Package 'ETC'

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Title Equivalence to control

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Description The package allows selecting those treatments of a one-way layout being equivalent to a control. Bonferroni adjusted ``two one-sided t-tests'' (TOST) and related simultaneous confidence intervals are given for both differences or ratios of means of normally distributed data. For the case of equal variances and balanced sample sizes for the treatment groups, the single-step procedure of Bofinger and Bofinger (1995) can be chosen. For non-normal data, the Wilcoxon test is applied.

License GPL

LazyLoad yes

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ETC-package *Equivalence to control*

Description

The package allows selecting those treatments of a one-way layout being equivalent to a control. Bonferroni adjusted "two one-sided t-tests" (TOST) and related simultaneous confidence intervals are given for both differences or ratios of means of normally distributed data. For the case of equal variances and balanced sample sizes for the treatment groups, the single-step procedure of Bofinger and Bofinger (1995) can be chosen. For non-normal data, the Wilcoxon test is applied.

Details

Package:	ETC
Type:	Package
Version:	1.3
Date:	2009-01-30
License:	GPL
LazyLoad:	yes

- etc.diffSimultaneous equivalence tests and related confidence intervals for differences to control
- etc.ratSimultaneous equivalence tests and related confidence intervals for ratios to control
- BWData set of body weights measured in a toxicological study

Author(s)

Mario Hasler

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References

Hothorn, L.A. and Hasler, M. (2008): Proof of hazard and proof of safety in toxicological studies using simultaneous confidence intervals for differences and ratios to control, Journal of Biopharmaceutical Statistics 18, 915-933;

Bofinger, E. and Bofinger M. (1995): Equivalence with respect to a control: Stepwise tests, Journal of the Royal Statistical Society B 57 (4), 721-733;

Bofinger, E. (1985): Expanded confidence intervals, Communications in Statistics - Theory and Methods 14 (8), 1849-1864

Examples

```
data(BW)
```

```
comp <- etc.diff(formula=Weight~Dose, data=BW, margin.up=30, method="Bofinger")
summary(comp)
```

BW *Body weights measured in a toxicological study*

Description

Body weights of a 90-day chronic toxicological study on rats with a control and three dose groups.

Usage

```
data(BW)
```

Format

A data frame with 60 observations on the following 2 variables.

`Weight` a numeric vector containing the bodyweights of rats

`Dose` a factor with levels `1` `2` `3` `4`, specifying the dose groups, where `1` is the control group

Source

Hothorn, L.A. (2004): Statistische Auswerteverfahren. In: Regulatorische Toxikologie (Reichl, F.X., ed.). Springer Verlag Heidelberg, pp. 167-181.

Examples

```
library(ETC)

data(BW)
boxplot(Weight~Dose, data=BW)
```

---

etc.diff *Simultaneous equivalence to control for differences of means*

Description

Performs simultaneous equivalence tests and related confidence intervals for differences to control in a one-way layout.

Usage

```
etc.diff(formula, data, base = 1, margin.up = NULL, margin.lo = -margin.up,
         method = "var.unequal", FWER = 0.05)
```

Arguments

formula	a formula specifying a numerical response and a grouping factor (e.g., response ~ treatment)
data	a data frame containing the response and group variable as columns
base	a single integer specifying the control group
margin.up	a single numerical value or a numeric vector (of lenght equal to the number of comparisons) for absolute upper margins under the null hypotheses
margin.lo	a single numerical value or a numeric vector (of lenght equal to the number of comparisons) for absolute lower margins under the null hypotheses, set to -margin.up by default if not given
method	a character string: • "var.unequal": possibly unequal group variances, • "var.equal": equal group variances, • "Bofinger": equal group variances and equal sample sizes for the non-control groups • "non.par": non-normally distributed data
FWER	a single numeric value specifying the familywise error rate to be controlled by the simultaneous confidence intervals

Details

Having several treatment groups and a control in a one-way layout, the object is to simultaneously select those treatments being equivalent to the control. Bonferroni adjusted "two one-sided t-tests" (TOST) and related simultaneous confidence intervals are used for differences of means of normally distributed data with equal group variances (method="var.equal"). A pooled sample variance over all treatments is taken in this case. Welch-t-Tests are applied for unequal variances (method="var.unequal"). If the sample sizes of the treatment groups are balanced in the case of equal variances, the single-step procedure of Bofinger and Bofinger (1995) can be chosen with p-values and quantiles coming from a multivariate t-distribution (method="Bofinger"). A warning is given in the output if the Bofinger method is applied for unbalanced treatment groups. For non-normal data, tests based on wilcox.test(..., exact=FALSE, correct=TRUE, ...) are used (method="non.par").

Value

An object of class etc.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 (method="var.equal" and method="Bofinger") or a (named) vector of degrees of freedom (method="var.unequal")
corr.mat	if method="Bofinger", the correlation matrix of the multivariate t-distribution
crit.value	either a single critical value (method="var.equal" and method="Bofinger") or a (named) vector of critical values (method="var.unequal")
p.value	a (named) vector of p-values adjusted for multiplicity
conf.int	a (named) matrix of simultaneous confidence intervals

Note

The confidence intervals related to the TOST method (method="var.equal", method="var.unequal", and method="non.par") have simultaneous coverage probability (1-2alpha), while the intervals according to Bofinger and Bofinger (1995) (method="Bofinger") have (1-alpha). All intervals are "expanded", see Bofinger (1985).

