Package 'metamisc'

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Description Meta-analysis of diagnostic and prognostic modeling studies. Summarize estimates of diagnostic test accuracy and prediction model performance. Validate, update and combine published prediction models.

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`metamisc-package` *Diagnostic and Prognostic Meta-Analysis*

Description

Meta-analysis of diagnostic and prognostic modeling studies. Summarize estimates of diagnostic test accuracy and prediction model performance. Validate, update and combine published prediction models.

Details

The following functionality is currently implemented: univariate meta-analysis of summary data (`uvmeta`), bivariate meta-analysis of correlated outcomes (`riley`), bivariate meta-analysis of diagnostic test accuracy data, meta-analysis of prediction model performance (`valmeta`).

Author(s)

Thomas Debray <thomas.debray@gmail.com> Valentijn de Jong

References

Debray TPA, Damen JAAG, Snell KIE, Ensor J, Hooft L, Reitsma JB, et al. A guide to systematic review and meta-analysis of prediction model performance. *BMJ*. 2017; **356**:i6460.

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.

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.

`DVTipd` *Hypothetical dataset for diagnosis of Deep Vein Thrombosis (DVT)*

Description

A hypothetical dataset with 500 subjects suspected of having deep vein thrombosis (DVT).

Usage

```
data(DVTipd)
```

Format

A data frame with 500 observations of 15 variables.

`sex` gender (0=female, 1=male)

`malign` active malignancy (0=no active malignancy, 1=active malignancy)

`par` paresis (0=no paresis, 1=paresis)

`surg` recent surgery or bedridden

`tend` tenderness venous system

`oachst` oral contraceptives or hst

`leg` entire leg swollen

`notraum` absence of leg trauma

`calfdif3` calf difference >= 3 cm

`pit` pitting edema

`vein` vein distension

`altdiagn` alternative diagnosis present

`histdvt` history of previous DVT

`ddimdich` dichotimized D-dimer value

`dvt` final diagnosis of DVT

Details

Hypothetical dataset derived from the Individual Participant Data Meta-Analysis from Geersing *et al* (2014). The dataset consists of consecutive outpatients with suspected deep vein thrombosis, with documented information on the presence or absence of proximal deep vein thrombosis (`dvt`) by an acceptable reference test. Acceptable such tests were either compression ultrasonography or venography at initial presentation, or, if venous imaging was not performed, an uneventful follow-up for at least three months.

Source

Geersing GJ, Zuithoff NPA, Kearon C, Anderson DR, Ten Cate-Hoek AJ, Elf JL, et al. Exclusion of deep vein thrombosis using the Wells rule in clinically important subgroups: individual patient data meta-analysis. *BMJ*. 2014;348:g1340.

Examples

```
data(DVTipd)
str(DVTipd)
summary(apply(DVTipd,2,as.factor))

## Develop a prediction model to predict presence of DVT
model.dvt <- glm("dvt~sex+oachst+malign+surg+notraum+vein+calfdif3+ddimdich",
                 family=binomial, data=DVTipd)
summary(model.dvt)
```

`DVTmodels` *Risk prediction models for diagnosing Deep Venous Thrombosis (DVT)*

Description

Previously published prediction models for predicting the presence of DVT.

Usage

```
data(DVTmodels)
```

Format

An object of the class `litmodels` with the following information for each literature model: the study-level descriptives (`"descriptives"`), the regression coefficient or weight for each predictor (`"weights"`) and the error variance for each regression coefficient or weight (`"weights.var"`).

Details

Previously, several models (Gagne, Oudega) and score charts (Wells, modified Wells, and Hamilton) have been published for evaluating the presence of DVT in suspected patients. These models combine information on mulitple predictors into a weighted sum, that can subsequently be used to obtain estimates of absolute risk. See `DVTipd` for more information on the predictors.

Source

Wells PS, Anderson DR, Bormanis J, Guy F, Mitchell M, Gray L, Clement C, Robinson KS, Lewandowski B. Value of assessment of pretest probability of deep-vein thrombosis in clinical management. *Lancet* 1997; **350**(9094):1795–1798. DOI: 10.1016/S0140-6736(97)08140-3.

