Package 'SAMURAI'

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Type Package

Title Sensitivity Analysis of a Meta-analysis with Unpublished but Registered Analytical Investigations

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Description This package contains R functions to gauge the impact of unpublished studies upon the meta-analytic summary effect of a set of published studies. (Credits: The research leading to these results has received funding from the European Union's Seventh Framework Programme (FP7/2007-2013) under grant agreement no. 282574.)

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BHHR2009p92 *Fictional Data Set, with Binary Outcomes*

Description

A fictional meta-analytic data set with 6 published studies and 2 unpublished studies. The binary outcome event is not desired.

Usage

```
data(BHHR2009p92)
```

Format

A data frame with 8 observations on the following 8 variables.

number	`integer`	Study numeric id (optional)
study	`character`	Name of study or principal investigator
year	`integer`	Year (optional)
outlook	`factor`	Denotes whether a study is unpublished, and if so, what outlook it has.
ctrl.n	`integer`	The sample size of the control arm.
expt.n	`integer`	The sample size of the experimental arm.
ctrl.events	`integer`	The number of (undesired) events within the control arm.
expt.events	`integer`	The number of (undesired) events within the experimental arm.

Details

The outlook of a study can be one of the following: `published`, `very positive`, `positive`, `negative`, `very negative`, `current effect`, `no effect`, `very positive CL`, `positive CL`, `negative CL`, or `very negative CL`.

Since the outcome event is undesired, when using the function `forestsens()`, specify the option `higher.is.better=FALSE`. Since this is the default setting for `forestsens()`, this does not need to be specified explicitly.

Source

Borenstein, Hedges, Higgins, and Rothstein. Introduction to Meta-analysis. Wiley, 2009, page 92.

Examples

```
library(SAMURAI)
data(BHHR2009p92)

forestsens(table=BHHR2009p92, binary=TRUE, higher.is.better=FALSE)

# To assign all unpublished studies to each of ten outlooks, one at a time,
# and then return a table of summary effects, their 95% confidence interval,
```

```
# and tau-squared.
summtab <- forestsens(table=BHHR2009p92, binary=TRUE, higher.is.better=FALSE, all.outlooks=TRUE)
summtab
```

`Fleiss1993` *Aspirin after Myocardial Infarction*

Description

A meta-analytic data set that includes 7 published placebo-controlled randomized studies of the effect of aspirin in preventing death after myocardial infarction. The data set also includes 2 (fictional) unpublished studies.

The defined binary outcome event is death, and is undesired. When using the function `forestsens()`, specify the option `higher.is.better=FALSE`.

Usage

```
data(Fleiss1993)
```

Format

A data frame with 9 observations on the following 8 variables.

number	`integer`	Study numeric id (optional)
study	`character`	Name of study or principal investigator
year	`integer`	Year (optional)
outlook	`factor`	Denotes whether a study is unpublished, and if so, what outlook it has.
ctrl.n	`integer`	The sample size of the control arm.
expt.n	`integer`	The sample size of the experimental arm.
ctrl.events	`integer`	The number of (undesired) events within the control arm.
expt.events	`integer`	The number of (undesired) events within the experimental arm.

Details

The outlook of a study can be one of the following: `published`, `very positive`, `positive`, `negative`, `very negative`, `current effect`, `no effect`, `very positive CL`, `positive CL`, `negative CL`, or `very negative CL`.

Since the outcome event is undesired, when using the function `forestsens()`, specify the option `higher.is.better=FALSE`.

Source

Fleiss, JL. (1993) "The statistical basis of meta-analysis." *Stat Methods Med Res.* 2(2):121-45.

References

Guido Schwartzer. meta package.

Examples

```
library(SAMURAI)
data(Fleiss1993)

forestsens(table=Fleiss1993, binary=TRUE, higher.is.better=FALSE)

# To assign all unpublished studies to each of ten outlooks, one at a time,
# and then return a table of summary effects, their 95% confidence interval,
# and tau-squared.
summtab <- forestsens(table=Fleiss1993, binary=TRUE, higher.is.better=FALSE, all.outlooks=TRUE)
summtab
```

---

forestsens *Forest Plot for Sensitivity Analysis*

Description

This function imputes missing effect sizes for unpublished studies and creates a forest plot. A set of forest plots can be generated for multiple imputations.

