Package 'metansue'

April 12, 2020

Type Package

Title Meta-Analysis of Studies with Non-Statistically Significant
Unreported Effects

Version 2.4

Date 2020-04-12

Author Joaquim Radua

Maintainer Joaquim Radua <radua@clinic.cat>

Description Novel method to unbiasedly include studies with Non-statistically Significant Unreported Effects (NSUEs) in a meta-analysis <doi:10.1001/jamapsychiatry.2015.2196> and <doi:10.1177/0962280218811349>. Briefly, the method first calculates the interval where the unreported effects (e.g. t-values) should be according to the threshold of statistical significance used in each study. Afterwards, maximum likelihood techniques are used to impute the expected effect size of each study with NSUEs, accounting for between-study heterogeneity and potential covariates. Multiple imputations of the NSUEs are then randomly created based on the expected value, variance and statistical significance bounds. Finally, a restricted-maximum likelihood random-effects meta-analysis is separately conducted for each set of imputations, and estimations from these meta-analyses are pooled. Please read the reference in 'metansue' for details of the procedure.

License GPL-3

NeedsCompilation no

Repository CRAN

Date/Publication 2020-04-12 09:20:02 UTC

R topics documented:

1

---

forest   *Forest Plots for "meta.nsue" Objects*

Description

Draws a forest plot.

Usage

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

Arguments

x	an object of class `"meta.nsue"`.
width	the width of the plot, expressed as the maximum effect size that would be still plotted.
...	other arguments (currently ignored).

Details

The plot shows the observed or imputed effect sizes of the studies with the corresponding 95% confidence intervals. A light gray shadow shows the interval containing 95% of the imputations for studies with Non-statistically Significant Unreported Effects (NSUEs).

The effect size of the hypothesis of the model with the corresponding 95% confidence intervals is added to the bottom of the forest plot.

Value

The function invisibly returns the optimal width and height of the plot, useful when calling the function [pdf](#).

Author(s)

Joaquim Radua

See Also

[funnel](#) for plotting funnel plots.

[meta](#) for conducting a meta-analysis.

[pdf](#) for saving the plot in a PDF file.

Examples

```
t <- c(3.4, NA, NA, NA, NA, 2.8, 2.1, 3.1, 2.0, 3.4)
n <- c(40, 20, 22, 24, 18, 30, 25, 30, 16, 22)
m <- meta(smc_from_t(t, n))
forest(m)
```

---

funnel	*Funnel Plots for "meta.nsue" Objects*

Description

Draws a funnel plot.

Usage

```
funnel(x, ...)
```

Arguments

x	an object of class `"meta.nsue"`.
...	other arguments (currently ignored).

Details

The plot shows the residual effect size of the studies on the x-axis against their standard errors on the y-axis. A light gray shadow shows the ellipse approximately containing 95% of the imputations for studies with Non-statistically Significant Unreported Effects (NSUEs). A pseudo confidence interval region is drawn with a dashed line.

Asymmetry in the funnel plot may be an indication of publication bias, but this should be taken with caution, especially if sample sizes are too similar, if there are subgroups, or if dichotomous outcomes have been used (some effect estimates are naturally correlated with their standard errors).

Also, publication bias cannot be excluded in case of negative results, whereas it is only one of the possible explanations in case of positive results - others being selective outcome reporting, poor methodological quality in the smaller studies, true heterogeneity (i.e. effect size truly depends on study size), and etcetera.

Author(s)

Joaquim Radua

References

Egger, M., Smith, G.D., Schneider, M., Minder, C. (1997) Bias in meta-analysis detected by a simple, graphical test. *BMJ*, **315**, 629–634, doi:10.1136/bmj.315.7109.629.

See Also

metabias for testing for funnel plot asymmetry.

forest for plotting forest plots.

meta for conducting a meta-analysis.

pdf for saving the plot in a PDF file.

Examples

```
t <- c(3.4, NA, NA, NA, NA, 2.8, 2.1, 3.1, 2.0, 3.4)
n <- c(40, 20, 22, 24, 18, 30, 25, 30, 16, 22)
m <- meta(smc_from_t(t, n))
funnel(m)
```

---

leave1out   *Compute Leave-One-Out Diagnostics for "nsue" Objects*

Description

Repeatedly fits the specified model, leaving out one study at a time.

