidence intervals for tausq when estimated with a frequentistic approach, as it is considered fixed.

Author(s)

Thomas Debray <thomas.debray@gmail.com>

References

DerSimonian R, Laird N. Meta-analysis in clinical trials. *Controlled Clinical Trials* 1986; **7**: 177–188.

Biggerstaff BJ, Tweedie RL. Incorporating variability in estimates of heterogeneity in the random effects model in meta-analysis. *Statistics in Medicine* 1997; **16**: 753–768.

Higgins JPT, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Statistics in Medicine* 2002; **21**: 1539–1558.

Borenstein M, Hedges LV, Higgins JPT, Rothstein HR. A basic introduction to fixed-effect and random-effects models for meta-analysis. *Research Synthesis Methods* 2010; **1**: 97–111.

Riley RD, Higgins JPT, Deeks JJ. Interpretation of random effects meta-analyses. *British Medical Journal* 2011; **342**: d549.

See Also

uvmeta

uvmeta *Univariate meta-analysis.*

Description

This function performs a univariate meta-analysis by assuming fixed or random effects. Whereas the fixed effects model assumes that all studies in the analysis share a common effect size, the random-effects model allows different study-specific effect sizes. Concretely, if we move from fixed-effect weights to random-effects weights, large studies lose influence and small studies gain influence (Borenstein 2010).

Usage

```
uvmeta(r, vars, model="random", method="MOM", labels, na.action, pars,
       verbose=FALSE, ...)
```

Arguments

r	vector of numerics containing the effect sizes
vars	vector of numerics containing the error variance of the effect sizes
model	Assume "random" or "fixed" effects.
method	Estimation method: use "MOM" to implement the non-parametric method-of-moment estimator from DerSimonian and Laird, "ml" to implement the maximum-likelihood estimator, "pl" to use the profile-likelihood estimator or "bayes" to implement a Bayesian meta-analysis assuming normality of the random effects (Higgins 2009).
labels	vector of characters containing the labels for the studies
na.action	a function which indicates what should happen when the data contain NAs. Defaults to "na.fail", other options are "na.omit", "na.exclude" or "na.pass".
pars	A list with additional arguments. Use "level" to specify the level of confidence or credibility intervals. The following parameters configure the MCMC sampling procedure and are ignored if `method="MOM"`: `hp.mu.mean` (Hyperparameter: mean of the prior distribution of the fixed/random effects model, defaults to zero), `hp.mu.var` (Hyperparameter: variance of the prior distribution of the fixed/random effects model, defaults to 1000), `n.chains` (specifies the number of parallel chains), `n.adapt` (specifies the number of iterations for adaptation), `n.init` (number of iterations to run for initializing the Markov chain) and `n.iter` (number of iterations to monitor).
verbose	if TRUE then messages generated during the fitting process will be displayed.
...	arguments to be passed on to other functions

Details

The Bayesian approach uses an uninformative Normal prior for the mean and an uninformative uniform prior for the variance of the pooled effect size (Higgins 2009). For random effects models, a prediction interval for the pooled effect size is displayed. This interval predicts in what range future effect sizes will fall given what has already been observed (Higgins 2009, Riley 2011).

Value

An object of the class `uvmeta` for which many standard methods are available.

Author(s)

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References

Biggerstaff BJ, Tweedie RL. Incorporating variability in estimates of heterogeneity in the random effects model in meta-analysis. *Statistics in Medicine* 1997; **16**: 753–768.

Borenstein M, Hedges LV, Higgins JPT, Rothstein HR. A basic introduction to fixed-effect and random-effects models for meta-analysis. *Research Synthesis Methods* 2010; **1**: 97–111.

DerSimonian R, Laird N. Meta-analysis in clinical trials. *Controlled Clinical Trials* 1986; **7**: 177–188.

Gasparrini A, Armstrong B, Kenward, MG. Multivariate meta-analysis for non-linear and other multi-parameter associations. *Statistics in Medicine* 2012; **31**: 3821–3839.

