

Package: dtametaTMB (via r-universe)

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Title Diagnostic Test Accuracy Meta-Analysis using Template Model Builder

Version 0.1.0

Description Fits the hierarchical summary receiver operating characteristic (HSROC) model of Rutter and Gatsonis (2001) <[doi:10.1002/sim.942](https://doi.org/10.1002/sim.942)>, the bivariate binomial-normal model of Reitsma et al. (2005) <[doi:10.1016/j.jclinepi.2005.02.022](https://doi.org/10.1016/j.jclinepi.2005.02.022)>, and the threshold-based bivariate time-to-event model of Hoyer et al. (2018) <[doi:10.1002/jrsm.1273](https://doi.org/10.1002/jrsm.1273)> using Template Model Builder (TMB). Provides subgroup analyses, HSROC meta-regression, likelihood-ratio tests, SROC plots, and coupled forest plots.

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anaemia

*Anaemia (synthetic data set)***Description**

This is a synthetic data set where haemoglobin was measured by a point-of-care device, with laboratory measurement acting as the reference standard. Lower values indicate disease (anaemia).

Usage

anaemia

Format

A data frame with 81 rows and 11 variables:

study Study identifier

threshold Haemoglobin in g/dL

TP Number of true positives

FN Number of false negatives

FP Number of false positives

TN Number of true negatives

D Number of diseased individuals

H Number of healthy individuals

sens Sensitivity

fpr False positive rate

testdirection Smaller values indicate disease (=less)

Source

Synthetic dataset.

anova.dtametaTMB

*Likelihood Ratio Tests for Diagnostic Test Accuracy Models***Description**

Compare nested diagnostic test accuracy meta-analysis models using likelihood ratio tests (LRTs).

Usage

```
## S3 method for class 'Reitsma'
anova(object, ..., test = "Chisq")

## S3 method for class 'ReitsmaSubgroup'
anova(object, ..., test = "Chisq")

## S3 method for class 'RutterGatsonis'
anova(object, ..., test = "Chisq")

## S3 method for class 'RutterGatsonisSubgroup'
anova(object, ..., test = "Chisq")

## S3 method for class 'RutterGatsonisReg'
anova(object, ..., test = "Chisq")
```

Arguments

<code>object</code>	A fitted model object.
<code>...</code>	Additional fitted model objects to be compared.
<code>test</code>	Character string specifying the test to perform. Currently, only "Chisq" is supported.

Details

These methods compute likelihood ratio statistics from the fitted model log-likelihoods and compare models ordered by increasing numbers of estimated parameters. The test statistic is

$$-2(\ell_0 - \ell_1)$$

where ℓ_0 and ℓ_1 are the log-likelihoods of two nested models. Under standard regularity conditions, the statistic follows a chi-squared distribution with degrees of freedom equal to the difference in the numbers of estimated parameters.

The models supplied should be nested and fitted to the same dataset. Warnings are issued when models have identical numbers of parameters or when the log-likelihood decreases for a more complex model, suggesting that the nesting assumptions may be violated.

Value

An object of class "anova" inheriting from "data.frame" with the following columns:

Df Number of estimated parameters in the model.

logLik Model log-likelihood.

Df.diff Difference in parameters compared with the previous model.

Chisq Likelihood ratio chi-squared statistic.

Pr(>Chisq) P-value from the chi-squared test.

See Also

`logLik()`, `anova()`

anticcp

Anticcp dataset

Description

This is the anticcp data set from Nishimura (2007) from a review of anti-cyclic citrullinated peptide antibody (anti-ccp) to diagnose rheumatoid arthritis.

Usage

anticcp

Format

A data frame with 37 rows and 7 variables:

study Study identifier

year Year of the study

TP Number of true positives

FP Number of false positives

FN Number of false negatives

TN Number of true negatives

generation First generation (CCP1) or second generation (CCP2) assay

Source

Nishimura, K. et al. (2007). *Meta-analysis: diagnostic accuracy of anti-cyclic citrullinated peptide antibody and rheumatoid factor for rheumatoid arthritis*. *Annals of Internal Medicine*, 146(11), 392-403. doi:[10.7326/000348191461120070605000008](https://doi.org/10.7326/000348191461120070605000008)

as_revman.dtametaTMB *Export Model Results for RevMan*

Description

Converts fitted model objects (Reitsma, ReitsmaSubgroup, RutterGatsonis, RutterGatsonisSubgroup) into a format suitable for manual entry into the Diagnostic Test Accuracy module of Review Manager (RevMan).

Usage

```
as_revman(x, ...)

## S3 method for class 'Reitsma'
as_revman(x, ...)

## S3 method for class 'RutterGatsonis'
as_revman(x, ...)

## S3 method for class 'ReitsmaSubgroup'
as_revman(x, ...)

## S3 method for class 'RutterGatsonisSubgroup'
as_revman(x, ...)
```

Arguments

x	A fitted model object.
...	Currently not used.

Value

A data frame with columns:

Subgroup Only returned for ReitsmaSubgroup and RutterGatsonisSubgroup objects.

Externally_Calculated_Parameters Revman model/parameter types.

Parameter RevMan parameter name.

Estimate Parameter estimate.

The returned table contains the model parameters displayed by RevMan:

- E(logitSe)
- E(logitSp)
- Var(logitSe)
- Var(logitSp)
- Cov(logits)

- `Corr(logits)`
- `Lambda`
- `Theta`
- `beta`
- `Var(accuracy)`
- `Var(threshold)`
- `SE(E(logitSe))`
- `SE(E(logitSp))`
- `Cov(Es)`
- `Studies`

Note

For Rutter and Gatsonis models `SE(E(logitSe))`, `SE(E(logitSp))`, and `Cov(Es)` are not computed.

diabetes

Diabetes dataset

Description

This is the diabetes data set from the supplementary material in Hoyer (2018).

Usage

diabetes

Format

A data frame with 124 rows and 9 variables

study Study identifier

threshold Threshold HbA1c used to derive TP, FN, FP, TN

TP Number of true positives

TN Number of true negatives

FP Number of false positives

FN Number of false negatives

D Number of diseased individuals

H Number of healthy individuals

originally_published Whether the data threshold/row was used in the original publication (1=yes, 0=no)

Source

Hoyer, A., Hirt, S., Kuss, O. (2018). *Meta-analysis of full ROC curves using bivariate time-to-event models for interval-censored data*. Research Synthesis Methods, 9(1), 62-72. doi:[10.1002/jrsm.1273](https://doi.org/10.1002/jrsm.1273)

dtametaTMB

dtametaTMB: Diagnostic Test Accuracy Meta-Analysis using Template Model Builder

Description

Functions for fitting diagnostic test accuracy (DTA) meta-analysis models using Template Model Builder (TMB).

Details

Implemented methods

- Reitsma model
- Rutter-Gatsonis HSROC model
- Hoyer multiple-threshold model

Main workflow

- `fitReitsma()` -> `plot()` -> `forest()`
- `fitReitsmaSubgroup()` -> `plot()` -> `forest()`
- `fitRutterGatsonis()` -> `plot()` -> `forest()`
- `fitRutterGatsonisSubgroup()` -> `plot()` -> `forest()`
- `fitHoyer()` -> `plot()` -> `forest()`

Included datasets

- anaemia
- anticcp
- diabetes
- FENO
- RF
- schuetz

See the package vignettes for worked examples and model descriptions.

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FENO*FENO dataset*

Description

This is the FENO data set from Schneider (2017) from a review of fractional exhaled nitric oxide (FeNO) for diagnosis of asthma.

Usage

FENO

Format

A data frame with 150 rows and 7 variables:

study Study identifier

study_id Study identifier (numeric)

cutoff Threshold for FeNO measured in ppb

TP Number of true positives

FN Number of false negatives

FP Number of false positives

TN Number of true negatives

Note

The data are reproduced from the original source and the supplementary material accompanying the Cochrane Handbook. However, the study 'Schneider 2013' contains inconsistent diseased counts (TP + FN). To illustrate the Hoyer analysis in the vignette, we modify the TP counts in rows 118–120 from 39 to 38. Other corrections restoring internal consistency are also conceivable.

