Package ‘MultEq’

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Description Equivalence tests and related confidence intervals for the comparison of two treatments, simultaneously for one or many normally distributed, primary response variables (endpoints). The step-up procedure of Quan et al. (2001) is both applied for differences and extended to ratios of means. A related single-step procedure is also available.

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Description

The package provides tests and confidence intervals for comparing two treatments when there is more than one primary response variable (endpoint). The step-up procedure of Quan et al. (2001) is both applied for differences and extended to ratios of means of normally distributed data with equal group variances. A related single-step procedure is also available.

Details

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- multeq.diffEquivalence tests and related confidence intervals for differences of normal means of multiple endpoints
- multeq.ratEquivalence tests and related confidence intervals for ratios of normal means of multiple endpoints
- clinicData set of body measurements in a clinical study

Author(s)

Mario Hasler
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References

Quan et al. (2001): Assessmant of equivalence on multiple endpoints, Statistics in Medicine 20, 3159-3173

Examples

data(clinic)

comp <- multeq.diff(data=clinic, grp="fact", method="step.up", margin.up=rep(0.6,5), margin.lo=-rep(0.6,5))
summary(comp)
Body measurements in a clinical study

Description
Measurements on six parts of patients' bodies in a clinical study for two competing treatments.

Usage
data(clinic)

Format
A data frame with 30 observations on the following 6 variables.

fact a factor with levels 1 2, specifying the treatment groups
var1 numeric vectors containing measurements on a first part of patients' bodies
var2 numeric vectors containing measurements on a second part of patients' bodies
var3 numeric vectors containing measurements on a third part of patients' bodies
var4 numeric vectors containing measurements on a fourth part of patients' bodies
var5 numeric vectors containing measurements on a fifth part of patients' bodies

Source
L"auter, and Kropf, (1998): Exact stable multivariate tests for application in clinical research. Joint statistical meeting Dallas (USA), conference proceedings, group 1

Examples
library(MultEq)
data(clinic)
plot(clinic[,c1])

multeq.diff
Equivalence for differences of means of multiple endpoints

Description
Performs equivalence tests and related confidence intervals for differences of two normal means of multiple endpoints.

Usage
multeq.diff(data, grp, resp = NULL, base = 1, margin.lo = NULL, margin.up = NULL, method = "single.step", var.equal = FALSE, FWER = 0.05)
Arguments

- **data**: a data frame containing response variables (endpoints) and the group variable as columns, the data must have exactly two treatment groups
- **grp**: the name of the group variable in " ", the data must have exactly two treatment groups
- **resp**: a vector of names of the response variables (endpoints) in " ", the data must have exactly two treatment groups
- **base**: a single integer specifying the base/control group
- **margin.lo**: a vector of absolute lower margins under the null hypotheses relating to the endpoints
- **margin.up**: a vector of absolute upper margins under the null hypotheses relating to the endpoints
- **method**: a character string:
  - "step.up": method of Quan et al. (2001),
  - "single.step": Bonferroni-adjusted single-step procedure
- **var.equal**: a logical indicating homogeneous or heterogeneous variances of the data
- **FWER**: a single numeric value specifying the familywise error rate to be controlled by the simultaneous confidence intervals

Details

The objective is to show equivalence for two treatment groups on multiple primary, normally distributed response variables (endpoints). If margin.up is not given, one-sided tests are applied for the alternative hypothesis that the differences (to the base group) of the means is larger than margin.lo. Analogously, same vice versa. Only if both margin.lo and margin.up are given, a two-sided equivalence test for differences is done. Bonferroni adjusted "two one-sided t-tests" (TOST) and related simultaneous confidence intervals are used for method "single.step"; the method of Quan et al. (2001) is applied for "step.up". Welch t-tests and related confidence intervals are used for var.equal=FALSE.

Value

An object of class multeq.diff containing:

- **estimate**: a (named) vector of estimated differences
- **test.stat**: a (named) vector of the calculated test statistics
- **degr.fr**: either a single degree of freedom (var.equal=TRUE) or a (named) vector of degrees of freedom (var.equal=FALSE)
- **p.value**: a (named) vector of p-values adjusted for multiplicity
- **lower**: a (named) vector of lower confidence limits
- **upper**: a (named) vector of upper confidence limits

Note

Because related to the TOST method, the two-sided confidence intervals for method="single.step" have simultaneous coverage probability (1-2alpha). The intervals for method="step.up" are step-wise adjusted and only applicable for test decisions, not for a simultaneous parameter estimation or comparing among each other.
multeq.rat

Author(s)
Mario Hasler

References
Quan et al. (2001): Assessment of equivalence on multiple endpoints, Statistics in Medicine 20, 3159-3173

See Also
multeq.rat

Examples

data(clinic)

comp <- multeqNdiff(data=clinic,grp="fact",method="step.up",margin.up=rep(0.6,5),
                margin.lo=-rep(0.6,5))
summary(comp)

Description
Equivalence for ratios of means of multiple endpoints

Usage
multeq.rat(data, grp, resp = NULL, base = 1, margin.lo = NULL, margin.up = NULL,
method = "single.step", var.equal = FALSE, FWER = 0.05)