Usage

```
forestsens(table,
  binary = TRUE, mean.sd = FALSE,
  higher.is.better = FALSE,
  outlook = NA, all.outlooks = FALSE,
  rr.vpos = NA, rr.pos = NA, rr.neg = NA, rr.vneg = NA,
  smd.vpos = NA, smd.pos = NA, smd.neg = NA, smd.vneg = NA,
  level = 95,
  binary.measure = "RR", continuous.measure="SMD",
  summary.measure="SMD", method = "DL",
  random.number.seed = NA, sims = 10, smd.noise = 0.01,
  plot.title = "", scale = 1, digits = 3)
```

Arguments

table	The name of the table containing the meta-analysis data.
binary	TRUE if the outcomes are binary events; FALSE if the outcome data is continuous.
mean.sd	TRUE if the data set includes the mean and standard deviation of the both the control and experimental arms of studies with continuous outcomes; FALSE otherwise.

`higher.is.better`
: `TRUE` if higher counts of binary events or higher continuous outcomes are desired; `FALSE` otherwise. For continuous outcomes, set as FALSE if a lower outcome (eg. a more negative number) is desired.

`outlook`
: If you want all unpublished studies to be assigned the same outcome, set this parameter to one of the following values: `"very positive"`, `"positive"`, `"current effect"`, `"negative"`, `"very negative"`, `"no effect"`, `"very positive CL"`, `"positive CL"`, `"negative CL"`, `"very negative CL"`.

`all.outlooks`
: If `TRUE`, then a forest plot will be generated for each possible outlook.

`rr.vpos`
: The user-defined relative risk for binary outcomes in unpublished studies with a `"very positive"` outlook.

`rr.pos`
: The user-defined relative risk for binary outcomes in unpublished studies with a "positive" outlook.

`rr.neg`
: The user-defined relative risk for binary outcomes in unpublished studies with a "negative" outlook.

`rr.vneg`
: The user-defined relative risk for binary outcomes in unpublished studies with a "very negative" outlook.

`smd.vpos`
: The user-defined standardized mean difference for continuous outcomes in unpublished studies with a "very positive" outlook.

`smd.pos`
: The user-defined standardized mean difference for continuous outcomes in unpublished studies with a "positive" outlook.

`smd.neg`
: The user-defined standardized mean difference for continuous outcomes in unpublished studies with a "negative" outlook.

`smd.vneg`
: The user-defined standardized mean difference for continuous outcomes in unpublished studies with a "very negative" outlook.

`level`
: The confidence level, as a percent.

`binary.measure`
: The effect size measure used for binary outcomes. "RR" for relative risk; "OR" for odds ratios.

`continuous.measure`
: The effect size measure used for continuous outcomes. "SMD" for standardized mean difference (with the assumption of equal variances).

`summary.measure`
: The measure used for summary effect sizes.

`method`
: The same parameter in the escalc() function of the metafor package. "DL" for the DerSimonian-Laird method.

`random.number.seed`
: Leave as `NA` if results are to be randomized each time. Set this value to a integer between 0 and 255 if results are to be consistent (for purposes of testing and comparison).

`sims`
: The number of simulations to run per study when imputing unpublished studies with binary outcomes.

`smd.noise`
: The standard deviation of Gaussian random noise to be added to standardized mean differences when imputing unpublished studies with continuous outcomes.

`plot.title`
: Main title of forest plot.

scale	Changes the scaling of fonts in the forest plot.
digits	The number of significant digits (decimal places) to appear in the table of summary results which appears if all.outlooks=TRUE.

Details

For unpublished studies with binary outcomes, random numbers are generated from binomial distributions to impute the number of events in the experimental arms of experimental studies. The parameter of these distributions depends out the outlook of the unpublished study and the rate of events in the control arms of published studies. By default, 10 simulations are run and their average is used to impute the number of events in the experimental arm.

For unpublished studies with continuous outcomes, a 'very good' approximator mentioned by Borenstein is used to impute the variance of the standardized mean difference. See Borenstein et al, 2009, pages 27-28.

Note

The function employs functions in the metafor package: escalc() and forest().

Author(s)

Noory Kim

References

Borenstein M, Hedges LV, Higgins JPT, and Rothstein HR (2009). Introduction to Meta-Analysis. Chichester UK: Wiley.

Cooper HC, Hedges LV, & Valentine JC, eds. (2009). *The handbook of research synthesis and meta-analysis* (2nd ed.). New York: Russell Sage Foundation.

DerSimonian R and Laird N (1986). "Meta-analysis in clinical trials." *Controlled Clinical Trials* 7:177-188 (1986).

Viechtbauer W (2010). Conducting meta-analyses in R with the metafor package. *Journal of Statistical Software*, **36**(3), 1–48. http://www.jstatsoft.org/v36/i03/.