Source

Schneider, A. et al. (2017). *A novel statistical model for analyzing data of a systematic review generates optimal cutoff values for fractional exhaled nitric oxide for asthma diagnosis*. Journal of Clinical Epidemiology, 92, 69-78. doi:[10.1016/j.jclinepi.2017.09.001](https://doi.org/10.1016/j.jclinepi.2017.09.001)

fitHoyer

Fit Threshold-Based Bivariate Time-to-Event Model (Hoyer)

Description

This is a high-level wrapper that performs the full workflow for fitting the Hoyer AFT model:

1. Restructuring of threshold-based data into interval format
2. Estimation of initial parameter values
3. Model fitting via likelihood maximization

The input data must contain cumulative counts for true positives, false positives, false negatives, and true negatives at multiple thresholds within each study.

Usage

```
fitHoyer(
  data,
  TP,
  FP,
  FN,
  TN,
  study,
  threshold,
  smallest,
  largest,
  testdirection = c("greater", "less"),
  eval_threshold = NULL,
  conflevel = 0.95,
  dist = "loglogistic",
  verbose = FALSE,
  ...
)
```

Arguments

data	A data.frame containing study-level data.
TP	True positives (column name).
FP	False positives (column name).
FN	False negatives (column name).
TN	True negatives (column name).
study	Study identifier (column name).
threshold	The observed threshold value (column name). Must be positive and strictly increasing within each study.

<code>smallest</code>	Positive lower bound used to define the leftmost interval. Must be smaller than minimum threshold.
<code>largest</code>	Positive upper bound used to define the rightmost interval. Must be greater than maximum threshold.
<code>testdirection</code>	Direction of the test. Enter "greater" when larger test values indicate disease. Conversely, enter "less" when lower test values indicate disease (e.g. anaemia-type tests). Defaults to "greater".
<code>eval_threshold</code>	Optional numeric value or vector specifying the prediction grid threshold(s) at which sensitivity and specificity should be evaluated. If NULL (default), the median threshold from the original data is used.
<code>conflevel</code>	Confidence level for confidence intervals for sensitivities and specificities at the chosen thresholds. Defaults to 0.95.
<code>dist</code>	Character string specifying the parametric distribution for the AFT model. One of "weibull", "lognormal", or "loglogistic" (default).
<code>verbose</code>	Whether TMB optimization output should be printed (default: FALSE).
<code>...</code>	Additional arguments passed to <code>fitHoyerAFT</code> .

Details

Fits the threshold-based bivariate accelerated failure time (AFT) model for diagnostic test accuracy (DTA) meta-analysis as described by Hoyer et al. (2018). The model is estimated using interval-censored likelihoods via Template Model Builder (TMB).

The function internally calls:

- `restructure_data` to convert cumulative counts into interval-censored data
- `initHoyerAFT` to estimate starting values
- `fitHoyerAFT` to fit the model

Missing values in the input data are removed prior to analysis. A message is issued listing the affected studies.

Value

An object of class "HoyerAFT" as returned by `fitHoyerAFT`, containing:

data Processed original data
restructured Interval-formatted data
fit Optimization output
sdreport TMB report object
sdreport2 Summary of reported parameters
sensspec Sensitivity and specificity estimates

Note

Requires a compiled TMB model named "Hoyer".

References

Hoyer, A., Hirt, S., Kuss, O. (2018). Meta-analysis of full ROC curves using bivariate time-to-event models for interval-censored data. *Research Synthesis Methods*, 9(1), 62-72. doi:[10.1002/jrsm.1273](https://doi.org/10.1002/jrsm.1273)

Examples

```
data("diabetes")
fit <- fitHoyer(
  data = diabetes,
  TP = TP,
  FP = FP,
  FN = FN,
  TN = TN,
  study = study,
  threshold = threshold,
  testdirection = "greater",
  smallest = 2,
  largest = 10
)
summary(fit)
```

fitHoyerAFT

Fit Threshold-Based Bivariate Time-to-Event Model (Hoyer AFT)

Description

Fits a bivariate accelerated failure time (AFT) model for diagnostic test accuracy (DTA) data using interval-censored likelihoods as described in Hoyer et al. (2018). The model is estimated using Template Model Builder (TMB) with study-specific random effects.

Usage

```
fitHoyerAFT(
  data,
  init,
  conflevel = 0.95,
  eval_threshold = NULL,
  verbose = FALSE
)
```

Arguments

data A list as produced by [restructure_data](#), containing:
restructured Interval-formatted data
original Processed original data with derived quantities

<code>init</code>	A data frame of initial parameter values as produced by <code>initHoyerAFT</code> .
<code>conflvel</code>	Confidence level for confidence intervals for sensitivities and specificities at the chosen thresholds. Defaults to 0.95.
<code>eval_threshold</code>	Optional numeric value or vector specifying the prediction grid threshold(s) at which sensitivity and specificity should be evaluated. If NULL (default), the median threshold from the original data is used.
<code>verbose</code>	Whether TMB optimization output should be printed (default: FALSE).

Details

The model reports logit-survival quantities, which correspond to sensitivity and false positive rate for `testdirection = "greater"`, and to false negative rate and specificity for `testdirection = "less"`.

Model fitting is performed using `nlminb`, and uncertainty estimates are obtained via `TMB::sdreport`. Parameter transformations include log-scale parameters and Fisher's Z-transform for correlations.

Value

An object of class "HoyerAFT" containing:

data Processed original data
restructured Interval-formatted data
fit Optimization output from `nlminb`
sdreport TMB report object from `sdreport`
sdreport2 Summary of reported parameters
distcode Distribution code used in the model
sensspec Sensitivities and specificities at the chosen thresholds

Note

Requires a compiled TMB model named "Hoyer".

References

Hoyer, A., Hirt, S., Kuss, O. (2018). Meta-analysis of full ROC curves using bivariate time-to-event models for interval-censored data. *Research Synthesis Methods*, 9(1), 62-72. doi:10.1002/jrsm.1273

Examples

```
data("diabetes")
res <- restructure_data(
  data = diabetes,
  TP = TP,
  FP = FP,
  FN = FN,
  TN = TN,
```

```

    threshold = threshold,
    study = study,
    smallest = 2,
    largest = 10
  )
  init <- initHoyerAFT(res$restructured)
  fit <- fitHoyerAFT(res, init)
  summary(fit)

```

fitReitsma

Fit Reitsma Model

Description

Fits the Reitsma bivariate random-effects model for diagnostic test accuracy (DTA) meta-analysis using a binomial-normal likelihood via `glmmTMB`.

Usage

```
fitReitsma(data, TP, FP, FN, TN, study, constrain = NULL, conflevel = 0.95)
```

Arguments

<code>data</code>	A <code>data.frame</code> containing study-level data.
<code>TP</code>	True positives (column name).
<code>FP</code>	False positives (column name).
<code>FN</code>	False negatives (column name).
<code>TN</code>	True negatives (column name).
<code>study</code>	Study identifier (column name).
<code>constrain</code>	Optional character string specifying a simplified covariance structure for the Reitsma model. This can be useful for sparse data, small meta-analyses, or for reproducing simplified bivariate models described in the Cochrane Handbook for Diagnostic Test Accuracy Reviews. Allowed values are: <code>NULL</code> The standard unconstrained Reitsma model is fitted. <code>"sigma_AB"</code> The covariance between logit-sensitivity and logit-specificity random effects is fixed at zero. Random effects remain independent. <code>"sigma2_A"</code> The between-study variance of logit-sensitivity is fixed at zero. This also implies a zero covariance. <code>"sigma2_B"</code> The between-study variance of logit-specificity is fixed at zero. This also implies a zero covariance. <code>"all"</code> All random-effects variance and covariance parameters are fixed at zero, resulting in a fixed-effects model.
<code>conflevel</code>	Confidence level for confidence intervals. Default is 0.95.

Value

A list of class "Reitsma" with components:

- data: the original data set with derived quantities
- glmmTMB: fitted model object.
- estimates: parameter estimates with SE.
- vcov: variance-covariance matrix.
- sensspec: sensitivity and specificity estimates.
- LRDOR: Diagnostic odds ratio and likelihood ratios.
- RutterGatsonis_recovered: Recovered parameters in the Rutter-Gatsonis (HSROC) parameterization.
- constrain: Random effects parameters fixed at zero.