Wells PS, Anderson DR, Rodger M, Forgie M, Kearon C, Dreyer J, Kovacs G, Mitchell M, Lewandowski B, Kovacs MJ. Evaluation of D-dimer in the diagnosis of suspected deep-vein thrombosis. *The New England Journal of Medicine* 2003; **349**(13):1227–1235. DOI: 10.1056/NEJMoa023153.

Gagne P, Simon L, Le Pape F, Bressollette L, Mottier D, Le Gal G. Clinical prediction rule for diagnosing deep vein thrombosis in primary care. *La Presse Medicale* 2009; **38**(4):525–533. DOI: 10.1016/j.lpm.2008.09.022.

Subramaniam RM, Snyder B, Heath R, Tawse F, Sleigh J. Diagnosis of lower limb deep venous thrombosis in emergency department patients: performance of Hamilton and modified Wells scores. *Annals of Emergency Medicine* 2006; **48**(6):678–685. DOI: 10.1016/j.annemergmed.2006.04.010.

Oudega R, Moons KGM, Hoes AW. Ruling out deep venous thrombosis in primary care. a simple diagnostic algorithm including D-dimer testing. *Thrombosis and Haemostasis* 2005; **94**(1):200–205. DOI: 10.1160/TH04-12-0829.

References

Debray TPA, Koffijberg H, Nieboer D, Vergouwe Y, Steyerberg EW, Moons KGM. Meta-analysis and aggregation of multiple published prediction models. *Stat Med*. 2014 Jun 30;33(14):2341–62.

Debray TPA, Koffijberg H, Vergouwe Y, Moons KGM, Steyerberg EW. Aggregating published prediction models with individual participant data: a comparison of different approaches. *Stat Med*. 2012 Oct 15;31(23):2697–712.

See Also

`DVTipd`

Examples

```
data(DVTmodels)
```

EuroSCORE *Predictive performance of EuroSCORE II*

Description

This data set contains estimates on the predictive performance of the European system for cardiac operative risk evaluation (EuroSCORE II) in patients undergoing cardiac surgery. Results are based on the original development study and 22 validations identified by Guida *et al*.

Usage

```
data("EuroSCORE")
```

Format

A data frame with 23 observations on the following 13 variables.

`Study` a vector with the first author of each validation study

`n` a numeric vector with the total number of patients on which performance estimates are based

`n.events` a numeric vector with the total number of observed events

`c.index` a numeric vector with the estimated concordance statistic of each validation

`se.c.index` a numeric vector with the standard error of the concordance statistics

`c.index.95CIl` a numeric vector with the lower bound of the 95% confidence interval of the estimated concordance statistics

`c.index.95CIu` a numeric vector with the upper bound of the 95% confidence interval of the estimated concordance statistics

`Po` a numeric vector with the overall observed event probability of each validation

`Pe` a numeric vector with the overall expected event probability of each validation

`SD.Pe` a numeric vector with the standard error of `Pe`

`e.events` a numeric vector with the total number of expected events in each validation

`multicentre` a logical vector describing whether the study was a multicentre study

`mean.age` a numeric vector describing the mean age of the patients

`sd.age` a numeric vector with the spread of the age of the patients

`pts.before.2010` a logical vector describing whether studies included patients before 2010 (i.e., before EuroSCORE II was developed)

Details

Published in 2012, EuroSCORE II was developed using logistic regression in a dataset comprising 16,828 adult patients undergoing major cardiac surgery from 154 hospitals in 43 countries over a 12-week period (May-July) in 2010. EuroSCORE II was developed to predict in-hospital mortality for patients undergoing any type of cardiac surgery. In 2014, a systematic review of published evidence on the performance value of the euroSCORE II was undertaken by Guida *et al*. Twenty-two validations, including more 145,592 patients from 21 external validation articles (one study included two validations) and a split-sample validation contained within original development article were included in the review; 23 validation studies in total.