See Also

Hpylori, greentea

Examples

```
library(SAMURAI)

data(Hpylori)
forestsens(Hpylori, binary=TRUE, higher.is.better=FALSE)
forestsens(Hpylori, binary=TRUE, higher.is.better=FALSE, plot.title="Test")
forestsens(Hpylori, binary=TRUE, higher.is.better=FALSE, random.number.seed=52)
forestsens(Hpylori, binary=TRUE, higher.is.better=FALSE, outlook="negative")
forestsens(Hpylori, binary=TRUE, higher.is.better=FALSE, all.outlooks=TRUE)
```

```
data(greentea)
forestsens(greentea, binary=FALSE, mean.sd=TRUE, higher.is.better=FALSE)
forestsens(greentea, binary=FALSE, mean.sd=TRUE, higher.is.better=FALSE,
  outlook="negative")
forestsens(greentea, binary=FALSE, mean.sd=TRUE, higher.is.better=FALSE,
  outlook="negative", smd.noise=0.3)
```

`funnelplot` *Funnel Plot*

Description

This function (1) imputes data for a meta-analytic data set with unpublished studies, then (2) generates a funnel plot.

Usage

```
funnelplot(table,
  binary=TRUE, mean.sd=TRUE,
  higher.is.better=NA,
  outlook=NA,
  vpos=NA, pos=NA, neg=NA, vneg=NA,
  level=95,
  binary.measure="RR", continuous.measure="SMD",
  summary.measure="SMD", method="DL",
  random.number.seed=NA, sims=1, smd.noise=0.01,
  title="", pch.pub=19, pch.unpub=0)
```

Arguments

`table`	The name of the table containing the meta-analysis data.
`binary`	`TRUE` if the outcomes are binary events; FALSE if the outcome data is continuous.
`mean.sd`	`TRUE` if the data set includes the mean and standard deviation of the both the control and experimental arms of studies with continuous outcomes; `FALSE` otherwise.
`higher.is.better`	`TRUE` if higher counts of binary events or higher continuous outcomes are desired; `FALSE` otherwise. For continuous outcomes, set as FALSE if a lower outcome (eg. a more negative number) is desired.
`outlook`	If you want all unpublished studies to be assigned the same outcome, set this parameter to one of the following values: `"very positive"`, `"positive"`, `"current effect"`, `"negative"`, `"very negative"`, `"no effect"`, `"very positive CL"`, `"positive CL"`, `"negative CL"`, `"very negative CL"`.
`vpos`	The user-defined effect size for unpublished studies with a `"very positive"` outlook.

pos	The user-defined effect size for unpublished studies with a "positive" outlook.
neg	The user-defined effect size for unpublished studies with a "negative" outlook.
vneg	The user-defined effect size for unpublished studies with a "very negative" outlook.
level	The confidence level, as a percent.
binary.measure	The effect size measure used for binary outcomes. "RR" for relative risk; "OR" for odds ratios.
continuous.measure	The effect size measure used for continuous outcomes. "SMD" for standardized mean difference (with the assumption of equal variances).
summary.measure	The measure used for summary effect sizes.
method	The same parameter in the escalc() function of the metafor package. "DL" for the DerSimonian-Laird method.
random.number.seed	Leave as NA if results are to be randomized each time. Set this value to a integer between 0 and 255 if results are to be consistent (for purposes of testing and comparison).
sims	The number of simulations to run per study when imputing unpublished studies with binary outcomes.
smd.noise	The standard deviation of Gaussian random noise to be added to standardized mean differences when imputing unpublished studies with continuous outcomes.
title	The title of the funnel plot.
pch.pub	The symbol used to denote a published study.
pch.unpub	The symbol used to denote an unpublished study.

Note

The function employs functions in the metafor package: escalc() and forest().

Author(s)

Noory Kim

See Also

forestsens

Examples

```
library(SAMURAI)

data(Hpylori)
funnelplot(Hpylori, binary=TRUE, higher.is.better=FALSE,
  outlook="very negative")

data(greentea)
funnelplot(greentea, binary=FALSE, higher.is.better=FALSE)
```

greentea *The effect of green tea on weight loss.*

Description

Randomized clinical trials of at least 12 weeks duration assessing the effect of green tea consumption on weight loss.

Usage

```
data(greentea)
```

Format

A data frame with 14 observations on the following 9 variables.

study	`character`	Name of study or principal investigator
year	`numeric (integer)`	Year (optional)
outlook	`factor`	Denotes whether a study is unpublished, and if so, what outlook it has.
ctrl.n	`numeric (integer)`	The sample size of the control arm.
expt.n	`numeric (integer)`	The sample size of the experimental arm.
ctrl.mean	`numeric`	The mean effect within the control arm.
expt.mean	`numeric`	The mean effect within the experimental arm.
ctrl.sd	`numeric`	The standard deviation of the outcome within the control arm.
expt.sd	`numeric`	The standard deviation of the outcome within the experimental arm.

Details

The outlook of a study can be one of the following: `published`, `very positive`, `positive`, `negative`, `very negative`, `current effect`, `no effect`, `very positive CL`, `positive CL`, `negative CL`, or `very negative CL`.