References

- Reitsma, J. B., et al. (2005). Bivariate analysis of sensitivity and specificity produces informative summary measures in diagnostic reviews. *Journal of Clinical Epidemiology*, 58(10), 982–990. doi:10.1016/j.jclinepi.2005.02.022
- Rutter, C. M., & Gatsonis, C. A. (2001). A hierarchical regression approach to meta-analysis of diagnostic test accuracy evaluations. *Statistics in Medicine*, 20(19), 2865–2884. doi:10.1002/sim.942
- Harbord, R. M., Deeks, J. J., Egger, M., Whiting, P., & Sterne, J. A. C. (2007). A unification of models for meta-analysis of diagnostic accuracy studies. *Biostatistics*, 8(2), 239–251. doi:10.1093/biostatistics/kx1004

Examples

```
data("anticcp")
fit <- fitReitsma(
  data = anticcp,
  TP = TP,
  FP = FP,
  FN = FN,
  TN = TN,
  study = study
)
fit$estimates
```

fitReitsmaSubgroup	<i>Fit Reitsma Subgroup Model</i>
--------------------	-----------------------------------

Description

Fits the Reitsma bivariate random-effects model with a single categorical covariate for diagnostic test accuracy (DTA) meta-analysis using a binomial-normal likelihood via `glmmTMB`. The model is fitted twice, once with dummy/reference cell coding, and once with central-mean parameterization.

Usage

```
fitReitsmaSubgroup(
  data,
  TP,
  FP,
  FN,
  TN,
  study,
  subgroup,
  constrain = NULL,
  sensspec_constrain = NULL,
  variances = c("common", "unequal"),
  conflevel = 0.95
)
```

Arguments

<code>data</code>	A <code>data.frame</code> containing study-level data.
<code>TP</code>	True positives (column name).
<code>FP</code>	False positives (column name).
<code>FN</code>	False negatives (column name).
<code>TN</code>	True negatives (column name).
<code>study</code>	Study identifier (column name).
<code>subgroup</code>	A single categorical study-level subgroup variable (column name).
<code>constrain</code>	Optional character string specifying a simplified covariance structure for the Reitsma model. This can be useful for sparse data, small meta-analyses, or for reproducing simplified bivariate models described in the Cochrane Handbook for Diagnostic Test Accuracy Reviews. Allowed values are: <code>NULL</code> The standard unconstrained Reitsma model is fitted. <code>"sigma_AB"</code> The covariance between logit-sensitivity and logit-specificity random effects is fixed at zero. Random effects remain independent.

"sigma2_A" The between-study variance of logit-sensitivity is fixed at zero. This also implies a zero covariance.

"sigma2_B" The between-study variance of logit-specificity is fixed at zero. This also implies a zero covariance.

"all" All random-effects variance and covariance parameters are fixed at zero, resulting in a fixed-effects model.

These random-effects simplifications are currently only available for `variances="common"`.

`sensspec_constrain`

Optional character vector specifying restrictions on subgroup-specific logit-sensitivity and/or logit-specificity parameters.

This can be useful for testing whether subgroup differences are present in sensitivity, specificity, or both.

Allowed values are:

"sens" Constrain all subgroup-specific logit-sensitivity parameters to be equal. Subgroup differences are therefore only allowed in logit-specificity.

"spec" Constrain all subgroup-specific logit-specificity parameters to be equal. Subgroup differences are therefore only allowed in logit-sensitivity.

Both constraints may be specified simultaneously, e.g. `sensspec_constrain = c("sens", "spec")`, which forces all subgroup-specific sensitivity and specificity parameters to be equal across subgroups.

If NULL (default), separate sensitivity and specificity parameters are estimated for each subgroup.

`variances`

Whether the between-study random-effects variance-covariance matrix should be assumed to be "common" (default) or "unequal" across subgroups. If "common", a single between-study variance-covariance matrix is estimated and shared across all subgroups. If "unequal", subgroup-specific variance-covariance matrices are estimated.

`conflvel`

Confidence level for confidence intervals. Default is 0.95.

Value

A list of class "ReitsmaSubgroup" with components:

- `data`: the original data set with derived quantities
- `glmmTMB_mu`: fitted model object with cell means parameterization.
- `estimates_mu`: parameter estimates with SE with cell means parameterization.
- `vcov_mu`: variance-covariance matrix with cell means parameterization.
- `sensspec`: sensitivity and specificity estimates.
- `glmmTMB_nu`: fitted model object with dummy/reference-cell parameterization
- `estimates_nu`: parameter estimates with SE with dummy/reference-cell parameterization.
- `vcov_nu`: variance-covariance matrix with dummy/reference-cell parameterization.
- `LRDOR`: Diagnostic odds ratios and likelihood ratios.
- `RutterGatsonis_recovered`: Recovered parameters in the Rutter-Gatsonis (HSROC) parameterization.

- subgroups: The subgroup levels used in the model fit.
- constrain: Random effects parameters fixed at zero.
- variances: Variance structure used in the fitted model.

References

- Reitsma, J. B., et al. (2005). Bivariate analysis of sensitivity and specificity produces informative summary measures in diagnostic reviews. *Journal of Clinical Epidemiology*, 58(10), 982–990. doi:10.1016/j.jclinepi.2005.02.022
- Rutter, C. M., & Gatsonis, C. A. (2001). A hierarchical regression approach to meta-analysis of diagnostic test accuracy evaluations. *Statistics in Medicine*, 20(19), 2865–2884. doi:10.1002/sim.942
- Harbord, R. M., Deeks, J. J., Egger, M., Whiting, P., & Sterne, J. A. C. (2007). A unification of models for meta-analysis of diagnostic accuracy studies. *Biostatistics*, 8(2), 239–251. doi:10.1093/biostatistics/kxl004

Examples

```
data("anticcp")
fit <- fitReitsmaSubgroup(
  data = anticcp,
  TP = TP,
  FP = FP,
  FN = FN,
  TN = TN,
  study = study,
  subgroup = generation
)
fit
summary(fit)
```

fitRutterGatsonis

Fit the Rutter and Gatsonis (HSROC) model

Description

Fits the hierarchical summary receiver operating characteristic (HSROC) model as proposed by Rutter and Gatsonis for meta-analysis of diagnostic test accuracy (DTA) studies using Template Model Builder (TMB).

Usage

```
fitRutterGatsonis(
  data,
  TP,
  FP,
```

```

    FN,
    TN,
    study,
    conflevel = 0.95,
    constrain = NULL,
    spec = NULL,
    verbose = FALSE
  )

```

Arguments

<code>data</code>	A data.frame containing study-level data.
<code>TP</code>	True positives (column name).
<code>FP</code>	False positives (column name).
<code>FN</code>	False negatives (column name).
<code>TN</code>	True negatives (column name).
<code>study</code>	Study identifier (column name).
<code>conflevel</code>	Confidence level for confidence intervals. Default is 0.95.
<code>constrain</code>	Optional character vector specifying model parameters that should be fixed at zero during estimation. This can be useful for sparse data, small meta-analyses, or for reproducing simplified HSROC models described in the Cochrane Handbook for Diagnostic Test Accuracy Reviews. Allowed values are: " sigma2_alpha " Fix the between-study variance of the HSROC accuracy random effect at zero. " sigma2_theta " Fix the between-study variance of the HSROC threshold random effect at zero. " shape " Fix the HSROC shape parameter (beta) at zero, resulting in a symmetric summary ROC curve. Multiple constraints may be specified simultaneously, e.g. <code>constrain = c("sigma2_alpha", "shape")</code> . If NULL (default), the unconstrained HSROC model is fitted.
<code>spec</code>	Optional specificity value at which sensitivity is estimated. If NULL, the median observed specificity is used as a proxy.
<code>verbose</code>	Whether TMB optimization output should be printed (default: FALSE).

Details

The function internally transforms the data into long format and fits the model via maximum likelihood using TMB. Random effects are included for study-specific accuracy and threshold parameters.

Reitsma parameterization is recovered from the fitted HSROC parameters.

The `constrain` argument allows simplified HSROC models to be fitted by fixing selected parameters at zero. These constrained models may improve numerical stability in sparse datasets and can

be used to reproduce several simplified models presented in the Cochrane Handbook for Diagnostic Test Accuracy Reviews.

Constraints are imposed using parameter mapping within Template Model Builder (TMB), so constrained parameters are excluded from numerical optimization and treated as fixed constants.

