Package ‘metaLik’

May 29, 2018

Version 0.43.0
Priority optional
Title Likelihood Inference in Meta-Analysis and Meta-Regression Models
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Depends R (>= 3.4.0)
Description First- and higher-order likelihood inference in meta-analysis and meta-regression models.
License GPL (>= 2)
NeedsCompilation no
Repository CRAN
Date/Publication 2018-05-29 10:15:04 UTC

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### Albumin Data

**Description**

Data from four experiments about the percentage of albumin in the plasma protein of the normal human subjects.

**Usage**

```r
data(albumin)
```

**Format**

- `y` mean albumin percentage.
- `sigma2` estimated within-study variance.

**Source**


**Examples**

```r
data(albumin)
```

### Cholesterol Data

**Description**

Data from 28 randomized trials about the effect of serum cholesterol reduction on the risk of ischaemic heart disease.

**Usage**

```r
data(cholesterol)
```

**Format**

- `heart_disease` log odds ratio of ischaemic heart disease.
- `cholesterol_reduction` average serum cholesterol reduction measured in mmol/l.
- `sigma2` estimated within-study variance.
diuretics

Source


Examples

data(cholesterol)

data(diuretics)

---

**Description**

Data from nine randomized trials on prevention of pre-eclampsia with diuretics.

**Usage**

data(diuretics)

**Format**

- `y` logarithm of the risk ratio in each study.
- `sigma2` estimated within-study variance.

**Source**


**Examples**

data(diuretics)
education

Open education data.

Description
Data from eleven studies on the effect of open versus traditional education on student attitude toward schools.

Usage
data(education)

Format
y standardized estimated mean difference in attitude according to the type of education.
sigma2 estimated within-study variance.

Source

Examples
data(education)

---

metaLik

First- and higher-order likelihood inference in meta-analysis and meta-regression models

Description
Implements first-order and higher-order likelihood methods for inference in meta-analysis and meta-regression models, as described in Guolo (2012). Higher-order asymptotics refer to the higher-order adjustment to the log-likelihood ratio statistic for inference on a scalar component of interest as proposed by Skovgaard (1996). See Guolo and Varin (2012) for illustrative examples about the usage of metaLik package.

Usage
metaLik(formula, data, subset, contrasts = NULL, offset, sigma2, weights=1/sigma2)
**Arguments**

- **formula**: an object of class "formula" (or one that can be coerced to that class): a symbolic description of the model to be fitted. The details of model specification are given under ‘Details’.
- **data**: an optional data frame, list or environment (or object coercible by `as.data.frame` to a data frame) containing the variables in the model. If not found in data, the variables are taken from `environment(formula)`, typically the environment from which `metaLik` is called.
- **subset**: an optional vector specifying a subset of observations to be used in the fitting process.
- **contrasts**: an optional list. See the contrasts.arg of `model.matrix.default`.
- **offset**: this can be used to specify an a priori known component to be included in the linear predictor during fitting. This should be NULL or a numeric vector of length equal to the number of cases. One or more `offset` terms can be included in the formula instead or as well, and if more than one are specified their sum is used. See `model.offset`.
- **sigma2**: a vector of within-study estimated variances. The length of the vector must be the same of the number of studies.
- **weights**: a vector of the inverse of within-study estimated variances. The length of the vector must be the same of the number of studies. If `sigma2` is supplied, the value of `weights` is discarded.

**Details**

Models for `metaLik.fit` are specified symbolically. A typical model has the form \( y \sim x_1 + \ldots + x_J \), where \( y \) is the continuous response term and \( x_j \) is the j-th covariate available at the aggregated meta-analysis level for each study. The case of no covariates corresponds to the classical meta-analysis model specified as \( y \sim 1 \).

Within-study variances are specified through `sigma2`: the rare case of equal within-study variances implies Skovgaard’s adjustment reaching a third-order accuracy.

DerSimonian and Laird estimates (DerSimonian and Laird, 1986) are also supplied.

**Value**

An object of class "metaLik" with the following components:

- **y**: the y vector used.
- **X**: the model matrix used.
- **fitted.values**: the fitted values.
- **sigma2**: the within-study variances used.
- **K**: the number of studies.
- **mle**: the vector of the maximum likelihood parameter estimates.
- **vcov**: the variance-covariance matrix of the parameter estimates.
- **max.lik**: the maximum log-likelihood value.
beta.mle the vector of fixed-effects parameters estimated according to maximum likelihood.

tau2.mle the maximum likelihood estimate of $\tau^2$.

DL the vector of fixed-effects parameters estimated according to DerSimonian and Laird’s approach.

tau2.DL the method of moments estimate of the heterogeneity parameter $\tau^2$.

vcov.DL the variance-covariance matrix of the DL parameter estimates.
call the matched call.

formula the `formula` used.
terms the `terms` object used.
offset the offset used.

contrasts (only where relevant) the `contrasts` specified.
xlevels (only where relevant) a record of the levels of the factors used in fitting.

model the model frame used.

Generic functions `coefficients`, `vcov`, `logLik`, `fitted`, `residuals` can be used to extract fitted model quantities.

Author(s)
Annamaria Guolo and Cristiano Varin.

References


See Also
Function `summary.metaLik` for summaries.
Function `test.metaLik` for hypothesis testing.

Examples
```r
## meta-analysis
data(education)
m <- metalik(y~1, data=education, sigma2=sigma2)
summary(m)
## meta-analysis
data(albumin)
```
**simulate.metaLik**

```r
m <- metaLik(y~1, data=albumin, sigma2=sigma2)
summary(m)
## meta-regression
data(vaccine)
m <- metaLik(y~latitude, data=vaccine, sigma2=sigma2)
summary(m)
## meta-regression
data(cholesterol)
m <- metaLik(heart_disease~chol_reduction, data=cholesterol, weights=1/sigma2)
summary(m)
```

---

**simulate.metaLik**  
*Simulate meta-analysis outcomes*

**Description**

Simulate one or more meta-analysis outcomes from a fitted `metaLik` object.

