Package ‘mada’

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Description

This package provides functions for diagnostic meta-analysis. Next to basic analysis and visualization the bivariate Model of Reitsma et al. (2005) that is equivalent to the HSROC of Rutter & Gatsonis (2001) can be fitted. A new approach based to diagnostic meta-analysis of Holling et al. (2012) is also available. Standard methods like summary, plot and so on are provided.

Details

The package provides tools for the meta-analysis of diagnostic accuracy data. For this the number true positives (TP), false negatives (FN), true negatives (TN) and false positives (FP) for each study must be known. The package can fit the bivariate model of Reitsma et al (2005), a bivariate random effects model. This model has been shown by Harbord et al. (2007) to be equivalent to the HSROC proposed by Rutter & Gatsonis (2001). We approach this model as a linear mixed effects model to avoid the complications of non-linear mixed effects model. The main function to fit such model is `reitsma` and standard methods are available for the output of this function.

Author(s)

Author and Maintainer: Philipp Doebler

References


See Also

reitsma

---

### AUC

#### Area under the curve (AUC)

**Description**

Calculates the area under the curve given a function or a fitted model.

**Usage**

```r
## Default S3 method:
AUC(x, fpr = 1:99/100, ...)  
## S3 method for class 'phm'
AUC(x, level = 0.95, ...)  
## S3 method for class 'reitsma'
AUC(x, fpr = 1:99/100, sroc.type = "ruttergatsonis", ...)  
```

**Arguments**

- `x`: a function with range and domain in ROC space (default method) or an object of class `phm` or `reitsma`.
- `fpr`: numeric vector, points on which the (S)ROC curve is evaluated.
- `level`: numeric, confidence level for the calculations of confidence intervals.
- `sroc.type`: character, which SROC curve should be used to calculate the AUC? Besides the default `ruttergatsonis` the option `naive` is available.
- `...`: further arguments, currently not used.

**Details**

The area under the curve is calculated using the trapezoidal rule. The argument `fpr` is the grid on which the (S)ROC curve is evaluated. In many cases the default grid will contain points on which the SROC curve can only be calculated by extrapolation; however if only a subinterval is specified a *partial AUC* is calculated and the AUC value might differ substantially.

For `phm` objects the AUC and its confidence interval is calculated analytically, for `reitsma` objects a call to the default method is invoked.
Value
An object of the class AUC which is really a list with component AUC and an optional component ci, which is currently only available from the AUC method for phm objects.

Author(s)
Philipp Doebler <philipp.doebler@googlemail.com>

Examples
data(AuditC)
AUC(phm(AuditC))

CIRho

Confidence intervals for Spearman’s $\rho$.

Description
Using Fisher’s z-transformation ($\text{atanh}$) and the classic normal approximation confidence intervals for a vector of correlations is computed.

Usage
CIRho(rho, N, level = 0.95)

Arguments
rho numeric vector, must be between -1 and 1.
N integer vector, sample sizes.
level numeric, confidence level.

Value
A matrix with first column rho and two further columns with the lower and upper bound.

Author(s)
Philipp Doebler <philipp.doebler@googlemail.com>

Examples
CIRho(c(0.34, 0.19), c(22, 48), level = 0.80)
cochran.Q

---

**cochran.Q**  
*Cochran’s Q statistic*

**Description**

Given estimates from primary studies and the weights of the single studies calculate Cochran’s Q as a measure of heterogeneity.

**Usage**

```r
cochran.Q(x, weights)
```

**Arguments**

- `x` numeric, typically a vector of effect sizes like (log-)OR
- `weights` numeric, see Details

**Details**

In fixed effects settings the weights are often inverse proportional to the variances of the primary studies. Cochran’s Q is known to have low power to detect heterogeneity.

**Value**

A named vector of length 3. First element is Q followed by the p-value and the degrees of freedom.

**Author(s)**

Philipp Doebler <philipp.doebler@googlemail.com>

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**crosshair**  
*Crosshair plot*

**Description**

Produces a crosshair plot or adds such a plot to an existing plot.

**Usage**

```r
## Default S3 method:
crosshair(x, correction = 0.5, level = 0.95, method = "wilson",
xlim = c(0,1), ylim = c(0,1), length = 0.1, pch = 1,
add = FALSE, suppress = TRUE, ...)
```
Arguments

- **x**: a data frame with variables including TP, FN, FP, TN, alternatively a matrix with column names including these.
- **correction**: numeric, continuity correction applied to zero cells.
- **level**: numeric, confidence level for the calculations of confidence intervals.
- **method**: character, method used to calculate the confidence intervals for sensitivities, specificities and false positive rates. One of "wald", "wilson", "agresti-coull", "jeffreys", "modified wilson", "modified jeffreys", "clopper-pearson", "arcsine", "logit", "witting".
- **xlim**: part of ROC space to be plotted
- **ylim**: part of ROC space to be plotted
- **length**: length of "whiskers" of the crosshair.
- **pch**: Symbol used to plot point estimates. Use pch = "" to suppress plotting point estimates.
- **add**: logical, should the plot be added to the current plot?
- **suppress**: logical, should the warnings produced by the internal call to madad be suppressed? Defaults to TRUE, since only the diagnostic accuracies and their confidence intervals are used in subsequent calculations.
- ... further arguments passed on to plot.

Details

Crosshair plots go back to Phillips et al. (2010). Note that for fits of the `reitsma` function a crosshair method is available to plot pooled estimate, see `reitsma-class`.

Value

Besides plotting, the function returns an invisible NULL.