Usage

```
leave1out(x, ...)

## S3 method for class 'nsue'
leave1out(x, formula = ~1, hypothesis = NULL,
    n.imp = 500, maxiter = 200, tol = 1e-06, ...)
```

Arguments

x	an object of class "nsue".
formula	an object of class "formula": a symbolic description of the model to be fitted.
hypothesis	a hypothesis, or NULL to simply test the coefficients of the model.
n.imp	number of imputations of NSUEs per study.
maxiter	maximum number of iterations in the REML estimation of τ^2.
tol	tolerance in the REML estimation of τ^2.
...	other arguments (currently ignored).

Details

Use [nsue](#), [smc_from_t](#), [smd_from_t](#) or [zcor_from_r](#) to create objects of class "nsue".

Models for [meta](#) and leave1out are specified symbolically. The formula is a series of terms which specify a linear predictor for x. A formula specification of the form first + second indicates a multiple regression by first and second. A specification of the form first:second indicates the interaction of first with second. The specification first*second is the same as first + second + first:second.

Each hypothesis must be a matrix (or vector) giving linear combinations of coefficients by rows.

Value

leave1out returns an object of class "leave1out.nsue", which is a list containing a list for each iteration with the component study (the study discarded) and the component meta, which is an object of class "meta.nsue".

The functions print and summary may be used to print the details or a summary of the results.

Author(s)

Joaquim Radua

References

Radua, J., Schmidt, A., Borgwardt, S., Heinz, A., Schlagenhauf, F., McGuire, P., Fusar-Poli, P. (2015) Ventral striatal activation during reward processing in psychosis. A neurofunctional meta-analysis. *JAMA Psychiatry*, **72**, 1243–51.

Albajes-Eizagirre, A., Solanes, A, Radua, J. (2018) Meta-analysis of non-statistically significant unreported effects. *Statistical Methods in Medical Research*, in Press.

See Also

nsue, smc_from_t, smd_from_t and zcor_from_r for creating objects of class "nsue".

meta for conducting a meta-analysis.

Examples

```
t <- c(3.4, NA, NA, NA, NA, 2.8, 2.1, 3.1, 2.0, 3.4)
n <- c(40, 20, 22, 24, 18, 30, 25, 30, 16, 22)
leave1out(smc_from_t(t, n))
```

---

meta	*Meta-Analysis of Studies with Non-statistically Significant Unreported Effects*

Description

Conduct a meta-analysis. MetaNSUE is a meta-analytic method that allows an unbiased inclusion of studies with Non-statistically Significant Unreported Effects (NSUEs).

Usage

```
meta(x, ...)

## S3 method for class 'nsue'
meta(x, formula = ~1, hypothesis = NULL,
    n.imp = 500, maxiter = 200, tol = 1e-06, ...)
```

Arguments

x	an object of class "nsue".
formula	an object of class "formula": a symbolic description of the model to be fitted.
hypothesis	a hypothesis, or NULL to test the main coefficient of the model.
n.imp	number of imputations of NSUEs.
maxiter	maximum number of iterations in the REML estimation of τ^2.
tol	tolerance in the REML estimation of τ^2.
...	other arguments (currently ignored).

Details

Use [nsue](), [smc_from_t](), [smd_from_t]() or [zcor_from_r]() to create objects of class `"nsue"`.

Models for `meta` and [leave1out]() are specified symbolically. The `formula` is a series of terms which specify a linear predictor for `x`. A formula specification of the form `first + second` indicates a multiple regression by `first` and `second`. A specification of the form `first:second` indicates the interaction of `first` with `second`. The specification `first*second` is the same as `first + second + first:second`.

Each hypothesis must be a matrix (or vector) giving linear combinations of coefficients by rows.

Value

`meta` returns an object of class `"meta.nsue"`, which is a list containing the following components:

`aux`	information required for `y2var`, `mi` and / or `backtransf`.
`y2var`	a function to derive the variances of the effect sizes.
`mi`	a function to multiply impute effect sizes.
`backtransf`	a function to back-transform the effect sizes.
`measure`	a description of the effect-size measure used.
`labels`	the labels of the studies.
`known`	a list with the known effect sizes and their indexs.
`unknown`	a list with the imputations of NSUEs and their indexs.
`model`	a list with the formula, matrix and coefficients of the model.
`heterogeneity`	a list with τ^2, H^2, I^2 and Q test.
`hypothesis`	the matrixs and coefficients of the hypothesis.

The functions `print` and `summary` may be used to print the details or a summary of the results. The generic accessor functions `coefficients`, `fitted.values` and `residuals` extract various useful features of the value returned by `meta`.