Source

Guida P, Mastro F, Scrascia G, Whitlock R, Paparella D. Performance of the European System for Cardiac Operative Risk Evaluation II: a meta-analysis of 22 studies involving 145,592 cardiac surgery procedures. *J Thorac Cardiovasc Surg*. 2014; **148**(6):3049–3057.e1.

Nashef SAM, Roques F, Sharples LD, Nilsson J, Smith C, Goldstone AR, et al. EuroSCORE II. *Eur J Cardiothorac Surg*. 2012; **41**(4):734-744; discussion 744-745.

Examples

```
data(EuroSCORE)
```

`Framingham` *Predictive performance of the Framingham Risk Score in male populations*

Description

This data set contains estimates on the performance of the Framingham model for predicting coronary heart disease in male populations (Wilson 1998). Results are based on the original development study and 20 validations identified by Damen *et al*.

Usage

```
data("Framingham")
```

Format

A data frame with 24 observations on the following 19 variables.

`AuthorYear` a vector describing the study authors

`n` a numeric vector with the total number of patients on which performance estimates are based

`n.events` a numeric vector with the total number of observed events

`c.index` a numeric vector with the estimated concordance statistic of each validation

`se.c.index` a numeric vector with the standard error of the concordance statistics

`c.index.95CIl` a numeric vector with the lower bound of the 95% confidence interval of the estimated concordance statistics

`c.index.95CIu` a numeric vector with the upper bound of the 95% confidence interval of the estimated concordance statistics

`Po` a numeric vector with the overall observed event probability of each validation

`Pe` a numeric vector with the overall expected event probability of each validation

`t.val` a numeric vector describing the time period in which predictive performance was assessed for each validation

`mean_age` a numeric vector describing the mean age of the patients

`sd_age` a numeric vector with the spread of the age of the patients

`mean_SBP` a numeric vector with the mean systolic blood pressure in the validation studies (mm Hg)

`sd_SBP` a numeric vector with the spread of systolic blood pressure in the validation studies

`mean_total_cholesterol` a numeric vector with the mean total cholesterol in the validation studies (mg/dL)

`sd_total_cholesterol` a numeric vector with the spread of total cholesterol in the validation studies

`mean_hdl_cholesterol` a numeric vector with the mean high-density lipoprotein cholesterol in the validation studies (mg/dL)

`sd_hdl_cholesterol` a numeric vector with the spread of high-density lipoprotein cholesterol in the validation studies

`pct_smoker` a numeric vector with the percentage smokers in the validation studies

Details

The Framingham Risk Score allows physicians to predict 10-year coronary heart disease (CHD) risk in patients without overt CHD. It was developed in 1998 from a middle-aged white population sample, and has subsequently been validated across different populations. The current dataset contains the original (internal validation) results, as well as 23 external validations which were identified through a systematic review. In this review, studies were eligible for inclusion if they described the validation of the original Framingham model and assessed its performance for fatal or nonfatal CHD in males from a general population setting.

Source

Damen JAAG, Hooft L, Schuit E, Debray TPA, Collins GS, Tzoulaki I, et al. Prediction models for cardiovascular disease risk in the general population: systematic review. *BMJ*. 2016;i2416.

Wilson PW, D'Agostino RB, Levy D, Belanger AM, Silbershatz H, Kannel WB. Prediction of coronary heart disease using risk factor categories. *Circulation*. 1998; **97**(18):1837–47.