In this setting, a more negative change in outcome is desired; specify the option `higher.is.better=FALSE` for the function `forestsens()`.

Source

Jurgens TM, Whelan AM, Killian L, Doucette S, Kirk S, Foy E. "Green tea for weight loss and weight maintenance in overweight or obese adults." *Cochrane Database of Systematic Reviews* 2012, Issue 12. Art. No.: CD008650. DOI: 10.1002/14651858.CD008650.pub2.

Figure 6. Forest plot of comparison: 1 Primary outcomes, outcome: 1.2Weight loss studies conducted in/outside Japan.

Examples

```
data(greentea)
greentea
```

```
forestsens(greentea, binary=FALSE, mean.sd=TRUE, higher.is.better=FALSE)

# To fix the random number seed to make the results reproducible.
forestsens(greentea, binary=FALSE, mean.sd=TRUE, higher.is.better=FALSE, random.number.seed=52)

# To modify the outlooks of all unpublished studies to, say, "negative".
forestsens(greentea, binary=FALSE,mean.sd=TRUE,higher.is.better=FALSE,random.number.seed=52,
  outlook="negative")

# To modify the outlooks of all unpublished studies to, say, "negative", and
# overruling the default standardized mean difference (SMD) assigned to "negative".
# (In this case, for a negative outlook we might assign a positive SMD, which corresponds to
# having weight loss under green tea treatment less than weight loss under control treatment,
# i.e. the green tea treatment is less effective at achieving weight loss than control treatment.
forestsens(greentea, binary=FALSE, mean.sd=TRUE, higher.is.better=FALSE,random.number.seed=52,
  outlook="negative", smd.neg=0.4)

# To generate a forest plot for each of the ten default outlooks defined by forestsens().
forestsens(greentea, binary=FALSE, mean.sd=TRUE, higher.is.better=FALSE, random.number.seed=52,
  all.outlooks=TRUE)
```

`Hpylori` *Healing of duodenal ulcers by Helicobacter pylori eradication therapy*

Description

Randomized clinical trials comparing duodenal ulcer acute healing among (1) patients on ulcer healing drug + Helicobacter pylori eradication therapy vs. (2) patients ulcer healing drug alone. The event counts represent the numbers of patients *not* healed.

Usage

```
data(Hpylori)
```

Format

A data frame with 33 observations on the following 7 variables.

study	`character`	Name of study or principal investigator
year	`numeric`	Year (optional)
outlook	`factor`	Denotes whether a study is unpublished, and if so, what outlook it has.
ctrl.n	`numeric`	The sample size of the control arm.
expt.n	`numeric`	The sample size of the experimental arm.
ctrl.events	`numeric`	The number of (undesired) events within the control arm.
expt.events	`numeric`	The number of (undesired) events within the experimental arm.

Details

The outlook of a study can be one of the following: `published`, `very positive`, `positive`, `negative`, `very negative`, `current effect`, `no effect`, `very positive CL`, `positive CL`, `negative CL`, or `very negative CL`.

Since the outcome event is undesired, when using the function `forestsens()`, specify the option `higher.is.better=FALSE`.

Source

Ford AC, Delaney B, Forman D, Moayyedi P. "Eradication therapy for peptic ulcer disease in *Helicobacter pylori* positive patients." *Cochrane Database of Systematic Reviews* 2006, Issue 2. Art No.: CD003840. DOI: 10.1002/14651858.CD003840.pub4.

Figure 3. Forest plot of comparison: 1 duodenal ulcer acute healing hp eradication + ulcer healing drug vs. ulcer healing drug alone, outcome: 1.1 Proportion not healed.

Examples

```
data(Hpylori)
Hpylori

forestsens(table=Hpylori, binary=TRUE, higher.is.better=FALSE, scale=0.8)

# To fix the random number seed to make the results reproducible.
forestsens(table=Hpylori, binary=TRUE, higher.is.better=FALSE, scale=0.8,
  random.number.seed=106)

# To modify the outlooks of all unpublished studies to, say, "very negative".
forestsens(table=Hpylori, binary=TRUE, higher.is.better=FALSE, scale=0.8,
  random.number.seed=106, outlook="very negative")

# To modify the outlooks of all unpublished studies to, say, "very negative",
# and overruling the default relative risk assigned to "very negative".
forestsens(table=Hpylori, binary=TRUE, higher.is.better=FALSE, scale=0.8,
  random.number.seed=106, outlook="very negative", rr.vneg=2.5)

# To generate a forest plot for each of the ten default outlooks
# defined by forestsens().
forestsens(table=Hpylori, binary=TRUE, higher.is.better=FALSE, scale=0.8,
  random.number.seed=106, all.outlooks=TRUE)
```

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