Author(s)

Philipp Doebler <philipp.doebler@googlemail.com>

References


See Also

`ROCellipse`, `reitsma-class`

Examples

data(AuditC)
crosshair(AuditC)
Description

Produce a forest plot. Includes graphical summary of results if applied to output of suitable model-fitting function. forest methods for madad and madauni objects are provided.

Usage

```r
## S3 method for class 'madad'
forest(x, type = "sens", log = FALSE, ...)
## S3 method for class 'madauni'
forest(x, log = TRUE, ...)
forestmada(x, ci, plotci = TRUE, main = "Forest plot", xlab = NULL,
digits = 2L, snames = NULL, subset = NULL, pch = 15,
cex = 1, cipoly = NULL, polycol = NA, ...)
```

Arguments

- `x` an object for which a forest method exists or (in the case of forestmada) a vector of point estimates.
- `ci` numeric matrix, each row corresponds to a confidence interval (the first column being the lower bound and the second the upper).
- `plotci` logical, should the effects sizes and their confidence intervals be added to the plot (as text)?
- `main` character, heading of plot.
- `xlab` label of x-axis.
- `digits` integer, number of digits for axis labels and confidence intervals.
- `snames` character vector, study names. If NULL, generic study names are generated.
- `subset` integer vector, allows to study only a subset of studies in the plot. One can also reorder the studies with the help of this argument.
- `pch` integer, plotting symbol, defaults to a small square. Also see `plot.default`.
- `cex` numeric, scaling parameter for study names and confidence intervals.
- `cipoly` logical vector, which confidence interval should be plotted as a polygon? Useful for summary estimates. If set to NULL, regular confidence intervals will be used.
- `polycol` color of the polygon(s), passed on to `polygon`. The default value of NA implies no color.
- `type` character, one of sens, spec, negLR, posLR or DOR.
- `log` logical, should the log-transformed values be plotted?
- `...` arguments to be passed on to forestmada and further on to other plotting functions
Details

Produces a forest plot to graphically assess heterogeneity. Note that forestmada is called internally, so that the ... argument can be used to pass on arguments to this function; see the examples.

Value

Returns and invisible NULL.

Author(s)

Philipp Doebler <philipp.doebler@googlemail.com>

See Also

madad, madauni

Examples

data(AuditC)

## Forest plot of log DOR with random effects summary estimate
forest(madauni(AuditC))

## Forest plot of negative likelihood ratio (no log transformation)
## color of the polygon: light grey
## draw the individual estimate as filled circles
forest(madauni(AuditC, type = "negLR"),
       log = FALSE, polycol = "lightgrey", pch = 19)

## Paired forest plot of sensitivities and specificities
## Might look ugly if device region is too small
old.par <- par()
AuditC.d <- madad(AuditC)

plot.new()
par(fig = c(0, 0.5, 0, 1), new = TRUE)
forest(AuditC.d, type = "sens", xlab = "Sensitivity")
par(fig = c(0.5, 1, 0, 1), new = TRUE)
forest(AuditC.d, type = "spec", xlab = "Specificity")
par(old.par)

## Including study names
## Using Letters as dummies
forest(AuditC.d, type = "spec", xlab = "Specificity",
       snames = LETTERS[1:14])
Description

Five data frames with diagnostic accuracy data from binary test outcomes.

Usage

```r
data("AuditC")
data("Dementia")
data("IAQ")
data("SAQ")
data("smoking")
```

Format

Five data frames. The data set `smoking` combines the IAQ and SAQ data sets and is the only one with 5 variables.

- **TP** numeric. number of true positives
- **FN** numeric. number of false negatives
- **FP** numeric. number of false positives
- **TN** numeric. number of true negatives
- **type** factor. self-administered or interviewer-administered questionnaire

Details

The `AuditC` data is from Kriston et al. (2008). The `Dementia` from Mitchell (2009) and the SAQ and IAQ data are subsets from the data in Patrick et al. (1994), while `smoking` is the complete data.

Source


**madad**

*Descriptive statistics for meta-analysis of diagnostic accuracy*

**Description**

Given the frequencies of true positives, false negative, false positives and true negatives from primary diagnostic studies madad calculates various summary statistics. Apart from sensitivities, specificities and false positive rates the function also calculates the diagnostic odds ratio (DOR) and the positive and negative likelihood ratios, together with their respective confidence intervals. Also two hypothesis tests are calculated: one testing the equality of the sensitivities and the same for the false positive rates.

**Usage**

```r
madad(x = NULL, TP, FN, FP, TN, level = 0.95, correction = 0.5,
     correction.control = "all", method = "wilson", yates = TRUE,
     suppress = TRUE, ...)  
```

```r
## S3 method for class 'madad'
print(x, digits = 3, ...)  
```

**Arguments**

- **x**
  - any object that can be converted to a data frame with integer variables TP, FN, FP and TN, alternatively a matrix with column names including TP, FN, FP and TN.
- **TP**
  - vector of integers, ingored if X is not NULL.
- **FN**
  - vector of integers, ingored if X is not NULL.
- **FP**
  - vector of integers, ingored if X is not NULL.
- **TN**
  - vector of integers, ingored if X is not NULL.
- **correction**
  - numeric, continuity correction applied to 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.
- **level**
  - numeric, confidence level for the calculations of confidence intervals.
- **method**
  - character, method used to calculate the confidence intervals for sensitivities, specificities and false positive rates. One of "wald", "wilson", "agresti-coull", "jeffreys", "modified wilson", "modified jeffreys", "clopper-pearson", "arcsine", "logit", "witting"
- **yates**
  - logical, should a Yates correction be used for testing the equality of sensitivities and specificities?
- **digits**
  - integer, to what decimal place is the output to be rounded?
- **suppress**
  - logical, suppress the warning that is generated by `prop.test` when Chi-square approximation may be incorrect.
- **...**
  - further arguments to be passed on the other functions (currently none).
Details

All calculations are performed using the continuity corrected cell counts, so if there are zero cells, the sensitivities and specificities not equal to 1. This can be avoided by setting `correction.control` to "none".

