Package ‘subgroup’

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Type Package
Title Methods for exploring treatment effect heterogeneity in subgroup analysis of clinical trials
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Description Produces various measures of expected treatment effect heterogeneity under an assumption of homogeneity across subgroups. Graphical presentations are created to compare these expected differences with the observed differences.
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subgroup  Compute measures for assessing treatment effect heterogeneity across subgroups in clinical trials and produce graphical presentations

Description

This function produces various measures of expected treatment effect heterogeneity and allows graphical comparisons with the observed counterparts. The resulting measures can also be saved for creation of user-specified graphics.
Usage

subgroup(data, overall.diff = NA, force.theoretical = FALSE, force.simulation = FALSE, design = FALSE, plots = TRUE)

Arguments

data A matrix of 2 columns containing the subgroup treatment effects and their associated standard errors. The treatment effects must be measured on a scale where 0 means no effect. For example, a mean difference, a log relative risk, log odds ratio, or log hazard ratio. Column 2 must contain the standard errors associated with the subgroup treatment effects in Column 1. Furthermore, a treatment effect that is > 0 is considered to favour the control.

overall.diff The overall treatment effect, provided optionally by the user. If not specified this is calculated within the subgroup routine as a reciprocal variance weighted mean.

force.theoretical The default value for this argument is FALSE. If TRUE, theoretical computations are conducted regardless of the number of subgroups, R. If the standard errors of the subgroup treatment effects is heterogeneous and R > 20, a warning is given to advise the user that the processing time may be significant. An error message is given if both force.theoretical and force.simulation are set to TRUE, and the routine will stop execution.

force.simulation The default value for this argument is FALSE. If TRUE, simulation based computations are conducted regardless of the number of subgroups, R. An error message is given if both force.theoretical and force.simulation are set to TRUE, and the routine will stop execution.

design The default value for this argument is FALSE. If TRUE, the plots will not include any observed measures.

plots The default value for this argument is TRUE. If FALSE, no plots will be displayed.

Details

Subgroup analysis principles require a significant test of interaction in order to claim heterogeneity of treatment effect. As clinical trials are typically underpowered for tests of interaction, overly optimistic expectations of treatment effect homogeneity can make interpretation difficult when treatment effects seemingly differ between subgroups. In addition to extending the ideas proposed by Marschner (2010), the package subgroup also implements some new measures, and provides a suite of graphical tools that allow visual comparison of the magnitude and nature of the observed and expected subgroup differences that can arise as an artefact of chance. These tools are intended to supplement a formal test of interaction in subgroup analyses, and are described in the manuscript Schou and Marschner (2014).

Three outputs are computed by the package. These include the following: the expectations of the ordered treatment effects, the probability density of the range, and the probability distribution of the number of subgroups favouring the control treatment. The user has the option to have the in-built plot suppressed. The content of the default plot produced will depend on the user choice of an
analysis stage evaluation or a design stage evaluation; if it is the former, the observed counterparts of the measures produced will be included in the plots.

Value

The following list of components is returned by the routine subgroup:

- **expectations**: A matrix of dimension $R \times 4$, where $R$ is the number of subgroups. The first two columns present the treatment differences and the standard errors contained in the dataset $data$ as submitted by the user. The third column contains the expected ordered treatment differences, and the fourth column the order number.

- **favourcontrol**: A matrix of dimension $(R+1) \times 2$, where $R$ is the number of subgroups. The first column contains the number of subgroups favouring control. The second contains the probability of that event. Here, a treatment effect that is $> 0$ is considered to favour the control.

- **rangedensity**: A matrix with 2 columns. The first column contains the sample space for the range which takes on values $> 0$. The second column contains the probability density.

- **overalldiff**: A numeric variable which returns the input argument `overall.diff` if specified by the user or the reciprocal variance weighted mean treatment difference as calculated within the routine `subgroup`.

Author(s)

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References


Examples

```r
# Create dataset containing treatment differences and standard errors. ----------
difference<-c(-0.163, -0.083, -0.030, 0.095)
se<-c(0.48, 0.27, 0.19, 0.39)
mydata<-cbind(difference, se)

# Example code to produce the expected measures together with the plot created ----
# by the subgroup routine for comparison against the observed differences. -------
# NOTE: The execution time increases as the number of subgroups increases. -------
test1<-subgroup(data=mydata)

# Expected measures produced by the subgroup routine that the user --------------
# can manipulate to produce own graphics. --------------------------------------
test1$overalldiff # Overall difference between treatment groups.
```
test1$expectations # Expectations of the ordered treatment differences.
test1$rangedensity[1:15,] # Sample of the probability density of the range.
test1$favourcontrol # Prob dist of subgroups favouring the control treatment.

# Example code for evaluation of chance heterogeneity at the design stage. --------
test2<-subgroup(data=mydata, design=TRUE)

# Example code for simulation based evaluation of chance heterogeneity. ----------
test3<-subgroup(data=mydata, force.simulation=TRUE)
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