Author(s)

Joaquim Radua

References

Radua, J., Schmidt, A., Borgwardt, S., Heinz, A., Schlagenhauf, F., McGuire, P., Fusar-Poli, P. (2015) Ventral striatal activation during reward processing in psychosis. A neurofunctional meta-analysis. *JAMA Psychiatry*, **72**, 1243–51.

Albajes-Eizagirre, A., Solanes, A, Radua, J. (2018) Meta-analysis of non-statistically significant unreported effects. *Statistical Methods in Medical Research*, in Press.

See Also

nsue, smc_from_t, smd_from_t and zcor_from_r for creating objects of class "nsue".

forest for plotting forest plots.

funnel for plotting funnel plots.

metabias for testing for funnel plot asymmetry.

leave1out for computing leave-one-out diagnostics.

Examples

```
t <- c(3.4, NA, NA, NA, NA, 2.8, 2.1, 3.1, 2.0, 3.4)
n <- c(40, 20, 22, 24, 18, 30, 25, 30, 16, 22)
meta(smc_from_t(t, n))
```

---

metabias	*Test for Funnel Plot Asymmetry for "meta.nsue" Objects*

Description

Test for funnel plot asymmetry.

Usage

```
metabias(x, ...)

## S3 method for class 'meta.nsue'
metabias(x, maxiter = 100, tol = 1e-06, ...)
```

Arguments

x	an object of class "meta.nsue".
maxiter	maximum number of iterations in the REML estimation of τ^2.
tol	tolerance in the REML estimation of τ^2.
...	other arguments (currently ignored).

Details

The test, based on a meta-regression by the standard error, aims to detect asymmetry in the funnel plot, which may be an indication of publication bias.

However, results should be taken with caution, especially if there are too few studies (at least 10 studies were suggested by Sterne et al. (2011)), if sample sizes are too similar, if there are outliers or influential studies or subgroups in the plot, or if dichotomous outcomes have been used (some effect estimates are naturally correlated with their standard errors).

Also, publication bias cannot be excluded in case of negative results, whereas it is only one of the possible explanations in case of positive results - others being selective outcome reporting, poor methodological quality in the smaller studies, true heterogeneity (i.e. effect size truly depends on study size), and etcetera (Egger 1997).

Value

A list with class `"htest"` containing the following components:

data.name   a character string giving the name of the data.

method   a character string indicating that a `"meta.nsue"` regression test for funnel plot
                asymmetry was performed.

statistic   the value of the z-statistic.

p.value   the p-value for the test.

Author(s)

Joaquim Radua

References

Egger, M., Smith, G.D., Schneider, M., Minder, C. (1997) Bias in meta-analysis detected by a simple, graphical test. *BMJ*, **315**, 629–634, doi:10.1136/bmj.315.7109.629.

Radua, J., Schmidt, A., Borgwardt, S., Heinz, A., Schlagenhauf, F., McGuire, P., Fusar-Poli, P. (2015) Ventral striatal activation during reward processing in psychosis. A neurofunctional meta-analysis. *JAMA Psychiatry*, **72**, 1243–51.

Albajes-Eizagirre, A., Solanes, A, Radua, J. (2018) Meta-analysis of non-statistically significant unreported effects. *Statistical Methods in Medical Research*, in Press.

Sterne, J.A., Sutton, A.J., Ioannidis, J.P., Terrin, N., Jones, D.R., Lau, J., Carpenter, J., Rucker, G., Harbord, R.M., Schmid, C.H., Tetzlaff, J., Deeks, J.J., Peters, J., Macaskill, P., Schwarzer, G., Duval, S., Altman, D.G., Moher, D., Higgins, J.P. (2011) Recommendations for examining and interpreting funnel plot asymmetry in meta-analyses of randomised controlled trials. *BMJ*, **343**, d4002, doi:10.1136/bmj.d4002.

See Also

funnel for plotting funnel plots.

meta for conducting a meta-analysis.

Examples

```
t <- c(3.4, NA, NA, NA, NA, 2.8, 2.1, 3.1, 2.0, 3.4)
n <- c(40, 20, 22, 24, 18, 30, 25, 30, 16, 22)
m <- meta(smc_from_t(t, n))
metabias(m)
```

---

nsue   *Calculate Effect Sizes for "meta.nsue" Objects*

Description

These functions create objects of class "nsue", ready to be used by meta and leave1out.