Value

An object of class "RutterGatsonis" containing:

data Processed input data with derived quantities.

fit Optimization result from nlminb.

sdreport TMB standard report.

sdreport2 Summary of reported parameters.

sensspec Estimated sensitivity at given specificity with confidence intervals.

Reitsma_recovered Recovered parameters in the Reitsma parameterization.

constrain Parameters fixed at zero.

Note

Requires a compiled TMB model named "RutterGatsonis".

References

Reitsma, J. B., et al. (2005). Bivariate analysis of sensitivity and specificity produces informative summary measures in diagnostic reviews. *Journal of Clinical Epidemiology*, 58(10), 982–990. doi:10.1016/j.jclinepi.2005.02.022

Rutter, C. M., & Gatsonis, C. A. (2001). A hierarchical regression approach to meta-analysis of diagnostic test accuracy evaluations. *Statistics in Medicine*, 20(19), 2865–2884. doi:10.1002/sim.942

Harbord, R. M., Deeks, J. J., Egger, M., Whiting, P., & Sterne, J. A. C. (2007). A unification of models for meta-analysis of diagnostic accuracy studies. *Biostatistics*, 8(2), 239–251. doi:10.1093/biostatistics/kx1004

Examples

```
data("RF")
fit <- fitRutterGatsonis(
  data = RF,
  TP = TP,
  FP = FP,
  FN = FN,
  TN = TN,
  study = study
)
summary(fit)
```

fitRutterGatsonisReg *Fit the Rutter and Gatsonis Regression Model*

Description

Fits a general HSROC meta-regression model using user-supplied design matrices for estimation and prediction.

Usage

```
fitRutterGatsonisReg(
  data,
  TP,
  FP,
  FN,
  TN,
  study,
  Z,
  Z_pred = NULL,
  map = NULL,
  init = NULL,
  spec = NULL,
  conflevel = 0.95,
  verbose = FALSE
)
```

Arguments

data	A data.frame containing study-level data.
TP	True positives (column name).
FP	False positives (column name).
FN	False negatives (column name).
TN	True negatives (column name).
study	Study identifier (column name).
Z	Design matrix containing covariate values for model fitting. The current implementation is intended primarily for study-level covariates. In the long-format representation, this typically means that each study is represented by two consecutive rows with identical covariate values. The number of rows of Z must equal twice the number of studies.
Z_pred	Prediction design matrix used to obtain covariate-specific parameter estimates and SROC curves. Each row defines a covariate pattern at which predictions are evaluated. The number of columns of Z_pred must equal the number of columns of Z. If NULL (default), a single row of zeros is used. For meaningful predictions, users will typically want to specify Z_pred explicitly.

map	Optional named list of parameter mappings passed to MakeADFun. Parameter mapping allows selected model parameters to be fixed or constrained during estimation. This can be useful for fitting simplified HSROC models, imposing equality constraints, or reproducing model specifications described in the literature. Each component of map should be a factor vector with the same length as the corresponding parameter. Parameters assigned NA levels are fixed at their initial values supplied via the <code>init</code> argument, whereas parameters sharing the same factor level are estimated as equal. This is an advanced feature intended primarily for users familiar with Template Model Builder (TMB). If NULL (default), all model parameters are estimated freely. Example <code>map = list(shape_coef=factor(c(1, rep(NA, ncol(Z) - 1))))</code>.
init	Optional list of initial parameter values. If NULL (default), all fixed and random effects are initialized to zero. Advanced users may provide a named list containing: accuracy_coef Initial values for the accuracy regression coefficients. threshold_coef Initial values for the threshold regression coefficients. shape_coef Initial values for the shape regression coefficients. log_sigma_alpha Initial value for the log standard deviation of the accuracy random effects. log_sigma_theta Initial value for the log standard deviation of the threshold random effects. alpha Initial values for the study-specific accuracy random effects. theta Initial values for the study-specific threshold random effects. The lengths of <code>accuracy_coef</code>, <code>threshold_coef</code>, and <code>shape_coef</code> must equal the number of columns in <code>Z</code>. The lengths of <code>alpha</code> and <code>theta</code> must equal the number of studies.
spec	Optional specificity value or vector of specificity values at which sensitivity is evaluated for each covariate pattern specified in <code>Z_pred</code> . If NULL, the median observed specificity is used.
conlevel	Confidence level for confidence intervals. Default is 0.95.
verbose	Logical indicating whether TMB optimization output should be printed (default: FALSE).

Details

This function is intended for advanced users who wish to specify design matrices directly. The user is responsible for constructing appropriate design matrices, choosing prediction covariate patterns through `Z_pred`, and interpreting or visualizing the resulting regression model.

By default, all fixed and random effects are initialized at zero. For difficult optimization problems, user-supplied starting values may be provided through the `init` argument.

The fitted model estimates covariate effects on the HSROC accuracy, threshold, and optionally shape parameters. Predicted sensitivities are obtained by evaluating the resulting SROC curve(s) at the specificity value(s) supplied through `spec` and the covariate patterns defined by `Z_pred`.

Value

An object of class "RutterGatsonisReg" containing:

data Processed input data with derived quantities.

fit Optimization result returned by nlminb.

sdreport TMB standard report object.

sdreport2 Summary of reported model parameters and derived quantities.

sensspec Estimated sensitivities at the specified specificity value(s), including confidence intervals.

constrain Constraints on parameters applied during model fitting.

Note

Requires a compiled TMB model named "RutterGatsonisReg".

References

Reitsma, J. B., Glas, A. S., Rutjes, A. W. S., Scholten, R. J. P. M., Bossuyt, P. M., & Zwinderman, A. H. (2005). Bivariate analysis of sensitivity and specificity produces informative summary measures in diagnostic reviews. *Journal of Clinical Epidemiology*, 58(10), 982–990. doi:10.1016/j.jclinepi.2005.02.022

Rutter, C. M., & Gatsonis, C. A. (2001). A hierarchical regression approach to meta-analysis of diagnostic test accuracy evaluations. *Statistics in Medicine*, 20(19), 2865–2884. doi:10.1002/sim.942

Harbord, R. M., Deeks, J. J., Egger, M., Whiting, P., & Sterne, J. A. C. (2007). A unification of models for meta-analysis of diagnostic accuracy studies. *Biostatistics*, 8(2), 239–251. doi:10.1093/biostatistics/kxl004

Examples

```
data("RF")
RF2      <- RF[RF$method %in% c("LA", "ELISA", "Nephelometry"),]
RF2$method <- factor(RF2$method, levels=c("LA", "ELISA", "Nephelometry"))
Z <- model.matrix(~ method, data = RF2)
Z <- Z[rep(seq_len(nrow(Z)), each = 2), , drop = FALSE]
Z_pred <- matrix(c(1,0,0,1,1,0,1,0,1), ncol=3, nrow=3, byrow=TRUE)

fit <- fitRutterGatsonisReg(
  data = RF2,
  TP = TP,
  FP = FP,
  FN = FN,
  TN = TN,
  study = study,
  Z = Z,
  Z_pred = Z_pred
)

summary(fit)
```

fitRutterGatsonisSubgroup

Fit the Rutter and Gatsonis Subgroup Model

Description

The function fits an HSROC model with a single categorical study-level covariate (subgroup).

Usage

```
fitRutterGatsonisSubgroup(
  data,
  TP,
  FP,
  FN,
  TN,
  study,
  subgroup,
  constrain = NULL,
  spec = NULL,
  conflevel = 0.95,
  verbose = FALSE
)
```

Arguments

data	A data.frame containing study-level data.
TP	True positives (column name).
FP	False positives (column name).
FN	False negatives (column name).
TN	True negatives (column name).
study	Study identifier (column name).
subgroup	A single categorical study-level subgroup variable (column name).
constrain	Optional character vector specifying model parameters that should be constrained during estimation. This can be useful for sparse data, small meta-analyses, or for reproducing simplified HSROC models described in the Cochrane Handbook for Diagnostic Test Accuracy Reviews. Allowed values are: "sigma2_alpha" Fix the between-study variance of the HSROC accuracy random effect at zero. "sigma2_theta" Fix the between-study variance of the HSROC threshold random effect at zero. "accuracy" No subgroup effect on accuracy.

