

Package ‘ipdmeta’

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Type Package

Title Functions for characterizing subgroup analyses with meta-analysis

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Author S. Kovalchik

Maintainer S. Kovalchik <s.a.kovalchik@gmail.com>

Description Assess heterogeneity of covariates defining subgroups;
estimate the power of a treatment-covariate interaction for an
individual patient data meta-analysis using aggregate data

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R topics documented:

get.diag	2
ipd.sep	3
ipdmeta	5
poynard	6
Qt	7

Index	9
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`get.diag`*Extract Diagonal Elements from Matrix*

Description

Wrapper for `diag` that allows for scalar argument.

Usage

```
get.diag(x,...)
```

Arguments

<code>x</code>	Matrix or scalar
<code>...</code>	Additional arguments to <code>diag</code>

Details

Same as `diag` but interprets scalar as scalar rather than the elements of an identity matrix. Thus if `x` is scalar or vector it is simply returned.

Value

Diagonal as vector.

Author(s)

S. Kovalchik <s.a.kovalchik@gmail.com>

See Also

[diag](#)

Examples

```
get.diag(matrix(1:4,2,2))
```

```
get.diag(4)
```

ipd.sep

*IPD meta-analysis Subgroup Effect Power Estimator***Description**

The function estimates the power of an IPD meta-analysis to detect a specified subgroup effect (covariate-treatment interaction) based on summary statistics.

Usage

```
ipd.sep(
  effect,
  event0=NULL,
  event1=NULL,
  mean0=NULL,
  mean1=NULL,
  var0=NULL,
  var1=NULL,
  x0=NULL,
  x1=NULL,
  s20=NULL,
  s21=NULL,
  n0=NULL,
  n1=NULL,
  data,
  alpha=.05
)
```

Arguments

All vector entries are grouped by study.

effect	scalar, subgroup effect under alternative hypothesis
event0	vector, for binary outcome, events in group 0
event1	vector, for binary outcome, events in group 1
mean0	vector, for continuous outcome, mean in group 0
mean1	vector, for continuous outcome, mean in group 1
var0	vector, for continuous outcome, sample variances for responses in group 0
var1	vector, for continuous outcome, sample variances for responses in group 1
x0	vector of subgroup covariate means for group 0
x1	vector of subgroup covariate means for group 1
s20	vector of covariate sample variances for control group
s21	vector of covariate sample variances for treatment group
n0	vector of number of subjects for group 0

n1	vector of number of subjects for group 1
data	data frame containing the objects specified in response or covariate arguments
alpha	scalar significance level of Wald test (two-sided)

Details

If a data frame is supplied, then the object indicated in each vector argument is looked for in data.

For a patient-level binary outcome, mean0, mean1, var0 and var1 should not be specified. Zero event counts will be corrected with a 0.5 factor. For a continuous response, event0 and event1 should not be specified.

For a covariate that is a mean proportion, such as proportion male, no sample variances need to be specified. If no values are given for the sample variances s20 and s21 it will be assumed that the covariate is a mean proportion and the sample variances will be determined from the proportions.

The SEP for the IPD meta-analysis is based on a generalized linear mixed model for the patient-level analysis. The model has intercept, treatment, covariate and interaction fixed effects and independent random effects for the baseline and treatment by study. Under this model, an estimator for the subgroup effect variance, that is, the variance for the estimate of the covariate-treatment interaction, for either an identity or logistic GLMM, can be obtained from the study sample statistics. This variance is then used to estimate the power of the IPD meta-analysis for a specified subgroup effect based on a two-sided Wald test.

Value

A list with the following named components:

estimated.power	The estimated IPD meta-analysis interactive effect power
power.lower	Lower bound for level CI
power.upper	Upper bound for level CI
estimated.se	Estimated standard error of IPD meta-analysis interaction effect
se.lower	Lower bound for level CI
se.upper	Upper bound for level CI
sigma	The mean of the study residual variance
sigma0	Estimate of intercept random effect variance from simple RE meta-analysis with DSL estimator
sigma1	Estimate of treatment random effect variance simple RE meta-analysis with DSL estimator
level	confidence level for Wald test

Author(s)