The test for the equality of sensitivities and its counterpart for the specificities is based on `prop.test`. This function will occasionally output warnings.

Value

An object of class `madad` which is essentially a list with the following components:

- `sens`: A list of two components, `sens` (the sensitivities) and `sens.ci` the confidence intervals (a matrix with 2 columns).
- `spec`: A list of two components, `spec` (the specificities) and `spec.ci` the confidence intervals (a matrix with 2 columns).
- `fpr`: A list of two components, `fpr` (the false positive rates) and `fpr.ci` the confidence intervals (a matrix with 2 columns).
- `sens.htest`: An object of class `htest`.
- `spec.htest`: An object of class `htest`.
- `DOR`: A list of two components, `DOR` the diagnostic odds ratios and `DOR.ci` the confidence intervals (a matrix with 2 columns).
- `posLR`: A list of two components, `posLR` the positive likelihood ratios and `posLR.ci` the confidence intervals (a matrix with 2 columns).
- `negLR`: A list of two components, `negLR` the negative likelihood ratios and `negLR.ci` the confidence intervals (a matrix with 2 columns).
- `cor_sens_fpr`: numeric, the correlation of the sensitivities and false-positive rates.
- `level`: numeric
- `method`: character
- `names`: character vector, if the main argument of `madad` is a data frame with a variable names these names are stored here.
- `nobs`: integer, number of primary studies.
- `data`: data frame, with columns TP, FN, FP and TN.
- `data.name`: character, name of the main argument.
- `correction`: numeric
- `correction.control`: character

Author(s)

Philipp Doebler <philipp.doebler@googlemail.com>

See Also

-madauni
Examples

```r
data(AuditC)
AuditC.d <- madad(AuditC)
print(AuditC.d, digits = 2) # round everything to 2 digits
```

### madauni

**Meta-Analysis of univariate measures of diagnostic accuracy**

### Description

The classic strategy to meta-analysis of diagnostic accuracy data is to pool a univariate measure of accuracy like the diagnostic odds ratio, the positive likelihood ratio or the negative likelihood ratio. For fixed effect estimation a Mantel-Haenszel estimator is implemented and for random effect estimation a DerSimonian-Laird estimator is available.

### Usage

```r
madauni(x, type = "DOR", method = "DSL", suppress = TRUE, ...)
```

### Arguments

- **x**
  - any object that can be converted to a data frame with integer variables TP, FN, FP and TN, alternatively a matrix with column names including TP, FN, FP and TN.
- **type**
  - character, what effect size should be pooled? Either "DOR", "posLR" or "negLR".
- **method**
  - character, method of estimation. Either "MH" or "DSL".
- **suppress**
  - logical, should warnings produced by the internal call to madad be suppressed?
- **...**
  - further arguments to be passed on to madad, for example correction.control.

### Details

First note that the function madad is used to calculate effect measures. You can pass on arguments to this function via the ... arguments. This is especially useful for the correction.control and correction arguments, see the example.

The Mantel-Haenszel method performs fixed effect estimation of the effect sizes. For the DOR the variance of this estimator is calculated according to Robins et al. (1986) and for the likelihood ratios the variance is based on Greenland et al. (1985).

The DerSimonian-Laird method performs a random effects meta-analysis. For this $\tau^2$, the variance of the log-transformed effect size (DOR, positive or negative likelihood ratio) is calculated by the DerSimonian and Laird (1986) method. The confidence interval for $\tau^2$ is derived by inverting the Q-Test of Viechtbauer (2007).

Zwindermann and Bossuyt (2008) argue, that univariate summary points like the likelihood ratios should be derived from the bivariate model of Reitsma et al (2005). The function SummaryPts, using output of reitsma supports this approach.
madauni

Value
An object of class madauni, for which some standard methods are available, see madauni-class

Note
Performing univariate meta-analysis of diagnostic studies can not be recommended anymore now that bivariate methods are available, at least not if a reasonable number of primary studies is available. The package mada provides this functionality for exploratory purposes and for meta-analysis of a small number of studies. The prefered way is to use reitsma in conjunction with SummaryPts.
The default value of correction.control used mada (and hence in the calculation of the effect sizes for madauni) is "all", i.e. the continuity correction is added to all studies if any has a zero cell. This is a different default value than the metafor package uses. Set correction.control to "single" to arrive at the same values.

Author(s)
Philipp Doebler <philipp.doebler@googlemail.com>

References

See Also
madauni-class, reitsma, SummaryPts

Examples
data(AuditC)

## First example: DOR meta-analysis
AuditC.uni <- madauni(AuditC)
summary(AuditC.uni)

## Second example: sensitivity analysis
## Do continuity corrections make a difference?
madauni-class

Description

Various methods for the output of the function `madauni`. Also the default method `confint` works for this class.