	"threshold" No subgroup effect on threshold.
	"shape" No subgroup effect on shape.
	"shape_zero" All shape parameters (beta's) are fixed at zero.
	Multiple constraints may be specified simultaneously, e.g. <code>constrain = c("sigma2_alpha", "shape")</code> .
	<code>shape_zero</code> overrides <code>shape</code> .
	If NULL (default), the unconstrained HSROC model is fitted.
<code>spec</code>	Optional specificity value or vector of specificity values at which sensitivity is estimated. If NULL, the median observed specificity is used as a proxy.
<code>conflevel</code>	Confidence level for confidence intervals. Default is 0.95.
<code>verbose</code>	Whether TMB optimization output should be printed (default: FALSE).

Details

The function fits an HSROC model with a single categorical study-level covariate (subgroup). Separate subgroup effects are estimated for the accuracy and threshold parameters. Optionally, subgroup-specific effects can also be estimated for the shape parameter.

The fitted model returns subgroup-specific summary sensitivity estimates evaluated at user-specified specificity values. If `spec = NULL`, the median observed specificity is used as a proxy.

This function is intended as a convenient wrapper for subgroup analyses with a single categorical covariate and provides output suitable for dedicated `summary()`, `plot()`, and `forest()` methods.

Value

An object of class "RutterGatsonisSubgroup" containing:

data Processed input data with derived quantities.

fit Optimization result from `nlmminb`.

sdreport TMB standard report.

sdreport2 Summary of reported subgroup-specific parameters.

sensspec Estimated subgroup-specific sensitivities at the given specificity value(s), with confidence intervals.

subgroups The subgroup levels used in the model fit.

constrain Constraints on parameters applied during model fitting.

Note

Requires a compiled TMB model named "RutterGatsonisReg".

References

Reitsma, J. B., et al. (2005). Bivariate analysis of sensitivity and specificity produces informative summary measures in diagnostic reviews. *Journal of Clinical Epidemiology*, 58(10), 982–990. [doi:10.1016/j.jclinepi.2005.02.022](https://doi.org/10.1016/j.jclinepi.2005.02.022)

Rutter, C. M., & Gatsonis, C. A. (2001). A hierarchical regression approach to meta-analysis of diagnostic test accuracy evaluations. *Statistics in Medicine*, 20(19), 2865–2884. doi:[10.1002/sim.942](https://doi.org/10.1002/sim.942)

Harbord, R. M., Deeks, J. J., Egger, M., Whiting, P., & Sterne, J. A. C. (2007). A unification of models for meta-analysis of diagnostic accuracy studies. *Biostatistics*, 8(2), 239–251. doi:[10.1093/biostatistics/kxl004](https://doi.org/10.1093/biostatistics/kxl004)

Examples

```
data("RF")
fit <- fitRutterGatsonisSubgroup(
  data = RF,
  TP = TP,
  FP = FP,
  FN = FN,
  TN = TN,
  study = study,
  subgroup = method
)
summary(fit)
```

forest

Forest plot generic

Description

Produces coupled forest plots.

Usage

```
forest(x, ...)
```

Arguments

x	Object
...	Additional arguments

Value

No return value. Called for its side effect of producing a plot.

forest.Cochrane	<i>Coupled Forest plot for diagnostic test accuracy meta-analysis</i>
-----------------	---

Description

Provides coupled forest plots of sensitivities and specificities with Clopper-Pearson confidence limits.

Usage

```
## S3 method for class 'Cochrane'
forest(x, conflevel = 0.95, ...)
```

Arguments

x	Object of class "Cochrane" such as "RutterGatsonis", "Reitsma" or "HoyerAFT"
conflevel	Confidence level for confidence intervals. Default is 0.95.
...	Additional graphical arguments (not currently in use)

Value

No return value. Called for its side effect of producing a plot.

forest.CochraneSubgroup	<i>Coupled Forest plot for diagnostic test accuracy meta-analysis</i>
-------------------------	---

Description

Provides coupled forest plots of sensitivities and specificities with Clopper-Pearson confidence limits.

Usage

```
## S3 method for class 'CochraneSubgroup'
forest(x, conflevel = 0.95, subgroup_label = "Subgroup", ...)
```

Arguments

x	Object of class "CochraneSubgroup" such as "RutterGatsonisSubgroup", "ReitsmaSubgroup"
conflevel	Confidence level for confidence intervals. Default is 0.95.
subgroup_label	Column name for the subgroup. Defaults to "Subgroup".
...	Additional graphical arguments (not currently in use)

Value

No return value. Called for its side effect of producing a plot.

initHoyerAFT

Compute Initial Parameter Values for Hoyer AFT Models

Description

Computes initial values for the threshold-based bivariate time-to-event model of Hoyer et al. (2018).

Usage

```
initHoyerAFT(restructured, dist = "loglogistic")
```

Arguments

restructured	A data frame in interval format as produced by restructure_data (specifically the restructured component of its output). Must contain the columns: study Study identifier lowerB Lower interval bound upperB Upper interval bound events0 Non-diseased counts within interval events1 Diseased counts within interval ctype Censoring type (1 = left, 2 = interval, 3 = right) lcutmean Midpoint of log-threshold interval
dist	Character string specifying the parametric distribution used in the survival regression models. Must be one of: "weibull", "lognormal", or "loglogistic". Default is "loglogistic".

Details

The function fits separate intercept-only parametric survival models for diseased and non-diseased groups using weighted interval-censored likelihoods. It further derives initial estimates of between-study variability based on study-specific weighted averages of log-thresholds.

To ensure compatibility with `survival::survreg`, interval bounds are modified as follows:

- Left-censored intervals (`ctype = 1`) are assigned a small positive lower bound.
- Right-censored intervals (`ctype = 3`) are assigned an infinite upper bound.

Value

A single-row data frame containing initial parameter values:

beta0_init Intercept for non-diseased group

lambda0_init Scale parameter for non-diseased group

beta1_init Intercept for diseased group

lambda1_init Scale parameter for diseased group

su0_init Standard deviation of random effects (non-diseased)

su1_init Standard deviation of random effects (diseased)

coru0u1_init Correlation between random effects

distcode Numeric code for the distribution (1 = Weibull, 2 = lognormal, 3 = loglogistic)

References

Hoyer, A., Hirt, S., Kuss, O. (2018). Meta-analysis of full ROC curves using bivariate time-to-event models for interval-censored data. *Research Synthesis Methods*, 9(1), 62-72. doi:10.1002/jrsm.1273

Examples

```
data("diabetes")
res <- restructure_data(
  data = diabetes,
  TP = TP,
  FP = FP,
  FN = FN,
  TN = TN,
  threshold = threshold,
  study = study,
  smallest = 2,
  largest = 10
)
init <- initHoyerAFT(res$restructured)
```

Description

Returns the maximized log-likelihood for a fitted diagnostic test accuracy meta-analysis model. The returned value is an object of class "logLik" and includes the number of estimated parameters (df) and the number of observations used in model fitting (nobs).

Usage

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

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

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

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

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

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

Arguments

object	A fitted model object.
...	Not used.

Value

An object of class "logLik".

See Also

[anova.dtametaTMB\(\)](#)

plot.HoyerAFT

Plot Results from a Hoyer Model

Description

Produces a hierarchical summary receiver operating characteristic (HSROC) plot from a fitted Hoyer AFT model. The plot shows study-level sensitivity and specificity estimates together with the meta-analytic HSROC curve derived from the fitted model.

Usage

```
## S3 method for class 'HoyerAFT'
plot(
  x,
  scale = 0.02,
```

```

size = c("equal", "sampsiz", "se"),
thresholdrange = NULL,
main = "Diagnostic Test Accuracy Meta-Analysis",
...
)

```

Arguments

x	An object of class "HoyerAFT" as returned by fitHoyerAFT. Must contain: original Original processed data including sensitivity (sens) and false positive rate (fpr) sdreport2 Summary of model parameters distcode Distribution code (1 = Weibull, 2 = lognormal, 3 = loglogistic)
scale	A numeric scaling factor controlling the size of the rectangles representing study weights. Default is 0.02.
size	Character string controlling study weight display: "equal" All studies shown with equal size. Default "sampsiz" Size proportional to sample size "se" Size proportional to precision on the logit scale
thresholdrange	A numeric vector of length 2 giving the range of threshold over which sensitivities and specificities are predicted. If NULL (default), then the minimum and maximum thresholds from the data are used.
main	Character string giving the main title of the plot. Defaults to "Diagnostic Test Accuracy Meta-Analysis".
...	Additional graphical arguments (currently unused).