S. Kovalchik <s.a.kovalchik@gmail.com>

Examples

```
data(poynard)

#AGE SEP FOR IPD META-ANALYSIS OF BETA-ANTAGONISTS TO PREVENT GI BLEEDING EVENTS

#ALTERNATIVE HYPOTHESIS FOR AGE-TREATMENT EFFECT
```

```
#WITH 10 YEARS CHANGE TO OR TREATMENT EFFECT exp(beta*10)
#EFFECT MODIFIER CHANGES TREATMENT EFFECT BY 30%

beta = log(1.3)/10

age.sep <-

ipd.sep(
  effect=beta,
  event0=bleed0,
  event1=bleed1,
  n0=n0,
  n1=n1,
  x0=age0,
  x1=age1,
  s20=age.s20,
  s21=age.s21,
  data=poynard
)

age.sep

#GENDER SUBGROUP EFFECT; 30% OR CHANGE BY GENDER

beta <- log(1.3)

gender.sep <-

ipd.sep(
  effect=beta,
  event0=bleed0,
  event1=bleed1,
  n0=n0,
  n1=n1,
  x0=male0,
  x1=male1,
  data=poynard
)

gender.sep
```

Description

Assess heterogeneity of covariates defining subgroups; estimate the power of a treatment-covariate interaction for an individual patient data meta-analysis using aggregate data

Details

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Author(s)

Maintainer: Stephanie A. Kovalchik <s.a.kovalchik@gmail.com>

poynard	<i>Meta-analysis data set for Poynard et al. review of beta-adrenergic-antagonist drugs</i>
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Description

Meta-analytic dataset of 4 trials of Beta-adrenergic-antagonist drugs in the prevention of gastrointestinal bleeding in patients with cirrhosis and esophageal varices.

Dataset used to illustrate power estimator [ipd.sep](#)

Format

study	Name of trial
n0	Control group sample size
n1	Beta-adrenergic-antagonist group sample size
bleed0	Control group number of bleeding events at 2 year follow-up
bleed1	Beta-adrenergic-antagonist group number of bleeding events at 2 year follow-up
age0	Control group mean age
age1	Beta-adrenergic-antagonist group mean age
age.s20	Control group variance age
age.s21	Beta-adrenergic-antagonist group variance age
male0	Control group sample proportion male
male1	Beta-adrenergic-antagonist sample proportion male
drug	Beta-adrenergic-antagonist studied

Author(s)

S. Kovalchik <s.a.kovalchik@gmail.com>

References

Poynard, T, Cales, P, Pasta, L, Ideo, G, Pascal, J P, Pagliaro, L, Lebrech, D, (1991), Beta-adrenergic-antagonist drugs in the prevention of gastrointestinal bleeding in patients with cirrhosis and esophageal varices. An analysis of data and prognostic factors in 589 patients from four randomized clinical trials. Franco-Italian Multicenter Study Group, *NEJM*, 324, 1532-8.

Qt *Measures of covariate heterogeneity*

Description

Measures of covariate heterogeneity proposed by Simmonds and Higgins (2007) for assessing the power of a meta-regression

Usage

Qt(m,n,sigma2)

Arguments

	All vector entries are grouped by study.
	vector of study-level covariate means
m	vector of study sample sizes
sigma2	vector of covariate sample variances

Value

A list with the following named components: t, Qd, Qe, bar.Qd,bar.Qe, tilde.Qd, tilde.Qe

Author(s)

S. Kovalchik <s.a.kovalchik@gmail.com>

References

Simmonds, M. C., Higgins, J. P. T., (2007), Covariate heterogeneity in meta-analysis: criteria for deciding between meta-regression and individual patient data, *Statistics in Medicine*, 26 (15): 2982-99.

Examples

```
data(poynard)

#COVARIATE HETEROGENEITY FOR AGE

m <- (poynard$n0*poynard$age0+poynard$n1*poynard$age1)/(poynard$n0+poynard$n1)
n <- poynard$n0+poynard$n1
sigma2 <- ((poynard$n0-1)*poynard$age.s20+(poynard$n1-1)*poynard$age.s21)/(poynard$n0+poynard$n1-2)

Q <- Qt(m,n,sigma2)

lapply(Q,function(x){x/Q$t})
```

Index

*Topic **package**
ipdmeta, [5](#)

diag, [2](#)

get.diag, [2](#)

ipd.sep, [3](#), [6](#)
ipdmeta, [5](#)

poynard, [6](#)

Qt, [7](#)