Usage

```r
AuditC.uni_low <- madauni(AuditC, correction = 0.1)
AuditC.uni_single <- madauni(AuditC, correction.control = "single") ## default is "all"
confint(AuditC.uni)
confint(AuditC.uni_low)
confint(AuditC.uni_single)
```

```r
madauni-class       Methods for the class madauni.

Description

Various methods for the output of the function `madauni`. Also the default method `confint` works for this class.

Usage

```r
## S3 method for class 'madauni'
print(x, digits = 3, ...)
## S3 method for class 'madauni'
vcov(object, ...)
## S3 method for class 'madauni'
summary(object, level = 0.95, ...)
## S3 method for class 'summary.madauni'
print(x, digits = 3, ...)
```

Arguments

- `x` An object of class `madauni`.
- `object` An object of class `madauni`.
- `level` numeric, the confidence level for the confidence intervals in the summary.
- `digits` integer indicating the number of decimal places to round to.
- `...` arguments to be passed to methods

Value

`summary.madauni` returns a list of class `summary.madauni` which is printed with `print.summary.madauni`.

Author(s)

Philipp Doebler <philipp.doebler@googlemail.com>

See Also

`madauni`
Plot the Moses-Shapiro-Littenberg SROC curve

Description

The approach to SROC curve modeling is described in the paper of Moses, Shapiro and Littenberg (1993). It is considered outdated and is included in mada so that users can reproduce older results and compare different SROC curves.

Usage

```r
mslsroc(data = NULL, subset=NULL,
         TP="TP", FN="FN", FP="FP", TN="TN",
         fpr = NULL, extrapolate = FALSE,
         correction = 0.5, correction.control = "all",
         add = FALSE, lty = 1, lwd = 1, col = 1, ...)
```

Arguments

- **data**: any object that can be converted to a data frame with integer variables for observed frequencies of true positives, false negatives, false positives and true negatives. The names of the variables are provided by the arguments TP, FN, FP and TN (see their defaults). Alternatively the data can be a matrix with column names including TP, FN, FP and TN. If no data is specified, the function will check the TP, FN, FP and TN arguments.
- **TP**: character or integer: name for vector of integers that is a variable of data or a vector of integers. If data is not NULL, names are expected, otherwise integers are.
- **FN**: character or integer: name for vector of integers that is a variable of data or a vector of integers. If data is not NULL, names are expected, otherwise integers are.
- **FP**: character or integer: name for vector of integers that is a variable of data or a vector of integers. If data is not NULL, names are expected, otherwise integers are.
- **TN**: character or integer: name for vector of integers that is a variable of data or a vector of integers. If data is not NULL, names are expected, otherwise integers are.
- **subset**: the rows of data to be used as a subset in all calculations. If NULL (the default) then the complete data is considered.
- **fpr**: Points between 0 and 1 on which to draw the SROC curve. Should be tightly spaced. If set to NULL, the default, it will be the vector of numbers 0.01, 0.02, ..., 0.99 and is truncated if the extrapolate argument is FALSE.
- **extrapolate**: logical, should the SROC curve be extrapolated beyond the region where false positive rates are observed?
- **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.

add
logical, should the SROC curve be added to an existing plot?

lty
line type, see lines.
lwd
line width, see lines.
col
color of SROC, see lines.
...arguments to be passed on to plotting functions.

Details
Details are found in the paper of Moses, Shapiro and Littenberg (1993).

Value
Besides plotting the SROC, an invisible list is returned which contains the parameters of the SROC.

Author(s)
Philipp Doebler <philipp.doebler@googlemail.com>

References

See Also
reitsma-class, talpha, SummaryPts

Examples
## First Example
data(Dementia)
ROCellipse(Dementia)
ms1SROC(Dementia, add = TRUE) # Add the MSL-SROC to this plot

## Second Example
# Make a fancy plot and look at the coefficients
ms1_Dementia <- ms1SROC(Dementia, col = 3, lwd = 3, lty = 3)
ms1_Dementia$A2 # intercept on logit SROC space
ms1_Dementia$B2 # slope on logit SROC space
Description

The function fits the model of Holling et al. (2012). The adjusted profile maximum likelihood estimator (APMLE) is implemented for homogeneity and heterogeneity of primary studies.

Usage

```r
phm(data, ...)  
## Default S3 method:  
phm(data = NULL, subset=NULL,  
    TP="TP", FN="FN", FP="FP", TN="TN",  
    correction = 0.5, correction.control = "all",  
    hetero = TRUE, estimator = "APMLE", l = 100, ...)
```

Arguments

data any object that can be converted to a data frame with integer variables TP, FN, FP and TN, alternatively a matrix with column names including TP, FN, FP and TN.

subset the rows of data to be used as a subset in all calculations. If NULL (the default) then the complete data is considered.

TP character or integer: name for vector of integers that is a variable of data or a vector of integers. If data is not NULL, names are expected, otherwise integers are.

FN character or integer: name for vector of integers that is a variable of data or a vector of integers. If data is not NULL, names are expected, otherwise integers are.

FP character or integer: name for vector of integers that is a variable of data or a vector of integers. If data is not NULL, names are expected, otherwise integers are.

TN character or integer: name for vector of integers that is a variable of data or a vector of integers. If data is not NULL, names are expected, otherwise integers are.

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.

hetero logical, should heterogeneity of studies be assumed? Will fit model for homogeneity otherwise.

estimator character, determines estimator used. Currently only APMLE is available.

l integer, number of iterations for fixed point algorithm

... arguments passed on to other functions (currently not used)
Details

The model of Holling et al. (2012) assumes that the relationship between false positive rates \( u \) and sensitivities \( p \) can be described by

\[
u^\theta = p,
\]

where \( \theta \) is the diagnostic accuracy parameter. If homogeneity of the studies can be assumed, \( \theta \) is estimated as a fixed effect. Under heterogeneity a random effect with variance \( \tau^2 \) describes the variation of the diagnostic accuracy parameter in the population of studies. Since the error of each observed \( \theta \) depends only on the sample size and \( \theta \) the model has only one parameter in the case of homogeneity and two parameters under heterogeneity, making it suitable for diagnostic meta-analysis with low sample size. Estimation proceeds by a fixed point algorithm derived from the adjusted profile likelihood. More details on the computational approach can be found in Holling et al. (2012).

Value

An object of the class `phm` for which many standard methods are available. See `phm-class` for details.

Author(s)

Philipp Doebler <philipp.doebler@googlemail.com>, Walailuck Boehning (original implementation of estimation algorithm)

References


See Also

`phm-class`

Examples

data(AuditC)
(fit <- phm(AuditC))
summary(fit)
plot(fit)
Methods for `phm` objects.

Description

Objects of the class `phm` are output by the function with the same name. Apart from standard methods the function `sroc` provides SROC curves and confidence bands for model fits.

Usage