Details

The plot includes:

- Study-specific sensitivity and false positive rate estimates
- Rectangular markers representing study observations
- Lines connecting thresholds within studies
- A meta-analytic HSROC curve based on the fitted AFT model

The HSROC curve is constructed using the estimated model parameters and depends on the specified distribution:

- Weibull
- Lognormal
- Loglogistic

The plot is constructed on the ROC scale with sensitivity on the y-axis and specificity on the x-axis (displayed as 1 - false positive rate on a reversed axis).

Value

No return value. Called for its side effect of producing a plot.

See Also

[fitHoyerAFT](#) [fitHoyer](#)

plot.Reitsma

Plot Results from a Reitsma Model

Description

Produces a summary ROC plot for objects of class "Reitsma" obtained from [fitReitsma](#). The plot displays study-level estimates of sensitivity and specificity, the summary operating point, and corresponding confidence and prediction regions. Optionally, the HSROC (hierarchical summary ROC) curve can be overlaid.

Usage

```
## S3 method for class 'Reitsma'
plot(
  x,
  scale = 0.02,
  size = c("fisher", "equal", "sampsize", "se"),
  main = "Diagnostic Test Accuracy Meta-Analysis",
  HSROC = FALSE,
  specrange = c(0.7, 0.995),
  conflevel = 0.95,
  predlevel = 0.95,
  ...
)
```

Arguments

x	An object of class "Reitsma", as returned by fitReitsma .
scale	A numeric scaling factor controlling the size of the rectangles representing study weights. Default is 0.02.
size	Character string controlling study weight display: "fisher" Size proportional to a decomposition of Fisher's Information matrix. Default. "equal" All studies shown with equal size "sampsize" Size proportional to sample size "se" Size proportional to precision on the logit scale
main	Character string giving the main title of the plot. Defaults to "Diagnostic Test Accuracy Meta-Analysis".

HSROC	if TRUE, the HSROC curve is added to the plot. Default is FALSE.
specrange	A numeric vector of length 2 giving the range of specificities over which the HSROC curve is plotted. Defaults to <code>c(0.7, 0.995)</code> .
conflvel	Confidence level for the confidence region. Default is 0.95.
predlevel	Confidence level for the prediction region. Default is 0.95.
...	Additional graphical arguments passed to plotting functions.

Details

The plot is constructed on the ROC scale with sensitivity on the y-axis and specificity on the x-axis (displayed as 1 - false positive rate on a reversed axis).

Study-specific estimates are shown as rectangles, where the size reflects approximate study weights derived from the Fisher information matrix.

The following elements are displayed:

- Study-level sensitivity and specificity estimates
- Summary (pooled) estimate
- confidence region around the summary point
- prediction region reflecting between-study variability
- Optional HSROC curve (if HSROC = TRUE)

Confidence and prediction regions are derived using the delta method based on the estimated variance-covariance structure of the model.

Value

No return value. Called for its side effect of producing a plot.

References

- Freeman, S. C., Kerby, C. R., Patel, A., Cooper, N. J., Quinn, T., & Sutton, A. J. (2019). Development of an interactive web-based tool to conduct and interrogate meta-analysis of diagnostic test accuracy studies: MetaDTA. *BMC Medical Research Methodology*, 19, 81. doi:10.1186/s12874-0190724x
- Harbord, R. M., Deeks, J. J., Egger, M., Whiting, P., & Sterne, J. A. C. (2007). A unification of models for meta-analysis of diagnostic accuracy studies. *Biostatistics*, 8(2), 239–251. doi:10.1093/biostatistics/kxl004
- Riley, R. D., Ensor, J., Jackson, D., & Burke, D. L. (2018). Deriving percentage study weights in multi-parameter meta-analysis models: with application to meta-regression, network meta-analysis and one-stage individual participant data models. *Statistical Methods in Medical Research*, 27(10), 2885–2905. doi:10.1177/0962280216688033

See Also

[fitReitsma](#)

plot.ReitsmaSubgroup *Plot Results from a Reitsma Subgroup Model*

Description

Produces a summary ROC plot for objects of class "ReitsmaSubgroup" obtained from [fitReitsmaSubgroup](#). The plot displays study-level estimates of sensitivity and specificity, the summary operating point, and corresponding confidence and prediction regions. Optionally, the HSROC (hierarchical summary ROC) curve can be overlaid.

Usage

```
## S3 method for class 'ReitsmaSubgroup'
plot(
  x,
  scale = 0.02,
  size = c("equal", "sampsiz", "se"),
  main = "Diagnostic Test Accuracy Meta-Analysis",
  col = NULL,
  nudge_legend = -0.4,
  HSROC = FALSE,
  specrange = c(0.7, 0.995),
  conflevel = 0.95,
  predlevel = 0.95,
  connectstudies = FALSE,
  ...
)
```

Arguments

x	An object of class "ReitsmaSubgroup", as returned by fitReitsmaSubgroup .
scale	A numeric scaling factor controlling the size of the rectangles representing study weights. Default is 0.02.
size	Character string controlling study weight display: "equal" All studies shown with equal size. Default "sampsiz" Size proportional to sample size "se" Size proportional to precision on the logit scale
main	Character string giving the main title of the plot. Defaults to "Diagnostic Test Accuracy Meta-Analysis".
col	Vector of colours used for subgroup-specific HSROC curves, study-level rectangles, summary points, confidence and prediction region. If NULL, colours are generated automatically.
nudge_legend	Numeric horizontal offset for the subgroup legend. More negative values move the legend further right, outside the plotting area. Values closer to zero move it closer to the panel. Default is -0.4.

HSROC	if TRUE, the HSROC curve is added to the plot. Default is FALSE.
specrange	A numeric vector of length 2 giving the range of specificities over which the HSROC curve is plotted. Defaults to <code>c(0.7, 0.995)</code> .
confllevel	Confidence level for the confidence region. Default is 0.95.
predlevel	Confidence level for the prediction region. Default is 0.95.
connectstudies	Whether the point estimates (rectangles) of two subgroups within the same study should be connected. Defaults to FALSE.
...	Additional graphical arguments passed to plotting functions.

Details

The plot is constructed on the ROC scale with sensitivity on the y-axis and specificity on the x-axis (displayed as 1 - false positive rate on a reversed axis).

Study-specific estimates are shown as rectangles, where the size reflects approximate study weights derived from the Fisher information matrix.

The following elements are displayed:

- Study-level sensitivity and specificity estimates
- Summary (pooled) estimate
- confidence region around the summary point
- prediction region reflecting between-study variability
- Optional HSROC curve (if HSROC = TRUE)

Confidence and prediction regions are derived using the delta method based on the estimated variance-covariance structure of the model.

Value

No return value. Called for its side effect of producing a plot.

References

Harbord, R. M., Deeks, J. J., Egger, M., Whiting, P., & Sterne, J. A. C. (2007). A unification of models for meta-analysis of diagnostic accuracy studies. *Biostatistics*, 8(2), 239–251. doi:10.1093/biostatistics/kxl004

See Also

[fitReitsmaSubgroup](#)

plot.RutterGatsonis *Plot Results from a Rutter and Gatsonis Model*

Description

Produces a summary ROC plot for objects of class "RutterGatsonis" obtained from [fitRutterGatsonis](#). The plot displays study-level estimates of sensitivity and specificity and the HSROC (hierarchical summary ROC).

Usage

```
## S3 method for class 'RutterGatsonis'
plot(
  x,
  scale = 0.02,
  size = c("equal", "sampsiz", "se"),
  specrange = c(0.7, 0.995),
  main = "Diagnostic Test Accuracy Meta-Analysis",
  ...
)
```

Arguments

x	An object of class "RutterGatsonis", as returned by fitRutterGatsonis .
scale	A numeric scaling factor controlling the size of the rectangles representing study weights. Default is 0.02.
size	Character string controlling study weight display: "equal" All studies shown with equal size. Default "sampsiz" Size proportional to sample size "se" Size proportional to precision on the logit scale
specrange	A numeric vector of length 2 giving the range of specificities over which the HSROC curve is plotted. Defaults to c(0.7, 0.995).
main	Character string giving the main title of the plot. Defaults to "Diagnostic Test Accuracy Meta-Analysis".
...	Additional graphical arguments passed to plotting functions.