Usage

```
nsue(y, y_lo = -y_up, y_up, aux, y2var, mi, backtransf = .backtransf_identity,
      measure = "effect size", labels = "study")
smc_from_t(t, n, alpha = 0.05, labels = "study")
smd_from_t(t, n1, n2, alpha = 0.05, labels = "study")
zcor_from_r(r, n, alpha = 0.05, labels = "study")
```

Arguments

y	a vector to specify the effect-sizes. Use NA in studies with Non-statistically Significant Unreported Effects (NSUEs).
t	a vector to specify the t-values of the studies. Use NA in studies with Non-statistically Significant Unreported Effects (NSUEs).
r	a vector to specify the correlation coefficients of the studies. Use NA in studies with Non-statistically Significant Unreported Effects (NSUEs).
y_lo	a vector to specify the effect-sizes corresponding to the lower statistical threshold.
y_up	a vector to specify the effect-sizes corresponding to the upper statistical threshold.
aux	a data.frame to specify information required for y2var, mi and / or backtransf.
n	a vector to specify the sample sizes of the studies.
n1	a vector to specify the sample sizes of the first group (e.g. patients) of studies.
n2	a vector to specify the sample sizes of the second group (e.g. controls) of the studies.
y2var	a function to derive the variances of the effect sizes.
mi	a function to multiply impute effect sizes.
backtransf	a function to back-transform the effect sizes.
measure	a description of the effect-size measure used.
labels	a vector to specify the labels of the studies.
alpha	a vector to specify the p-value thresholds used in the studies (e.g. 0.05).

Details

Use nsue for creating an object of class "nsue".

Use smc_from_t for creating an object of class "nsue" for standardized mean changes from the t-values of the paired Student t-tests, e.g. in repeated-measures studies analyzing the amount of change in within a group.

Use smd_from_t for creating an object of class "nsue" for standardized mean differences from t-values of the two-sample Student t-tests, e.g. in studies comparing a quantitative (normally-distributed) variable between two groups.

Use zcor_from_r for creating an object of class "nsue" for Pearson correlation coefficients (using the Fisher's transform), e.g. in studies examining the association between two quantitative (normally-distributed) variables.

Value

nsue, smc_from_t, smd_from_t, and zcor_from_r return objects of class "nsue".

The function print may be used to print a summary of the results. The function subset returns the subset of studies that meets a condition.

An object of class "nsue" is a list containing the following components:

y	the effect-sizes.
y_lo	the effect-sizes corresponding to the lower statistical threshold.
y_up	the effect-sizes corresponding to the upper statistical threshold.
aux	information required for y2var, mi and / or backtransf.
y2var	a function to derive the variances of the effect sizes.
mi	a function to multiply impute effect sizes.
backtransf	a function to back-transform the effect sizes.
measure	a description of the effect-size measure used.
labels	the labels of the studies.

Users can create their objects of class "nsue" for effect sizes not included in the package.

Author(s)

Joaquim Radua

References

Radua, J., Schmidt, A., Borgwardt, S., Heinz, A., Schlagenhauf, F., McGuire, P., Fusar-Poli, P. (2015) Ventral striatal activation during reward processing in psychosis. A neurofunctional meta-analysis. *JAMA Psychiatry*, **72**, 1243–51.

Albajes-Eizagirre, A., Solanes, A, Radua, J. (2018) Meta-analysis of non-statistically significant unreported effects. *Statistical Methods in Medical Research*, in Press.

See Also

meta for conducting a meta-analysis.

leave1out for computing leave-one-out diagnostics.

Examples

```
# Standardized mean change in one sample:
t <- c(3.4, NA, NA, NA, 3.2, 2.8, 2.1, 3.1, 2.0, 3.4)
n <- c(40, 20, 22, 24, 18, 30, 25, 30, 16, 22)
smc <- smc_from_t(t, n)
m0 <- meta(smc)
smc
m0

# Standardized mean difference between two samples:
t <- c(4.8, 3.2, NA, NA, NA, 3.2, 2.0, 2.3, 2.7, 3.1)
n1 <- c(40, 20, 22, 24, 18, 30, 25, 30, 16, 22)
n2 <- c(38, 20, 22, 25, 20, 28, 25, 30, 18, 23)
smd <- smd_from_t(t, n1, n2)
m1 <- meta(smd)
smd
m1

# Pearson correlation:
r <- c(0.80, NA, NA, NA, 0.32, 0.45, 0.53, 0.67, 0.74, 0.56)
n <- c(40, 22, 13, 12, 28, 22, 27, 28, 15, 23)
zr <- zcor_from_r(r, n)
m2 <- meta(zr)
zr
m2
```

Index