```r
## S3 method for class 'phm'
print(x, ...)  
## S3 method for class 'phm'
summary(object, level = 0.95, ...)  
## S3 method for class 'phm'
sroc(fit, fpr = 1:99/100, ...)  
## S3 method for class 'phm'
plot(x, extrapolate = FALSE, confband = TRUE, level = 0.95,
     ylim = c(0,1), xlim = c(0,1), sroclty = 1, sroclwd = 1,
     confbandlty = 2, confbandlwd = 0.5, ...)
```

Arguments

- `x`: a `phm` object.
- `object`: a `phm` object.
- `fit`: a `phm` object.
- `level`: numeric, the confidence level for calculations of confidence intervals (`summary`) or confidence bands (`plot`).
- `fpr`: numeric, the false positives rates for which to calculate the predicted sensitivities.
- `extrapolate`: logical, should the sroc curve be plotted beyond the observed false positive rates?
- `confband`: logical, should confidence bands be plotted?
- `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?
- `sroclty`: integer, line type of the SROC curve
- `sroclwd`: integer, line width of the SROC curve
- `confbandlty`: integer, line type of the SROC curve’s confidence band
- `confbandlwd`: integer, line width of the SROC curve’s confidence band
- `...`: arguments to be passed on to other functions
Details

The SROC curve is derived from the model formula. The confidence bands are calculated from the bounds of the confidence interval for the diagnostic accuracy parameter $\theta$. The parameter and its confidence interval are then also used to calculate the AUC and partial AUC using the formulae

$$AUC(a, b) = \int_a^b u^\theta du = \frac{1}{\theta + 1} [b^{\theta+1} - a^{\theta+1}],$$

$$AUC = AUC(0, 1)$$

and

$$pAUC = \frac{1}{b - a} AUC(a, b),$$

where $a$ is the lower bound of the observed false positive rates and $b$ the upper.

Value

The sroc function returns a matrix ready for plotting. Each row corresponds to one point in ROC space.

Author(s)

Philipp Doebler <philipp.doebler@googlemail.com>

References


See Also

phm

Examples

# load data
data(AuditC)
# fit model
fit <- phm(AuditC)
# calculate a SROC curve, but do not plot it
sroc.AuditC <- sroc(fit)
# plot the SROC curve in ROC space as a line
plot(sroc.AuditC, type = "l")
# Fancy version using plot
plot(fit)
Fit the bivariate model of Reitsma et al. (2005) and extensions.

Description

The function fits the bivariate model of Reitsma et al. (2005) that Harbord et al. (2007) have shown to be equivalent to the HSROC of Rutter&Gatsonis (2001). We specify the model as a linear mixed model with known variances of the random effects, similar to the computational approach by Reitsma et al. (2005). Variance components are estimated by restricted maximum likelihood (REML) as a default but ML estimation is available as well. In addition meta-regression is possible and the use of other transformations than the logit, using the approach of Doebler et al. (2012).

Usage

reitsma(data, ...) ## Default S3 method:
reitsma(data = NULL, subset=NULL, formula = NULL,
TP="TP", FN="FN", FP="FP", TN="TN",
alphasens = 1, alphafpr = 1,
correction = 0.5, correction.control = "all",
method = "reml",
control = list(), ...)

Arguments

data any object that can be converted to a data frame with integer variables for observed frequencies of true positives, false negatives, false positives and true negatives. The names of the variables are provided by the arguments TP, FN, FP and TN (see their defaults). Alternatively the data can be a matrix with column names including TP, FN, FP and TN. If no data is specified, the function will check the TP, FN, FP and TN arguments.

TP character or integer: name for vector of integers that is a variable of data or a vector of integers. If data is not NULL, names are expected, otherwise integers are.

FN character or integer: name for vector of integers that is a variable of data or a vector of integers. If data is not NULL, names are expected, otherwise integers are.

FP character or integer: name for vector of integers that is a variable of data or a vector of integers. If data is not NULL, names are expected, otherwise integers are.

TN character or integer: name for vector of integers that is a variable of data or a vector of integers. If data is not NULL, names are expected, otherwise integers are.

subset the rows of data to be used as a subset in all calculations. If NULL (the default) then the complete data is considered.
Formula for meta-regression using standard *formula*. The left hand side of this formula must be `cbind(tsens, tfpr)` and if `formula` is NULL (the default), then the formula `cbind(tsens, tfpr) ~ 1` is used, i.e. a model without covariates.

Transformation parameter for (continuity corrected) sensitivities, see details. If set to 1 (the default) the logit transformation is used.

Transformation parameter for (continuity corrected) false positive rates, see details.

numeric, continuity correction applied if zero cells

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.

character, either "fixed", "ml", "mm", "vc" or "reml" (the default)

a list of control parameters, see the documentation of `mvmeta`.

arguments to be passed on to other functions, currently ignored

In a first step the observed frequencies are continuity corrected if values of 0 or 1 would result for the sensitivity or false positive rate otherwise. Then the sensitivities and false positive rates are transformed using the transformation

