

# Package ‘metaLik’

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**Title** Likelihood Inference in Meta-Analysis and Meta-Regression Models

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

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`albumin`*Albumin data.*

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**Description**

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

**Usage**

```
data(albumin)
```

**Format**

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

**Source**

Meier, P. (1953). Variance of a Weighted Mean. *Biometrics* **9**, 59–73.

**Examples**

```
data(albumin)
```

---

`cholesterol`*Serum cholesterol data.*

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**Description**

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

**Usage**

```
data(cholesterol)
```

**Format**

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

**Source**

Law, M.R., Wald, N.J., and Thompson, S.G. (1994). By How Much and How Quickly Does Reduction in Serum Cholesterol Concentration Lower Risk of Ischaemic Heart Disease? *British Medical Journal* **308**, 367–373.

Thompson, S.G. and Sharp, S.J. (1999). Explaining Heterogeneity in Meta-Analysis: A Comparison of Methods. *Statistics in Medicine* **18**, 2693–2708.

**Examples**

```
data(cholesterol)
```

---

diuretics

*Diuretics data.*

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**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**

Biggerstaff, B. and Tweedie, R. (1997). Incorporating Variability in Estimates of Heterogeneity in the Random Effects Model in Meta-Analysis. *Statistics in Medicine* **16**, 753–768.

**Examples**

```
data(diuretics)
```

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education	<i>Open education data.</i>
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### 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

Hedges, L.V. and Olkin, I. (1985). *Statistical Methods for Meta-Analysis*. Academic Press, Orlando.

### Examples

```
data(education)
```

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metaLik	<i>First- and higher-order likelihood inference in meta-analysis and meta-regression models</i>
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### 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 " <a href="#">formula</a> " (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 <a href="#">as.data.frame</a> to a data frame) containing the variables in the model. If not found in data, the variables are taken from <code>environment(formula)</code> , 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 <a href="#">model.matrix.default</a> .
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 <a href="#">offset</a> terms can be included in the formula instead or as well, and if more than one are specified their sum is used. See <a href="#">model.offset</a> .
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  $y \sim x_1 + \dots + x_J$ , 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 <code>formula</code> used.
terms	the <code>terms</code> object used.
offset	the offset used.
contrasts	(only where relevant) the <code>contrasts</code> 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

- DerSimonian, R. and Laird, N. (1986). Meta-Analysis in Clinical Trials. *Controlled Clinical Trials* **7**, 177–188.
- Guolo, A. (2012). Higher-Order Likelihood Inference in Meta-Analysis and Meta-Regression. *Statistics in Medicine* **31**, 313–327.
- Guolo, A. and Varin, C. (2012). The R Package metaLik for Likelihood Inference in Meta-Analysis. *Journal of Statistical Software* **50** (7), 1–14. <https://www.jstatsoft.org/v50/i07/>.
- Skovgaard, I. M. (1996). An Explicit Large-Deviation Approximation to One-Parameter Tests. *Bernoulli* **2**, 145–165.

### See Also

- Function `summary.metaLik` for summaries.
- Function `test.metaLik` 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)

```

---

simulate.metaLik	<i>Simulate meta-analysis outcomes</i>
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---

## Description

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

## Usage

```

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

```

## Arguments

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

## Value

A dataframe containing the simulated meta-analysis outcomes.

## Author(s)

Annamaria Guolo and Cristiano Varin.

## References

DerSimonian, R. and Laird, N. (1986). Meta-Analysis in Clinical Trials. *Controlled Clinical Trials* **7**, 177–188.

## Examples

```

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 " <a href="#">metaLik</a> ".
...	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	<i>Hypothesis testing on a scalar fixed-effect component in meta-analysis and meta-regression models</i>
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---

## 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 " <b>metaLik</b> ".
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

$$\bar{r}(\beta) = r(\beta) + \frac{1}{r(\beta)} \log \frac{u(\beta)}{r(\beta)},$$

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:

<code>r</code>	the value of the signed profile log-likelihood ratio statistic.
<code>pvalue.r</code>	the p-value of the signed profile log-likelihood ratio test.
<code>rskov</code>	the value of the Skovgaard's statistic.
<code>pvalue.rskov</code>	the p-value of the Skovgaard's test.

**Author(s)**

Annamaria Guolo and Cristiano Varin.

**References**

Guolo, A. (2012). Higher-Order Likelihood Inference in Meta-Analysis and Meta-Regression. *Statistics in Medicine* **31**, 313–327.

Guolo, A. and Varin, C. (2012). The R Package metaLik for Likelihood Inference in Meta-Analysis. *Journal of Statistical Software* **50** (7), 1–14. <https://www.jstatsoft.org/v50/i07/>.

Skovgaard, I. M. (1996). An Explicit Large-Deviation Approximation to One-Parameter Tests. *Bernoulli* **2**, 145–165.

**See Also**

Function [metaLik](#) for fitting meta-analysis and meta-regression models. Function [summary.metaLik](#) for summaries.

**Examples**

```
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.

latitude latitude, distance of each study from the equator, surrogate for the presence of environmental mycobacteria providing a level of natural immunity against tuberculosis.

year year of the study.

sigma2 estimated within-study variance.

**Source**

Berkey, C.S., Hoaglin, D.C., Mosteller, F. and Colditz, G.A. (1995). A random-effects regression model for meta-analysis. *Statistics in Medicine* **14**, 395–411.

**Examples**

```
data(vaccine)
```

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