Examples

```
data(Framingham)
```

---

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
```

`plot.valmeta` *Forest Plots*

Description

Function to create forest plots for objects of class `"valmeta"`.

Usage

```
## S3 method for class 'valmeta'
plot(x, ...)
```

Arguments

`x`	an object of class `"valmeta"`
`...`	Additional arguments which are passed to `forest` from the package `metafor`.

Details

Plots are generated using functionalities provided by the `metafor` pacakge. The forest plot shows the performance estimates of each validation with corresponding confidence intervals. A polygon is added to the bottom of the forest plot, showing the summary estimate based on the model (with the outer edges of the polygon indicating the confidence interval limits). A 95% prediction interval is added by default, the dotted line indicates its (approximate) bounds.

Note

As indicated by `metafor`, the labels, annotations, and symbols may become quite small and impossible to read when the number of studies is quite large. Stretching the plot window vertically may then provide a more readable figure (one should call the function again after adjusting the window size, so that the label/symbol sizes can be properly adjusted). Also, the `cex`, `cex.lab`, and `cex.axis` arguments are then useful to adjust the symbol and text sizes.

Author(s)

Thomas Debray <thomas.debray@gmail.com>

References

Debray TPA, Damen JAAG, Snell KIE, Ensor J, Hooft L, Reitsma JB, et al. A guide to systematic review and meta-analysis of prediction model performance. *BMJ*. 2017;356:i6460.

Lewis S, Clarke M. Forest plots: trying to see the wood and the trees. *BMJ*. 2001; 322(7300):1479–80.

Riley RD, Higgins JPT, Deeks JJ. Interpretation of random effects meta-analyses. *BMJ*. 2011 342:d549–d549.

Viechtbauer W. Conducting Meta-Analyses in R with the metafor Package. *Journal of Statistical Software*. 2010; 36(3). Available from: http://www.jstatsoft.org/v36/i03/

Examples

```
data(EuroSCORE)
attach(EuroSCORE)

fit <- valmeta(cstat=c.index, cstat.se=se.c.index,
               cstat.95CI=cbind(c.index.95CIl,c.index.95CIu),
               N=n, O=n.events)
plot(fit)

detach(EuroSCORE)
```

`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`

`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)

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.

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>

`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)

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References

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

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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.

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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

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)

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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, r.se, method="REML", test="knha", labels, na.action, n.chains=4, pars,
       verbose=FALSE, ...)
```

Arguments

r	vector of numerics containing the effect sizes
r.se	vector of numerics containing the standard error of the effect sizes
method	character string specifying whether a fixed- or a random-effects model should be fitted. A fixed-effects model is fitted when using method="FE". Random-effects models are fitted by setting method equal to one of the following: "REML" (Default), "DL", "HE", "SJ", "ML", "EB", "HS", "GENQ" or "BAYES". See 'Details'.
test	character string specifying how test statistics and confidence intervals for the fixed effects should be computed. By default (test="knha"), the method by Knapp and Hartung (2003) is used for adjusting test statistics and confidence intervals. Type '?rma' for more details.
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".
n.chains	the number of chains to use in the Gibbs sampler (method="BAYES"). More chains will improve the sensitivity of the convergence diagnostic, but will cause the simulation to run more slowly. The default number of chains is 4.
pars	A list with additional arguments. The following parameters configure the MCMC sampling procedure: 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)
verbose	if TRUE then messages generated during the fitting process will be displayed.
...	Additional arguments that are passed to **rma** or **runjags** (if method="BAYES").

Details

Unless specified otherwise, all meta-analysis models assume random effects and are fitted using restricted maximum likelihood estimation with the **metafor** package (Viechtbauer 2010). Further, confidence intervals for the average performance are based on the Hartung-Knapp-Sidik-Jonkman method, to better account for the uncertainty in the estimated between-study heterogeneity (Debray 2016). A Bayesian meta-analysis can be performed by specifying `method="BAYES"`. In that case, the R packages **runjags** and **rjags** must be installed.

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).

Bayesian meta-analysis models

For Bayesian meta-analysis models that involve the Gibbs sampler (`method="BAYES"`), the R packages `runjags` and `rjags` must be installed. The Bayesian approach uses an uninformative Normal prior for the mean and a uniform prior for the between-study variance of the pooled effect size (Higgins 2009). By default, the Normal prior has a mean of 0 and a variance of 1000. These hyperparameters can, however, be altered through the variables `hp.mu.mean` and `hp.mu.var` in the argument `pars`. The prior distribution of the between-study standard deviation is given by a uniform distribution, bounded between 0 and 100. Future versions of `metamisc` will allow to alter these boundaries.