\[ x \mapsto t_\alpha(x) := \alpha \log(x) - (2 - \alpha) \log(1 - x). \]

Note that for \( \alpha = 1 \), the default value, the logit transformation results, i.e. the approach of Reitsma et al. (2005). A bivariate random effects model is then fitted to the pairs of transformed sensitivities and false positive rates.

Parameter estimation makes use of the fact that the fixed effect parameters can be profiled in the likelihood. Internally the function `mvmeta` is called. Currently only standard errors for the fixed effects are available. Note that when using `method = "mm"` or `method = "vc"`, no likelihood can be computed and hence no AIC or BIC values.

If you want other summary points like negative or positive likelihood ratios, see `SummaryPts`.

An object of the class `reitsma` for which many standard methods are available. See `reitsma-class` for details.

Philipp Doebler <philipp.doebler@googlemail.com>
References


See Also

`reitsma-class, talpha, SummaryPts`

Examples

data(Dementia)
(fit <- reitsma(Dementia))
summary(fit)
plot(fit)

## Meta-Regression

data(smoking)
## use type of questionnaire as covariate
(fit <- reitsma(smoking, formula = cbind(tsens, tfpr) ~ type))
summary(fit) ## sensitivities significantly lower for SAQ

---

reitsma-class

Methods for `reitsma` objects.

Description

Objects of the class `reitsma` are output by the function with the same name. Apart from standard methods the functions `sroc`, `mcsroc` and `ROCellipse` provide SROC curves and confidence regions for fits.

Usage

## S3 method for class 'reitsma'
print(x, digits = 4, ...)
## S3 method for class 'reitsma'
summary(object, level = 0.95, sroc.type = "ruttergatsonis", ...)
## S3 method for class 'reitsma'
sroc(fit, fpr = 1:99/100, type = "ruttergatsonis", return_function = FALSE, ...)
## S3 method for class 'reitsma'
mcsroc(fit, fpr = 1:99/100, replications = 10000, lambda = 100, ...)
## S3 method for class 'reitsma'

ROCCellipse(x, level = 0.95, add = FALSE, pch = 1, ...)

## S3 method for class 'reitsma'

crosshair(x, level = 0.95, length = 0.1, pch = 1, ...)

## S3 method for class 'reitsma'

plot(x, extrapolate = FALSE, plotsumm = TRUE, level = 0.95,
    ylim = c(0,1), xlim = c(0,1), pch = 1, sroclty = 1, sroclwd = 1,
    predict = FALSE, predlty = 3, predlwd = 1, type = "ruttergatsonis", ...)

## S3 method for class 'reitsma'

anova(object, fit2, ...)

## S3 method for class 'anova.reitsma'

print(x, digits = 4, ...)

### Arguments

- **x**: a `reitsma` object.
- **object**: a `reitsma` object.
- **fit**: a `reitsma` object.
- **fit2**: a `reitsma` object.
- **digits**: number of decimal digits to print.
- **level**: numeric, the level for calculations of confidence intervals (summary) or regions (ROCellipse)
- **sroc.type**: character, which SROC curve should be used to calculate the AUC in the summary? Besides the default `ruttergatsonis` the option `naive` is available.
- **return_function**: logical. Should a function on ROC space be returned or the values at the points given by `fpr`?
- **fpr**: numeric, the false positives rates for which to calculate the predicted sensitivities
- **replications**: integer, the number of replications for the Monte-Carlo SROC curve
- **lambda**: numeric, the parameter lambda of the Monte-Carlo run, see details
- **add**: logical, should the confidence region be added to the current plot? If set to `FALSE` a matrix of points of the ellipse is returned
- **extrapolate**: logical, should the SROC curve be plotted beyond the observed false positive rates?
- **plotsumm**: logical, should the summary pair of sensitivity and false positive rate together with its confidence region be plotted?
- **length**: positive numeric, length of the "whiskers" of the crosshairs.
- **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
- **sroclty**: integer, line type of the SROC curve
- **sroclwd**: integer, line width of the SROC curve
- **predict**: logical, draw prediction region?
The confidence regions of `ROCellipse` are first calculated as ellipses on logit-ROC space, so the back-transformed regions that are output are not necessarily ellipses. The Monte-Carlo SROC curves are generated from random samples from the fitted model and a `lowess` smooth through them is output. Many computational details are to be found in Doebler et al. (2012).

The summary function for `reitsma` objects also contains the five parameters of the HSROC model by Rutter & Gatsonis (2001) if no regression is performed. These values are calculated by using the formulae from Harbord et al. (2007).

The plot method for `reitsma` objects will plot the generalization of the Rutter-Gatsonis curve. If you require positive or negative likelihood ratios, you should use `summarypts`.

### Value

`sroc` returns a matrix ready for plotting. Each row corresponds to one point in ROC space. `mcsroc` returns a `lowess` smooth. `ROCellipse` returns a list, the first element being a matrix of points in ROC space that delimit the confidence region and the second is the point estimate of the pair of sensitivity and false positive rate in ROC space.

### Author(s)

Philipp Doebler <philipp.doebler@googlemail.com>

### References


### See Also

`reitsma`, `SummaryPts`

### Examples

