Package ‘metamisc’

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Description This package provides functions for diagnostic and
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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.

Details

Package: metamisc
Type: Package
Version: 0.1.1
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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 \texttt{uvmeta}) and bivariate (with \texttt{riley}) summary data using frequentist and Bayesian approaches.

Author(s)

Thomas Debray <thomas.debray@gmail.com>

References


**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**

```r
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**


**Examples**

```r
data(Collins)
```
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


inv.logit

**Apply the inverse logit transformation**

### 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


---

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

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
```r
## S3 method for class 'riley'
plot(xL 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

See Also
riley
predict.riley

Examples

data(Scheidler)

d1 <- Scheidler[which(Scheidler$modality==1),]
d2 <- Scheidler[which(Scheidler$modality==2),]
d3 <- 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>
**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

```r
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 restricted 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)
Thomas Debray <thomas.debray@gmail.com>

References

See Also
$logLik.riley$, plot.riley, predict.riley, rileyDA, rileyES, summary.riley, vcov.riley

Examples
```r
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")
```
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 (\(beta_1\)), logit of false positive rate (\(beta_2\)), additional variation of \(beta_1\) beyond sampling error (\(psi_1\)), additional variation of \(beta_2\) beyond sampling error (\(psi_2\)) and a transformation of the correlation between \(psi_1\) and \(psi_2\) (\(rho_T\)). The original correlation is given as \(\text{inv.logit}(rhot_I \times RMQ)\). The results from a univariate random-effects meta-analysis with a method-of-moments estimator are used as starting values for \(beta_1\), \(beta_2\), \(psi_1\) and \(psi_2\) 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>

Usage

```r
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 restricted 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(rhotI*RMQ)`. 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


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**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**


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

Parameter summaries

Description

Provides the summary estimates 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

```r
## 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


See Also

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

Usage

```r
## 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 `I^2` (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


See Also

`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)

Thomas Debray <thomas.debray@gmail.com>

References


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.


See Also

`uvmeta-class`

Examples

```r
data(Roberts)

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

#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`
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)

Thomas Debray <thomas.debray@gmail.com>

References


See Also

riley
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