Value

An object of the class `uvmeta` for which many standard methods are available. If `method="BAYES"`, the results contain an object of the class `runjags`.

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.

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.

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.

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Viechtbauer W. Conducting Meta-Analyses in R with the metafor Package. *Journal of Statistical Software*. 2010; 36(3). Available from: http://www.jstatsoft.org/v36/i03/

See Also

uvmeta-class

Examples

```
data(Roberts)

# Frequentist random-effects meta-analysis
fit1 <- with(Roberts, uvmeta(r=SDM, r.se=SE, labels=rownames(Roberts)))
summary(fit1)
plot(fit1, main="Forest plot") #show a forest plot
fit1

## Not run:
# Bayesian random effects meta-analysis
fit2 <- with(Roberts, uvmeta(r=SDM, r.se=SE, labels=rownames(Roberts), method="BAYES"))
plot(fit2)

## End(Not run)
```

---

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
```

---

valmeta *Meta-analysis of prediction model performance*

Description

This function allows to meta-analyze the performance of a prediction model, and to obtain summary estimates of the concordance statistic, the total observed-expected ratio and the calibration slope. Where appropriate, data transformations are applied and missing information is derived from available quantities.

Usage

```
valmeta(measure="cstat", cstat, cstat.se, cstat.95CI, OE, OE.se, OE.95CI, citl, citl.se,
        N, O, E, Po, Po.se, Pe, t.val, t.ma, t.extrapolate=FALSE, method="REML",
         test="knha", verbose=FALSE, slab, n.chains=4, pars, ...)
```

Arguments

measure	a character string indicating which performance measure should be calculated. See 'Details' for possible options and how the data should be specified.
cstat	vector with the estimated c-statistic for each valiation
cstat.se	vector with the standard error of the estimated c-statistics
cstat.95CI	2-dimensional array with the lower (first column) and upper (second column) boundary of the 95% confidence interval of the estimated c-statistics
OE	vector with the estimated ratio of total observed versus total expected events
OE.se	vector with the standard error of the estimated O:E ratios
OE.95CI	2-dimensional array with the lower (first column) and upper (second column) boundary of the 95% confidence interval of the total O:E ratio
citl	vector with the estimated calibration-in-the-large for each valiation
citl.se	vector with the standard error of the estimated calibration-in-the-large statistics
N	vector with the total number of participants for each valiation.
O	vector with the total number of observed events for each valiation.
E	vector with the total number of expected events for each valiation
Po	vector with the (cumulative) observed event probability for each valiation
Po.se	vector with the standard errors of Po. Note that when Po is derived from Kaplan-Meier estimates, Po.se is equal to the standard error of the (cumulative) observed survival probability.
Pe	vector with the (cumulative) expected event probability for each validation
t.val	optional vector for prognostic models, containing the time period for which performance was assessed
t.ma	optional numeric value for prognostic models, containing the time period of primary interest for meta-analysis
t.extrapolate	logical indicating whether calibration performance of the prognostic model should be extrapolated to time t.ma
method	character string specifying whether a fixed- or a random-effects model should be fitted. A fixed-effects model is fitted when using method="FE". Random-effects models are fitted by setting method equal to one of the following: "REML" (Default), "DL", "HE", "SJ", "ML", "EB", "HS", "GENQ" or "BAYES". See 'Details'.
test	character string specifying how test statistics and confidence intervals for the fixed effects should be computed. By default (test="knha"), the method by Knapp and Hartung (2003) is used for adjusting test statistics and confidence intervals. Type '?rma' for more details.
verbose	if TRUE then messages generated during the fitting process will be displayed.
slab	optional vector with labels for the k studies.
n.chains	the number of chains to use in the Gibbs sampler (method="BAYES"). More chains will improve the sensitivity of the convergence diagnostic, but will cause the simulation to run more slowly. The default number of chains is 4.

pars — A list with additional arguments. The following parameters configure the MCMC sampling procedure: hp.mu.mean (mean of the prior distribution of the random effects model, defaults to 0), hp.mu.var (variance of the prior distribution of the random effects model, defaults to 1E6), hp.tau.min (minimum value for the between-study standard deviation, defaults to 0), hp.tau.max (maximum value for the between-study standard deviation, defaults to 2), hp.tau.sigma (standard deviation of the prior distribution for the between-study standard-deviation), hp.tau.dist (prior distribution for the between-study standard-deviation. Defaults to "dunif"), hp.tau.df (degrees of freedom for the prior distribution for the between-study standard-deviation. Defaults to 3), method.restore.c.se (method for restoring missing estimates for the standard error of the c-statistic. So far, only "Newcombe.2" and "Newcombe.4" are supported. These methods have been described by Newcombe in 2006.), model.cstat (The likelihood/link for modeling the c-statistic; see "Details"), model.oe (The likelihood/link for modeling the O:E ratio; see "Details")