```r
# load data
data(Dementia)
# fit model
fit <- reitsma(Dementia)
# calculate a confidence region but do not plot it
cr.Dementia <- ROCellipse(fit)
# calculate a SROC curve
sroc.Dementia <- sroc(fit)
```
# plot the confidence region in ROC space as a line
plot(cr.Dementia$ROCellipse, type = "l", xlim = c(0,1), ylim = c(0,1))
# add the point estimate of the mean
points(cr.Dementia$tfprsens)
# add the SROC curve
lines(sroc.Dementia)

---

**ROCellipse**  
*Confidence Regions on ROC space*

**Description**

Plot individual confidence regions for the estimate from each primary study on ROC space or add such regions to an existing plot.

**Usage**

```r
## Default S3 method:
ROCellipse(x, correction = 0.5, level = 0.95,
xlim = c(0, 1), ylim = c(0, 1), method = "wilson",
pch = 1, add = FALSE, corr = 0, suppress = TRUE,
ellipsecol = "grey", ...)
```

**Arguments**

- `x`: a data frame with variables including TP, FN, FP, TN, alternatively a matrix with column names including these.
- `correction`: numeric, continuity correction applied to zero cells.
- `level`: numeric, confidence level for the calculations of confidence intervals.
- `xlim`: numeric of length 2, which portion of ROC space should be plotted? All reasonable values should be within (0,1).
- `ylim`: numeric of length 2, which portion of ROC space should be plotted? All reasonable values should be within (0,1).
- `method`: character, method used to calculate the confidence intervals for sensitivities, specificities and false positive rates. One of "wald", "wilson", "agresti-coull", "jeffreys", "modified wilson", "modified jeffreys", "clopper-pearson", "arcsine", "logit", "witting"
- `pch`: Symbol used to plot point estimates. Use `pch = ""` to suppress plotting point estimates.
- `add`: logical, should the plot be added to the current plot?
- `corr`: numeric or character, the correlation assumed in the calculation of the confidence ellipsoids on logit-ROC space. If set to "logit", the correlation of the logit-transformed sensitivities and false positive rates will be used in the correlations. See details for further explanation.
suppress logical, should the warnings produced by the internal call to madad be suppressed? Defaults to "TRUE", since only the diagnostic accuracies and their confidence intervals are used in subsequent calculations.

ellipsecol The color used for plotting the ellipses.

... further arguments passed on to plot.

Details

The confidence regions are ellipses on logit-ROC space, hence the name of the function. The standard deviations underlying confidence intervals for the sensitivities and false positive rates are used to determine the scale of the ellipses on logit-ROC space. These ellipses get backtransformed to ROC space and plotted. As a default no correlation is assumed on logit-ROC space.

The objects of class reitsma have their own ROCellipse method to add a confidence region for the pooled estimate, see reitsma-class.

Value

Besides plotting an invisible NULL is returned.

Author(s)

Philipp Doebler <philipp.doebler@googlemail.com>

See Also

crosshair, reitsma-class

Examples

data(AuditC)
ROCellipse(AuditC)

---

rsSROC  

Plot the Ruecker-Schumacher (2010) SROC curve

Description

Assuming that a weighted Youden index is maximized in all primary studies, the Ruecker-Schumacher approach estimates individual ROC curves and then averages them.

Usage

rsSROC(data = NULL, subset=NULL,
   TP="TP", FN="FN", FP="FP", TN="TN",
   lambda = "from_bivariate",
   fpr = NULL, extrapolate = FALSE, plotstudies = FALSE,
   correction = 0.5, correction.control = "all",
   add = FALSE, lty = 1, lwd = 1, col = 1, ...)
Arguments

data any object that can be converted to a data frame with integer variables for observed frequencies of true positives, false negatives, false positives and true negatives. The names of the variables are provided by the arguments TP, FN, FP and TN (see their defaults). Alternatively the data can be a matrix with column names including TP, FN, FP and TN. If no data is specified, the function will check the TP, FN, FP and TN arguments.

TP character or integer: name for vector of integers that is a variable of data or a vector of integers. If data is not NULL, names are expected, otherwise integers are.

FN character or integer: name for vector of integers that is a variable of data or a vector of integers. If data is not NULL, names are expected, otherwise integers are.

FP character or integer: name for vector of integers that is a variable of data or a vector of integers. If data is not NULL, names are expected, otherwise integers are.

TN character or integer: name for vector of integers that is a variable of data or a vector of integers. If data is not NULL, names are expected, otherwise integers are.

subset the rows of data to be used as a subset in all calculations. If NULL (the default) then the complete data is considered.

lambda numeric or "from_bivariate", the weight of the weighted Youden index. Must be between 0 and 1. If set to "from_bivariate", the reitsma function is used to calculate lambda from the data.

fpr Points between 0 and 1 on which to draw the SROC curve. Should be tightly spaced. If set to NULL, the default, it will be the vector of numbers 0.01, 0.02, ..., 0.99 and is truncated if the extrapolate argument is FALSE.

extrapolate logical, should the SROC curve be extrapolated beyond the region where false positive rates are observed?

plotstudies logical, should the ROC curves for the individual studies be added to the plot? The plot will become crowded if set to TRUE.

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.

add logical, should the SROC curve be added to an existing plot?

lty line type, see lines.

lwd line width, see lines.

col color of SROC, see lines.

... arguments to be passed on to plotting functions.
Details

Details are found in the paper of Ruecker and Schumacher (2010).

Value

Besides plotting the SROC, an invisible list is returned which contains the parameters of the SROC.

Author(s)

Philipp Doebler <philipp.doebler@googlemail.com> Original code kindly supplied by G. Ruecker.

References


See Also

reitsma-class, talpha, SummaryPts

Examples

## First Example
data(Dementia)
ROCellipse(Dementia)
rsSROC(Dementia, add = TRUE) # Add the RS-SROC to this plot

## Second Example
# Make a crowded plot and look at the coefficients
rs_Dementia <- rsSROC(Dementia, col = 3, lwd = 3, lty = 3, plotstudies = TRUE)
rs_Dementia$lambda
rs_Dementia$aa # intercepts of primary studies on logit ROC space
rs_Dementia$bb # slopes

---

sens  

Sensitivity, Specificity and False Positive Rate

Description

Calculate basic measures of diagnostic accuracy for a number of studies.

Usage

sens(x)  
spec(x)  
fpr(x)
Arguments

\texttt{x} \hspace{1cm} \text{a data frame with variables including TP, FN, FP, TN, alternatively a matrix with column names including these.}

Details

These functions are the basic building blocks of many procedures to assess diagnostic accuracy. For a decent summary of set of primary studies it is better to use \texttt{madad}, for graphical summaries \texttt{crosshair} and \texttt{ROCellipse} are available.

Value

A numeric vector.

Author(s)

Philipp Doebler <philipp.doebler@googlemail.com>

See Also

\texttt{madad}, \texttt{crosshair}, \texttt{link\{ROC.ellipse\}}

Examples