Author(s)

Mario Hasler

References

Hothorn, L.A. and Hasler, M. (2008): Proof of hazard and proof of safety in toxicological studies using simultaneous confidence intervals for differences and ratios to control, Journal of Biopharmaceutical Statistics 18, 915-933;

Bofinger, E. and Bofinger M. (1995): Equivalence with Respect to a Control: Stepwise Tests, Journal of the Royal Statistical Society B 57 (4), 721-733;

Bofinger, E. (1985): Expanded confidence intervals, Communications in Statistics - Theory and Methods 14 (8), 1849-1864

See Also

etc.rat

Examples

```
data(BW)

comp <- etc.diff(formula=Weight~Dose, data=BW, margin.up=30, method="Bofinger")
summary(comp)
```

---

etc.rat *Simultaneous equivalence to control for ratios of means*

Description

Performs simultaneous equivalence tests and related confidence intervals for ratios to control in a one-way layout.

Usage

```
etc.rat(formula, data, base = 1, margin.up = NULL, margin.lo = 1/margin.up,
        method = "var.unequal", FWER = 0.05)
```

Arguments

formula	a formula specifying a numerical response and a grouping factor (e.g., response ~ treatment)
data	a data frame containing the response and group variable as columns
base	a single integer specifying the control group
margin.up	a single numerical value or a numeric vector (of lenght equal to the number of comparisons) for relative upper margins under the null hypotheses
margin.lo	a single numerical value or a numeric vector (of lenght equal to the number of comparisons) for relative lower margins under the null hypotheses, set to 1/margin.up by default if not given
method	a character string: • "var.unequal": possibly unequal group variances, • "var.equal": equal group variances
FWER	a single numeric value specifying the familywise error rate to be controlled by the simultaneous confidence intervals

Details

Having several treatment groups and a control, the object is to simultaneously select those treatments being equivalent to the control. Bonferroni adjusted "two one-sided t-tests" (TOST) and related simultaneous confidence intervals are used for ratios of means of normally distributed data with equal group variances (method="var.equal"). A pooled sample variance over all treatments is taken in this case. Welch-t-Tests are applied for unequal variances (method="var.unequal").

Value

An object of class etc.rat containing:

estimate	a (named) vector of estimated ratios
test.stat	a (named) vector of the calculated test statistics (method="var.equal")
test.stat.up	a (named) vector of the calculated test statistics (up) (method="var.unequal")
test.stat.do	a (named) vector of the calculated test statistics (do) (method="var.unequal")
degr.fr	a single degree of freedom (method="var.equal")
degr.fr.up	a (named) vector of degrees of freedom for test statistics (up) (method="var.unequal")
degr.fr.do	a (named) vector of degrees of freedom for test statistics (do) (method="var.unequal")
degr.fr.ci	a (named) vector of degrees of freedom used for the confidence intervals (method="var.unequal")
crit.value	a single critical value (method="var.equal")
crit.value.up	a (named) vector of critical values for test statistics (up) (method="var.unequal")
crit.value.do	a (named) vector of critical values for test statistics (do) (method="var.unequal")
crit.value.ci	a (named) vector of critical values for the confidence intervals (method="var.unequal")
p.value	a (named) vector of p-values adjusted for multiplicity
conf.int	a (named) matrix of simultaneous confidence intervals

Note

Because related to the TOST method, the confidence intervals have simultaneous coverage probability (1-2alpha). The intervals are "expanded", see Bofinger (1985).

Author(s)

Mario Hasler

References

Hothorn, L.A. and Hasler, M. (2008): Proof of hazard and proof of safety in toxicological studies using simultaneous confidence intervals for differences and ratios to control, Journal of Biopharmaceutical Statistics 18, 915-933;

Bofinger, E. (1985): Expanded confidence intervals, Communications in Statistics - Theory and Methods 14 (8), 1849-1864

See Also

etc.diff

Examples

```
data(BW)

comp <- etc.rat(formula=Weight~Dose, data=BW, margin.up=1.25, method="var.equal")
summary(comp)
```

---

print.etc.diff *Print out of the results of etc.diff*

Description

A short print out of the results of etc.diff.

Usage

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

Arguments

x	an object of class "etc.diff" as obtained by calling etc.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 etc.diff.

Author(s)

Mario Hasler

See Also

print.etc.rat

`print.etc.rat` *Print out of the results of etc.rat*

Description

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

Usage

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

Arguments

`x`	an object of class "etc.rat" as obtained by calling etc.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 etc.rat.

Author(s)

Mario Hasler

See Also

print.etc.diff

summary.etc.diff *Summary function for etc.diff*

Description

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

Usage

```
## S3 method for class 'etc.diff'
summary(object, digits = 4, ...)
```

Arguments

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

Value

A print out containing the margins, degrees of freedom (not for method="non.par"), correlation matrix (if method="Bofinger"), estimates, critical values (not for method="non.par"), test statistics, confidence intervals, and p.values computed by etc.diff.

Author(s)

Mario Hasler

See Also

summary.etc.rat

summary.etc.rat *Summary function for etc.rat*

Description

A detailed print out of the results of etc.rat.

Usage

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

Arguments

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

Value

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

Author(s)

Mario Hasler

See Also

summary.etc.diff

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