... — Additional arguments that are passed to **rma** or **runjags** (if method="BAYES").

Details

Unless specified otherwise, all meta-analysis models assume random effects and are fitted using restricted maximum likelihood estimation with the **metafor** package (Viechtbauer 2010). Further, confidence intervals for the average performance are based on the Hartung-Knapp-Sidik-Jonkman method, to better account for the uncertainty in the estimated between-study heterogeneity (Debray 2016). A Bayesian meta-analysis can be performed by specifying method="BAYES". In that case, the R packages **runjags** and **rjags** must be installed.

Performance measures: The measure argument is a character string specifying which performance measure should be calculated and meta-analyzed. The options for the measure argument are as follows:

- "cstat" for meta-analysis of the concordance statistic
- "OE" for meta-analysis of the total observed-expected ratio

Meta-analysis of the concordance statistic (c-statistic):

The c-statistic is a measure of discrimination, and indicates the ability of a prediction model to distinguish between patients developing and not developing the outcome. The c-statistic typically ranges from 0.5 (no discriminative ability) to 1 (perfect discriminative ability). A meta-analysis for the c-statistic will be performed if the c-statistics (cstat) and their respective standard errors (cstat.se) are defined. For studies where the standard error is unknown, it can be derived from the 95% confidence interval, or from cstat, O and N (Newcombe 2006). By default, the meta-analysis model assumes Normality for the logit of the c-statistic (model.cstat = "normal/logit"). Alternatively, it is possible to summarize raw estimates of the c-statistic by setting model.cstat = "normal/identity".

Meta-analysis of the total observed versus expected ratio (O:E ratio):

The total O:E ratio provides a rough indication of the overall model calibration (across the entire range of predicted risks). Currently, three methods have been implemented to obtain a summary estimate of the total O:E ratio. By default, the meta-analysis model assumes Normality for the (natural) logarithm of the O:E ratios (model.oe = "normal/log"). Continuity corrections are applied when necessary by adding 0.5 to O, E and N. Alternatively, it is possible to model the

total number of observed and expected events using a Poisson likelihood (Stijnen 2010). The resulting model does not require continuity corrections for O and can be implemented by setting model.oe = "poisson/log" (note that hp.mu.var is truncated to a maximum value of 100 for method="BAYES"). Finally, it is possible to summarize raw estimates of the O:E ratio by setting model.oe = "normal/identity".

When unkown, the standard error of the O:E ratio will be approximated in the following order from (1) the 95% confidence interval, (2) the standard error of Po, (3) the error variance of the binomial distribution, (4) the error variance of the Poisson distribution, or from (5) the calibration-in-the-large statistic.

For meta-analysis of prognostic models, it is recommended to provide information on the time period (t.val) during which calibration was assessed in the validation study. When the time period of the validation study does not correspond to the time period of interest (t.ma), observed and expected survival probabilities will be extrapolated using Poisson distributions. Currently, extrapolation of event rates is only supported for model.oe = "normal/log" and model.oe = "normal/identity". Note that values for O and N should take the presence of drop-out into account. This implies that O is ideally based on Kaplan-Meier estimates, or that N should represent the total number of participants with complete follow-up.

Bayesian meta-analysis:

The prior distribution for the between-study standard deviation can be specified by hp.tau.dist, and is always truncated by hp.tau.min and hp.tau.max. Initial values for the between-study standard deviation are sampled from a uniform distribution with aformentioned boundaries. The following distributions are supported for modeling the prior of the between-study standard deviation: Uniform distribution (hp.tau.dist="dunif"; default), truncated Student-t distribution (hp.tau.dist="dhalft").

Value

An object of class valmeta with the following elements:

data	array with (transformed) data used for meta-analysis
lme4	a fitted object of class glmerMod (if lme4 was used for meta-analysis)
measure	character string specifying the performance measure that has been meta-analysed.
method	character string specifying the meta-analysis method.
model	character string specifying the meta-analysis model (link function).
results	numeric vector containing the meta-analysis results
rma	a fitted object of class rma (if metafor was used for meta-analysis)
runjags	a fitted object of class runjags (if runjags was used for meta-analysis)
se.source	character vector specifying the source of the studies' standard errors
slab	vector specifying the label of each study

Author(s)

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References

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Viechtbauer W. Conducting Meta-Analyses in R with the metafor Package. *Journal of Statistical Software*. 2010; 36(3). Available from: http://www.jstatsoft.org/v36/i03/

See Also

plot.valmeta

Examples