```r
data(AuditC)
plot(fpr(AuditC), sens(AuditC), main = "AUDIT-C data on ROC space",
     ylab = "Sensitivity", xlab = "False Positive Rate")
```

---

**SummaryPts**

Use the Zwindermann & Bossuyt (2008) MCMC procedure to generate summary points (positive and negative likelihood ratio, diagnostic odds ratio) for the Reitsma et al. (2005) bivariate model

Description

Zwindermann & Bossuyt (2008) argue that likelihood ratios should not be pooled by univariate meta-analysis. They propose a sampling based approach that uses the parameters of a fit to the bivariate model (implemented in \texttt{reitsma}) to generate samples for observed sensitivities and false positive rates. From these samples the quantities of interest (and their confidence intervals) are estimated.
Usage

SummaryPts(object, ...)  
## Default S3 method:
SummaryPts(object, mu, Sigma, alphasens = 1, alphafpr = 1,  
n.iter = 10^6, FUN, ...)
## S3 method for class 'reitsma'
SummaryPts(object, n.iter = 10^6, FUN = NULL, ...)
## S3 method for class 'SummaryPts'
print(x, ...)
## S3 method for class 'SummaryPts'
summary(object, level = 0.95, digits = 3, ...)

Arguments

object an object for which a method exists
x An object of class SummaryPts
mu numeric of length 2, expected to be the mean parameter of a bivariate model
Sigma 2x2 variance covariance matrix, expected to be the matrix representing the standard error of mu and the covariance of these two estimates
alphasens numeric, alpha parameter for the sensitivities. Amounts to logit transformation if set to 1 (the default). See reitsma.
alphafpr numeric, alpha parameter for the false positive rates. Amounts to logit transformation if set to 1 (the default). See reitsma.
n.iter number of samples
FUN A list of functions with 2 arguments (sens and fpr); if set to NULL in SummaryPts.reitsma, the positive, negative and inverse negative likelihood ratios are calculated and also the diagnostic odds ratio (DOR). See the example on how to supply other functions.
level numeric, confidence level for confidence intervals
digits number of significant digits to display
... arguments to be passed on to other functions, currently ignored

Details

Samples are generated from a bivariate normal using rmvnorm. Note that the FUN argument

Value

An object of the class SummaryPts for which print and summary methods are available.

Author(s)

Philipp Doebler <philipp.doebler@googlemail.com>
References


See Also

`reitsma, talpha`

Examples

```r
data(Dementia)
(fit <- reitsma(Dementia))
mcnc_sum <- SummaryPts(fit, n.iter = 1e+3)
## n.iter should be larger in applications!
mcnc_sum #just the means
summary(mcmc_sum) # 95% CIs by default
summary(mcmc_sum, level = 0.80, digits = 5) ## more digits, smaller CIs

## Supplying other functions

# Example 1: theta parameter of proportional hazards model
# see "phm" in mada's documentation for details on theta
theta <- function(sens, fpr)(log(sens) / log(fpr))
theta_sum <- SummaryPts(fit, FUN = list(theta = theta), n.iter = 1e+3)
## n.iter should be larger in applications!
summary(theta_sum)
# compare with phm:
summary(phm(Dementia)) # the two estimators almost agree in this example

# Example 2: Youden index
Youden <- function(sens, fpr)(sens - fpr)
Youden_sum <- SummaryPts(fit, FUN = list(Youden = Youden), , n.iter = 1e+3)
## n.iter should be larger in applications!
summary(Youden_sum)
```

talpha

*The $t_\alpha$ transformation as a link function for binary GLMs.*

Description

A parametric link function, i.e. a family of link functions intended for binary data.

Usage

talpha(alpha, verbose = FALSE,
    splineinv = TRUE, eps = 2 * .Machine$double.eps, maxit = 100)
**Arguments**

- **alpha**: numeric, must be larger than 0 and smaller than 2.
- **verbose**: logical, warn if truncation occurs when link function or inverse are used.
- **splineinv**: logical, use spline interpolation for calculation of inverse link?
- **eps**: if splineinv is FALSE, a Newton-Raphson algorithm is run to calculate the inverse. The argument eps determines when to terminate this algorithm. Ignored if splineinv is TRUE.
- **maxit**: maximum number of iterations for Newton-Raphson. Ignored if splineinv is TRUE.

**Value**

An object of class "link-glm", see `family` and `family`. Intended for use with `glm`.

**Author(s)**

Philipp Doebler <philipp.doebler@googlemail.com>

**Examples**

```r
canonical <- binomial(link = talpha(1)) # logit-link
talpha_fam <- function(alpha)binomial(link = talpha(alpha)) # talpha family

## A call to glm might look like this: glm(formula, family = talpha_fam(1.5))
```
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