Graham PL, Moran JL. Robust meta-analytic conclusions mandate the provision of prediction intervals in meta-analysis summaries. *Journal of Clinical Epidemiology* 2012; **65**: 503–510.

Higgins JPT, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Statistics in Medicine* 2002; **21**: 1539–1558.

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Rucker G, Schwarzer G, Carpenter JR, Schumacher M . Undue reliance on I2 in assessing heterogeneity may mislead. *BMC Medical Research Methodology* 2008; **8**: 79.

See Also

`uvmeta-class`

Examples

```
data(Roberts)

#Extract effect size and error variance
r <- Roberts$SDM
vars <- Roberts$SE**2
```

```
#Frequentist random-effects meta-analysis
fit1 <- uvmeta(r,vars,labels=rownames(Roberts))
plot(fit1, main="Forest plot") #show a forest plot
fit1


#Bayesian random-effects meta-analysis
#fit2 <- uvmeta(r,vars,method="bayes")
#fit2
```

---

uvmeta-class *Class "uvmeta". Result of a univariate meta-analysis.*

Description

This class encapsulates results of a univariate meta-analysis.

Objects from the Class

Objects can be created by calls of the form uvmeta.

Slots

call: (language) The call to uvmeta.

data: (data frame) The data used for the meta-analysis.

results: (data frame) Contains the pooled effect size (mu), the between-study variability (tausq), Cochran's Q statistic (Q) and Higgins' and Thompson's I square statistic (Isq). For each estimate, error variances are provided with predefined confidence (method="MOM") or credibility (method="bayes") intervals.

model: (character) The meta-analysis model used.

method: (character) The estimator used.

na.action: (character) Information from the action which was applied to object if NAs were handled specially, or NULL.

df: (numeric) Degrees of freedom.

numstudies: (numeric) The amount of studies used in the meta-analysis.

pred.int: (data frame) A prediction interval, predicting in what range future effect sizes will fall given what has already been observed (based on a Student's t-distribution, cfr. Riley 2011)

formula: (character) If a formula was specified, a character vector giving the formula and parameter specifications.

Methods

print signature(object = "uvmeta"): Print object summary.

forest signature(object = "uvmeta"): Plot a forest plot with the summary estimate.

summary signature(object = "uvmeta"): Generate object summary.

Examples

```
data(Collins)

#Extract effect size and error variance
r <- Collins$logOR
vars <- Collins$SE**2

#Frequentist random-effects meta-analysis
fit1 <- uvmeta(r,vars)

#Extract results
fit1$results
```

`vcov.riley` *Calculate Variance-Covariance Matrix for a Fitted Riley Model Object*

Description

Returns the variance-covariance matrix of the main parameters of a fitted model object.

Usage

```
## S3 method for class 'riley'
vcov(object, ...)
```

Arguments

`object`	a `riley` object.
`...`	arguments to be passed on to other functions

Details

The variance-covariance matrix is obtained from the inverse Hessian as provided by `optim`.

Value

A matrix of the estimated covariances between the parameter estimates in the Riley model: logit of sensitivity (`mu1`), logit of false positive rate (`mu2`), additional variation of `mu1` beyond sampling error (`psi1`), additional variation of `mu2` beyond sampling error (`psi2`) and a transformation of the correlation between `psi1` and `psi2` (`rhoT`). The original correlation is given as `inv.logit(rhoT)*2-1`.

Note

A warning message is casted when the Hessian matrix contains negative eigenvalues. This implies that the identified minimum for the (restricted) negative log-likelihood is a saddle point, and that the solution is therefore not optimal.

Author(s)

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References

Riley, RD., Thompson, JR., & Abrams, KR. (2008). "An alternative model for bivariate random-effects meta-analysis when the within-study correlations are unknown." *Biostatistics*, **9**, 172–186.

See Also

riley

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