```
######### Validation of prediction models with a binary outcome #########
data(EuroSCORE)

# Meta-analysis of the c-statistic (random effects)
fit <- with(EuroSCORE, valmeta(cstat=c.index, cstat.se=se.c.index,
               cstat.95CI=cbind(c.index.95CIl,c.index.95CIu),
               N=n, O=n.events, slab=Study))
plot(fit)

# Nearly identical results when we need to estimate the SE
with(EuroSCORE, valmeta(cstat=c.index,  N=n, O=n.events, slab=Study))

# Meta-analysis of the total O:E ratio (random effects)
with(EuroSCORE, valmeta(measure="OE", O=n.events, E=e.events, N=n))
with(EuroSCORE, valmeta(measure="OE", O=n.events, E=e.events))
with(EuroSCORE, valmeta(measure="OE", Po=Po, Pe=Pe, N=n))
with(EuroSCORE, valmeta(measure="OE", O=n.events, E=e.events, pars=list(model.oe="poisson/log")))

## Not run:
# Bayesian meta-analysis of the c-statistic (random effects)
fit2 <- with(EuroSCORE, valmeta(cstat=c.index, cstat.se=se.c.index,
                cstat.95CI=cbind(c.index.95CIl,c.index.95CIu),
                N=n, O=n.events, method="BAYES", slab=Study))
plot(fit2)

# Bayesian meta-analysis of the O:E ratio
pars <- list(model.oe="poisson/log", # Use a Poisson-Normal model
             hp.tau.dist="dhalft",   # Prior for the between-study standard deviation
             hp.tau.sigma=1.5,       # Standard deviation for 'hp.tau.dist'
             hp.tau.df=3,            # Degrees of freedom for 'hp.tau.dist'
           hp.tau.max=10)        # Maximum value for the between-study standard deviation
```

```
with(EuroSCORE, valmeta(measure="OE", O=n.events, E=e.events, N=n, method="BAYES",
     slab=Study, pars=pars))

## End(Not run)


######### Validation of prediction models with a time-to-event outcome #########
data(Framingham)

# Meta-analysis of total O:E ratio after 10 years of follow-up
with(Framingham, valmeta(measure="OE", Po=Po, Pe=Pe, N=n, t.val=t.val, t.ma=10))
with(Framingham, valmeta(measure="OE", Po=Po, Pe=Pe, N=n, t.val=t.val, t.ma=10, t.extrapolate=TRUE))
```

`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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See Also

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