**Usage**

```r
## S3 method for class 'metaLik'
simulate(object, nsim=1, seed=NULL, ...)  
```

**Arguments**

- `object` an object of class "`metaLik`".
- `nsim` number of outcome vectors to simulate. Default is 1.
- `seed` an object specifying if and how the random number generator should be initialized, see `simulate` for details.
- `...` additional optional arguments.

**Value**

A dataframe containing the simulated meta-analysis outcomes.

**Author(s)**

Annamaria Guolo and Cristiano Varin.

**References**


**Examples**

```r
data(vaccine)
m <- metaLik(y~latitude, data=vaccine, sigma2=sigma2)
sim <- simulate(m, nsim=2)
sim
```
**summary.metaLik**

*Summarizing meta-analysis and meta-regression model fits*

### Description

Summary method for class "metaLik".

### Usage

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

### Arguments

- **object**: an object of class "metaLik", usually a result of a call to "metaLik".
- **...**: additional arguments

### Details

`summary.metaLik` prints summary information about within-study heterogeneity, parameter estimates, standard errors, first- and higher-order log-likelihood ratio statistics. See `test.metaLik` for more details about the first- and higher-order statistics.

### Value

The function `summary.metaLik` returns the `metaLik` object from which `summary.metaLik` is called.

### See Also

The generic functions `coefficients`, `confint` and `vcov`. Function `test.metaLik` allows for hypothesis testing.

### Examples

```
## meta-analysis
data(education)
m <- metaLik(y~1, data=education, sigma2=sigma2)
summary(m)
## meta-analysis
data(albumin)
m <- metaLik(y~1, data=albumin, sigma2=sigma2)
summary(m)
## meta-regression
data(vaccine)
m <- metaLik(y~latitude, data=vaccine, sigma2=sigma2)
summary(m)
## meta-regression
data(cholesterol)
```
```
m <- metaLik(heart_disease~chol_reduction, data=cholesterol, weights=1/sigma2)
summary(m)
```

---

**test.metaLik**  

_Hypothesis testing on a scalar fixed-effect component in meta-analysis and meta-regression models_

**Description**

Performs hypothesis testing on a scalar component of the fixed-effects vector in meta-analysis and meta-regression models, using the signed profile log-likelihood ratio test and its higher-order Skovgaard’s adjustment (Skovgaard, 1996), as described in Guolo (2012). See Guolo and Varin (2012) for illustrative examples about the usage of _metaLik_ package.

**Usage**

```
test.metaLik(object, param=1, value=0, alternative=c("two.sided", "less", "greater"), print=TRUE)
```

**Arguments**

- **object**: an object of class "metaLik".
- **param**: a specification of which parameter is to be given confidence interval, either a number or a name. Default is 1 corresponding to the intercept.
- **value**: a single number indicating the value of the fixed-effect parameter under the null hypothesis. Default is 0.
- **alternative**: a character string specifying the alternative hypothesis, must be one of "two.sided" (default), "greater" or "less". Just the initial letter can be specified.
- **print**: logical, whether output information should be printed or not; default is _TRUE_.

**Details**

`test.metaLik` allows hypothesis testing on a scalar component of interest in the fixed-effects vector. The signed profile log-likelihood ratio statistic for inference on scalar component \( \beta \) of \( \theta \) is

\[
r(\beta) = \text{sign}(\hat{\beta} - \beta) \sqrt{2(l(\hat{\theta}) - l(\theta))},
\]

where \( l \) is the log-likelihood function and \( \hat{\theta} \) is the maximum likelihood estimate of \( \theta \). The Skovgaard’s adjustment is defined as

\[
\tau(\beta) = r(\beta) + \frac{1}{r(\beta)} \log \frac{u(\beta)}{u(\beta)},
\]

where \( u(\beta) \) is a correction term involving the observed and the expected information matrix and covariances of likelihood quantities, as described in Guolo (2012). Skovgaard’s statistic has a second-order accuracy in approximating the standard normal distribution. In the rare case of equal within-study variances, Skovgaard’s statistic reaches third-order accuracy.
Value

A list with the following components:

- \( r \) the value of the signed profile log-likelihood ratio statistic.
- \( p\text{value}.r \) the p-value of the signed profile log-likelihood ratio test.
- \( rskov \) the value of the Skovgaard’s statistic.
- \( p\text{value}.rskov \) the p-value of the Skovgaard’s test.

Author(s)

Annamaria Guolo and Cristiano Varin.

References


See Also

Function `metalik` for fitting meta-analysis and meta-regression models. Function `summary.metalik` for summaries.

Examples

```r
data(vaccine)
m <- metalik(y~latitude, data=vaccine, sigma2=sigma2)
## significance test for the intercept coefficient
test.metalik(m)
## significance test for the 'latitude' coefficient
test.metalik(m, param=2)
## testing for the 'latitude' coefficient less than 0
test.metalik(m, param=2, value=0, alternative='less')
```

---

**vaccine**

*Data for Bacillus Calmette-Guerin (BCG) vaccine studies.*

**Description**

Data from thirteen clinical studies evaluating the efficacy of the BCG vaccine for the prevention of tuberculosis.
Usage
data(vaccine)

Format

\( y \) log odds ratio in each study.

\( \text{latitude} \) latitude, distance of each study from the equator, surrogate for the presence of environmental mycobacteria providing a level of natural immunity against tuberculosis.

\( \text{year} \) year of the study.

\( \text{sigma2} \) estimated within-study variance.

Source


Examples

data(vaccine)
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