Details

The plot is constructed on the ROC scale with sensitivity on the y-axis and specificity on the x-axis (displayed as 1 - false positive rate on a reversed axis).

Study-specific estimates are shown as rectangles.

The following elements are displayed:

- Study-level sensitivity and specificity estimates
- HSROC curve

Value

No return value. Called for its side effect of producing a plot.

References

Freeman, S. C., Kerby, C. R., Patel, A., Cooper, N. J., Quinn, T., & Sutton, A. J. (2019). Development of an interactive web-based tool to conduct and interrogate meta-analysis of diagnostic test accuracy studies: MetaDTA. *BMC Medical Research Methodology*, 19, 81. doi:10.1186/s12874-0190724x

See Also

[fitRutterGatsonis](#)

plot.RutterGatsonisSubgroup

Plot Results from a Rutter and Gatsonis Subgroup Model

Description

Produces summary ROC plots for objects of class "RutterGatsonisSubgroup" obtained from [fitRutterGatsonisSubgroup](#). The plot displays study-level estimates of sensitivity and specificity, stratified by subgroup, together with subgroup-specific HSROC (hierarchical summary ROC) curves.

Usage

```
## S3 method for class 'RutterGatsonisSubgroup'
plot(
  x,
  scale = 0.02,
  size = c("equal", "sampsiz", "se"),
  nudge_legend = -0.4,
  specrange = c(0.7, 0.995),
  col = NULL,
  main = "Diagnostic Test Accuracy Meta-Analysis",
  connectstudies = FALSE,
  ...
)
```

Arguments

x	An object of class "RutterGatsonisSubgroup", as returned by fitRutterGatsonisSubgroup .
scale	A numeric scaling factor controlling the size of the rectangles representing study weights. Default is 0.02.
size	Character string controlling study weight display:

	"equal" All studies shown with equal size. Default.
	"sampsiz" Size proportional to sample size.
	"se" Size proportional to precision on the logit scale.
nudge_legend	Numeric horizontal offset for the subgroup legend. More negative values move the legend further right, outside the plotting area. Values closer to zero move it closer to the panel. Default is -0.4.
specrange	A numeric vector of length 2 giving the range of specificities over which the HSROC curve is plotted. Defaults to c(0.7, 0.995).
col	Vector of colours used for subgroup-specific HSROC curves and study-level rectangles. If NULL, colours are generated automatically.
main	Character string giving the main title of the plot. Defaults to "Diagnostic Test Accuracy Meta-Analysis".
connectstudies	Whether the point estimates (rectangles) of two subgroups within the same study should be connected. Defaults to FALSE.
...	Additional graphical arguments passed to plotting functions.

Details

The plot is constructed on the ROC scale with sensitivity on the y-axis and specificity on the x-axis (displayed as 1 - false positive rate on a reversed axis).

Study-specific estimates are shown as rectangles, with subgroup-specific colours.

The following elements are displayed:

- Study-level sensitivity and specificity estimates by subgroup
- Subgroup-specific HSROC curves
- A legend identifying the subgroups

Value

No return value. Called for its side effect of producing a plot.

References

Freeman, S. C., Kerby, C. R., Patel, A., Cooper, N. J., Quinn, T., & Sutton, A. J. (2019). Development of an interactive web-based tool to conduct and interrogate meta-analysis of diagnostic test accuracy studies: MetaDTA. *BMC Medical Research Methodology*, 19, 81. doi:10.1186/s12874-0190724x

See Also

[fitRutterGatsonisSubgroup](#)

print.HoyerAFT	<i>Print Hoyer AFT Model Object</i>
----------------	-------------------------------------

Description

Displays a concise summary of a fitted Hoyer AFT model, including distribution, number of studies, convergence status, and likelihood-based fit statistics.

Usage

```
## S3 method for class 'HoyerAFT'  
print(x, ...)
```

Arguments

x	An object of class "HoyerAFT".
...	Further arguments (unused).

Value

Invisibly returns the input object.

See Also

[summary.HoyerAFT](#)

print.Reitsma	<i>Print Method for Reitsma Objects</i>
---------------	---

Description

Displays a concise summary of a fitted Reitsma diagnostic test accuracy model, including number of studies, convergence status and likelihood-based fit statistics.

Usage

```
## S3 method for class 'Reitsma'  
print(x, ...)
```

Arguments

x	An object of class "Reitsma".
...	Additional arguments (unused).

Value

Invisibly returns the input object.

See Also

[summary.Reitsma](#)

`print.ReitsmaSubgroup` *Print Method for ReitsmaSubgroup Objects*

Description

Displays a concise summary of a fitted Reitsma Subgroup diagnostic test accuracy model, including number of studies, convergence status, and likelihood-based fit statistics.

Usage

```
## S3 method for class 'ReitsmaSubgroup'
print(x, ...)
```

Arguments

<code>x</code>	An object of class "ReitsmaSubgroup".
<code>...</code>	Additional arguments (unused).

Value

Invisibly returns the input object.

See Also

[summary.ReitsmaSubgroup](#)

`print.RutterGatsonis` *Print Method for RutterGatsonis Objects*

Description

Displays a concise summary of a fitted HSROC model, including number of studies, convergence status, and likelihood-based fit statistics.

Usage

```
## S3 method for class 'RutterGatsonis'
print(x, ...)
```

Arguments

x	An object of class "RutterGatsonis".
...	Additional arguments (unused).

Value

Invisibly returns the input object.

See Also

[summary.RutterGatsonis](#)

`print.RutterGatsonisReg`

Print Method for RutterGatsonisReg Objects

Description

Displays a concise summary of a fitted HSROC model, including number of studies, convergence status, and likelihood-based fit statistics.

Usage

```
## S3 method for class 'RutterGatsonisReg'  
print(x, ...)
```

Arguments

x	An object of class "RutterGatsonisReg".
...	Additional arguments (unused).

Value

Invisibly returns the input object.

See Also

[summary.RutterGatsonisReg](#)

```
print.RutterGatsonisSubgroup
```

Print Method for RutterGatsonisSubgroup Objects

Description

Displays a concise summary of a fitted HSROC model, including number of studies, convergence status, and likelihood-based fit statistics.

Usage

```
## S3 method for class 'RutterGatsonisSubgroup'
print(x, ...)
```

Arguments

`x` An object of class "RutterGatsonisSubgroup".
`...` Additional arguments (unused).

Value

Invisibly returns the input object.

See Also

[summary.RutterGatsonisSubgroup](#)

```
restructure_data
```

Construct Interval Data for Threshold-Based Bivariate Time-to-Event Models

Description

Transforms study-level diagnostic test accuracy (DTA) data with multiple thresholds into interval-censored format suitable for likelihood-based modelling (Hoyer et al., 2018).

Usage

```
restructure_data(
  data,
  TP,
  FP,
  FN,
  TN,
  threshold,
  study,
```

```

    smallest,
    largest,
    testdirection = c("greater", "less")
)

```

Arguments

<code>data</code>	A data.frame containing study-level data.
<code>TP</code>	True positives (column name).
<code>FP</code>	False positives (column name).
<code>FN</code>	False negatives (column name).
<code>TN</code>	True negatives (column name).
<code>threshold</code>	The observed threshold value (column name). Must be positive and strictly increasing within each study.
<code>study</code>	Study identifier (column name).
<code>smallest</code>	Positive lower bound used to define the leftmost interval. Must be smaller than minimum threshold.
<code>largest</code>	Positive upper bound used to define the rightmost interval. Must be greater than maximum threshold.
<code>testdirection</code>	Direction of the test. Enter "greater" when larger test values indicate disease. Conversely, enter "less" when lower test values indicate disease (e.g. anaemia-type tests). Defaults to "greater".

Details

The function constructs:

- A left-censored interval (below the first threshold)
- Intermediate intervals between adjacent thresholds
- A right-censored interval (above the last threshold)

Event counts are derived from cumulative counts to represent the number of observations falling within each interval for diseased and non-diseased groups. Therefore, input counts must be cumulative over increasing thresholds within each study.

The function first validates that counts are numeric, non-negative integers and that threshold values are positive.