Arguments
data a data frame containing response variables (endpoints) and the group variable as columns, the data must have exactly two treatment groups
grp the name of the group variable in ""
resp a vector of names of the response variables (endpoints) in ""
base a single integer specifying the base/control group
margin.lo a vector of relative lower margins under the null hypotheses relating to the endpoints
margin.up a vector of relative upper margins under the null hypotheses relating to the endpoints
method a character string:
• "step.up": method of Quan et al. (2001),
• "single.step": Bonferroni-adjusted single-step procedure

`var.equal` a logical indicating homogeneous or heterogeneous variances of the data

`FWER` a single numeric value specifying the familywise error rate to be controlled by the simultaneous confidence intervals

**Details**

The objective is to show equivalence for two treatment groups on multiple primary, normally distributed response variables (endpoints). If `margin.up` is not given, one-sided tests are applied for the alternative hypothesis that the ratios (to the base group) of the means is larger than `margin.lo`. Analogously, same vice versa. Only if both `margin.lo` and `margin.up` are given, a two-sided equivalence tests for ratios is done. Bonferroni adjusted "two one-sided t-tests" (TOST) and related simultaneous confidence intervals are used for method "single.step"; an extended version of the method of Quan et al. (2001) is applied for "step.up". Welch t-tests and related confidence intervals are used for `var.equal=FALSE`.

**Value**

An object of class `multeq.rat` containing:

- `estimate` a (named) vector of estimated ratios
- `test.stat` a (named) vector of the calculated test statistics (var.equal=TRUE)
- `test.stat.up` a (named) vector of the calculated test statistics (up) (var.equal=FALSE)
- `test.stat.do` a (named) vector of the calculated test statistics (do) (var.equal=FALSE)
- `degr.fr` a single degree of freedom (var.equal=TRUE)
- `degr.fr.up` a (named) vector of degrees of freedom for test statistics (up) (var.equal=FALSE)
- `degr.fr.do` a (named) vector of degrees of freedom for test statistics (do) (var.equal=FALSE)
- `degr.fr.ci` a (named) vector of degrees of freedom used for the confidence intervals (var.equal=FALSE)
- `p.value` a (named) vector of p-values adjusted for multiplicity
- `lower` a (named) vector of lower confidence limits
- `upper` a (named) vector of upper confidence limits

**Note**

Because related to the TOST method, the two-sided confidence intervals for method="single.step" have simultaneous coverage probability (1-2alpha). The intervals for method="step.up" are step-wise adjusted and only applicable for test decisions, not for a simultaneous parameter estimation or comparing among each other.

**Author(s)**

Mario Hasler
References
Quan et al. (2001): Assessmant of equivalence on multiple endpoints, Statistics in Medicine 20, 3159-3173

See Also
multeq.diff

Examples

data(clinic)

comp <- multeq.rat(data=clinic,grp="fact",method="step.up",margin.up=rep(1.25,5),
    margin.lo=1/rep(1.25,5))
summary(comp)

print.multeq.diff  
Print out of the results of multeq.diff

Description
A short print out of the results of multeq.diff.

Usage

## S3 method for class 'multeq.diff'
print(x, digits = 4, ...)

Arguments

x an object of class "multeq.diff" as obtained by calling multeq.diff
digits digits for rounding the results
... arguments to be passed to print

Value
A print out containing the margins, estimates, confidence intervals, and p.values computed by multeq.diff.

Author(s)
Mario Hasler

See Also

print.multeq.rat
print.multeq.rat  

Print out of the results of multeq.rat

Description

A short print out of the results of multeq.rat.

Usage

## S3 method for class 'multeq.rat'
print(x, digits = 4, ...)  

Arguments

- **x**: an object of class "multeq.rat" as obtained by calling multeq.rat
- **digits**: digits for rounding the results
- **...**: arguments to be passed to print

Value

A print out containing the margins, estimates, confidence intervals, and p.values computed by multeq.rat.

Author(s)

Mario Hasler

See Also

- print.multeq.diff

summary.multeq.diff  

Summary function for multeq.diff

Description

A detailed print out of the results of multeq.diff.

Usage

## S3 method for class 'multeq.diff'
summary(object, digits = 4, ...)
**summary.multeq.rat**

**Arguments**

- `object`: an object of class "multeq.diff" as obtained by calling `multeq.diff`
- `digits`: digits for rounding the results
- `...`: arguments to be passed to `print`

**Value**

A print out containing the margins, degrees of freedom, estimates, test statistics, confidence intervals, and `p`-values computed by `multeq.diff`.

**Author(s)**

Mario Hasler

**See Also**

`summary.multeq.rat`

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**Description**

A detailed print out of the results of `multeq.rat`.

**Usage**

```r
## S3 method for class 'multeq.rat'
summary(object, digits = 4, ...)
```

**Arguments**

- `object`: an object of class "multeq.rat" as obtained by calling `multeq.rat`
- `digits`: digits for rounding the results
- `...`: arguments to be passed to `print`

**Value**

A print out containing the margins, degrees of freedom, estimates, test statistics, confidence intervals, and `p`-values computed by `multeq.rat`.

**Author(s)**

Mario Hasler

**See Also**

`summary.multeq.diff`
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