Within each study, total numbers of diseased (n_1) and non-diseased (n_0) individuals are required to be constant across thresholds. Intermediate interval counts are computed as differences between cumulative counts.

The log-scale midpoint (`lcutmean`) is provided to support initialization of random effects in subsequent Hoyer AFT models.

For `testdirection = "greater"`, the function assumes that sensitivity decreases and specificity increases with increasing thresholds. For `testdirection = "less"`, the reverse monotonicity is required. Internally, the function standardizes the definition of a positive test result so that it always corresponds to values above the threshold. For `testdirection = "less"`, this is achieved by re-labeling the observed counts. This does not affect the resulting sensitivity, specificity, or ROC curve, but ensures compatibility with the model formulation.

Value

A list with two components:

restructured A data frame with one row per constructed interval containing:

study Study identifier

TP, TN, n1, n0 Original counts carried forward

threshold Threshold associated with the interval

lowerB Lower interval bound (NA for left-censored)

upperB Upper interval bound (NA for right-censored)

events1 Number of diseased observations in the interval

events0 Number of non-diseased observations in the interval

ctype Censoring type (1 = left, 2 = interval, 3 = right)

lcutmean Midpoint of log-thresholds defining the interval

original The processed original data including (derived) quantities:

n1 Total number of diseased individuals (TP + FN)

n0 Total number of non-diseased individuals (TN + FP)

sens Sensitivity (TP / n1)

spec Specificity (TN / n0)

fpr False positive rate (FP / n0)

testdirection As specified by testdirection

References

Hoyer, A., Hirt, S., Kuss, O. (2018). Meta-analysis of full ROC curves using bivariate time-to-event models for interval-censored data. *Research Synthesis Methods*, 9(1), 62-72. doi:10.1002/jrsm.1273

Examples

```
data("diabetes")
res <- restructure_data(
  data = diabetes,
  TP = TP,
  FP = FP,
  FN = FN,
  TN = TN,
  threshold = threshold,
  study = study,
  smallest = 2,
  largest = 10
)
```

RF	<i>RF dataset</i>
----	-------------------

Description

This is the RF data set from Nishimura (2007) from a review of rheumatoid factor (RF) to diagnose rheumatoid arthritis.

Usage

RF

Format

A data frame with 50 rows and 8 variables:

study Study identifier

year Year of the study

TP Number of true positives

FP Number of false positives

FN Number of false negatives

TN Number of true negatives

cutoff Threshold used in U/mL for test positivity

method Different methods used to perform the test

Source

Nishimura, K. et al. (2007). *Meta-analysis: diagnostic accuracy of anti-cyclic citrullinated peptide antibody and rheumatoid factor for rheumatoid arthritis*. *Annals of Internal Medicine*, 146(11), 392-403. doi:[10.7326/000348191461120070605000008](https://doi.org/10.7326/000348191461120070605000008)

schuetz	<i>Schuetz dataset</i>
---------	------------------------

Description

This is the schuetz data set from Schuetz (2010) from a meta-analysis of non-invasive coronary angiography using computer tomography (CT) versus magnetic resonance imaging (MRI)

Usage

schuetz

Format

A data frame with 108 rows and 7 variables:

test Which test was used, CT or MRI

study Study identifier

TP Number of true positives

FP Number of false positives

FN Number of false negatives

TN Number of true negatives

indirect whether the comparison is indirect (=1) or direct (=0)

Source

Schuetz, K., et al. (2010). *Meta-analysis: noninvasive coronary angiography using computed tomography versus magnetic resonance imaging*. *Annals of Internal Medicine*, 152(3), 167-177.
doi:[10.7326/00034819152320100202000008](https://doi.org/10.7326/00034819152320100202000008)

summary.HoyerAFT

Summary Method for HoyerAFT Objects

Description

Extracts and returns the summary information stored in a fitted HoyerAFT model object.

Usage

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

Arguments

object	An object of class "HoyerAFT", typically the result of a call to fitHoyerAFT .
...	Additional arguments (currently unused).

Details

This method is part of the standard S3 `summary()` generic and provides access to summary statistics computed from the fitted model, as stored in the `sdreport2` and `sensspec` component of the object.

Value

A list with two data frames containing summary statistics derived from the fitted model.

- `sdreport2`: Parameter estimates with standard errors as returned from TMB reported parameters.
- `sensspec`: Estimated sensitivity and specificity with confidence intervals at the specified thresholds.

See Also[fitHoyer](#) [fitHoyerAFT](#)

`summary.Reitsma`*Summary Method for Reitsma Objects*

Description

Extracts key results from an object of class "Reitsma", including parameter estimates, sensitivity and specificity summaries, and recovered HSROC parameters from the Rutter–Gatsonis parameterization.

Usage

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

Arguments

<code>object</code>	An object of class "Reitsma" as returned by fitReitsma .
<code>...</code>	Additional arguments (currently ignored).

Value

A list with the following components:

- `estimates`: Parameter estimates with standard errors.
- `sensspec`: Estimated sensitivity and specificity with confidence intervals.
- `RutterGatsonis_recovered`: Recovered parameters in the Rutter-Gatsonis (HSROC) parameterization.

See Also[fitReitsma](#)

summary.ReitsmaSubgroup

Summary Method for ReitsmaSubgroup Objects

Description

Extracts key results from an object of class "ReitsmaSubgroup", including parameter estimates, sensitivity and specificity summaries, and recovered HSROC parameters from the Rutter–Gatsonis parameterization.

Usage

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

Arguments

object	An object of class "ReitsmaSubgroup" as returned by fitReitsmaSubgroup .
...	Additional arguments (currently ignored).

Value

A list with the following components:

- estimates: Parameter estimates with standard errors.
- sensspec: Estimated sensitivity and specificity with confidence intervals.
- RutterGatsonis_recovered: Recovered parameters in the Rutter-Gatsonis (HSROC) parameterization.
- subgroups Subgroup names.

See Also

[fitReitsmaSubgroup](#)

summary.RutterGatsonis

Summary Method for RutterGatsonis Objects

Description

This method extracts key components from a fitted HSROC model object returned by [fitRutterGatsonis](#). It returns parameter estimates, sensitivity/specificity summaries, and the recovered Reitsma parametrization.

Usage

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

Arguments

object An object of class "RutterGatsonis" as returned by [fitRutterGatsonis](#).
... Additional arguments (currently unused).

Details

Provides a concise summary of a fitted "RutterGatsonis" model.

Value

A list containing the following components:

- **estimates** Parameter estimates with standard errors as returned from TMB reported parameters.
- **sensspec** Estimated sensitivity at the specified specificity, including confidence intervals.
- **Reitsma_recovered** Recovered parameters in the Reitsma parameterization.

See Also

[fitRutterGatsonis](#)

summary.RutterGatsonisReg

Summary Method for RutterGatsonisReg Objects

Description

This method extracts key components from a fitted HSROC model object returned by [fitRutterGatsonisReg](#). It returns parameter estimates, sensitivity/specificity summaries.

Usage

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

Arguments

object An object of class "RutterGatsonisReg" as returned by [fitRutterGatsonisReg](#).
... Additional arguments (currently unused).

Details

Provides a concise summary of a fitted "RutterGatsonisReg" model.

Value

A list containing the following components:

- estimates Parameter estimates with standard errors as returned from TMB reported parameters.
- sensspec Estimated sensitivity at the specified specificity, including confidence intervals.

See Also

[fitRutterGatsonisReg](#)

summary.RutterGatsonisSubgroup

Summary Method for RutterGatsonisSubgroup Objects

Description

This method extracts key components from a fitted HSROC model object returned by [fitRutterGatsonisSubgroup](#). It returns parameter estimates and sensitivity/specificity summaries.

Usage

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

Arguments

object	An object of class "RutterGatsonisSubgroup" as returned by fitRutterGatsonisSubgroup .
...	Additional arguments (currently unused).

Details

Provides a concise summary of a fitted "RutterGatsonisSubgroup" model.

Value

A list containing the following components:

- estimates Parameter estimates with standard errors as returned from TMB reported parameters.
- sensspec Estimated sensitivity at the specified specificity, including confidence intervals.
- Reitsma_recovered Recovered parameters in the Reitsma parameterization.
- subgroups Subgroup names.

summary.RutterGatsonisSubgroup

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See Also

[fitRutterGatsonisSubgroup](#)

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