

# Package ‘SimComp’

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**Type** Package

**Title** Simultaneous Comparisons for Multiple Endpoints

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**Depends** R (>= 2.10.0)

**Imports** mvtnorm, multcomp, mratios

**Suggests** mvtnorm, multcomp, mratios

**Description** Simultaneous tests and confidence intervals for one-way experimental designs with one or many normally distributed, primary response variables (end-points). The procedure of Hasler and Hothorn (2011) is applied for differences or ratios of means. Various contrasts can be chosen, unbalanced sample sizes are allowed as well as heterogeneous variances or covariance matrices.

**License** GPL

**LazyLoad** yes

**Repository** CRAN

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|                 |  |
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| SimComp-package | <i>Simultaneous Comparisons for Multiple Endpoints</i> |
|-----------------|--|

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## Description

This package provides simultaneous tests and confidence intervals for one-way experimental designs with one or many normally distributed, primary response variables (endpoints). Means of several groups or dose levels can be compared

- by arbitrary contrasts, like the Dunnett or the Tukey test,
- for balanced or unbalanced sample sizes,
- for a single endpoint or for many endpoints simultaneously,
- for homogeneous or heterogeneous variances/ covariance matrices of the groups, and
- in terms of differences or ratios.

Exact or approximate multivariate  $t$ -distributions, respectively, are used for quantiles or  $p$ -values.

For example, the well-known conventional all-pair comparison of Tukey (1953) can be performed by specifying only a single endpoint and homogeneous (co-)variances. On the other hand, it's also possible to do the same, but for many endpoints simultaneously, with heterogeneous covariance matrices and in terms of ratios.

For multiple comparisons of means of heteroscedastic data, see Hasler and Hothorn (2008). The test procedure for multiple endpoints is described by Hasler and Hothorn (2011).

## Details

|           |            |
|-----------|------------|
| Package:  | SimComp    |
| Type:     | Package    |
| Version:  | 1.6.0      |
| Date:     | 2011-03-25 |
| License:  | GPL        |
| LazyLoad: | yes        |

## Index:

- SimCiDiff: Simultaneous Confidence Intervals for Differences of Means of Multiple Endpoints
- SimCiRat: Simultaneous Confidence Intervals for Ratios of Means of Multiple Endpoints

- SimTestDiff: Simultaneous Tests for Differences of Means of Multiple Endpoints
- SimTestRat: Simultaneous Tests for Ratios of Means of Multiple Endpoints
- coagulation: Data from a clinical study of three sets of extracorporeal circulation in heart-lung machines
- ermvnorm: Multivariate Normal Random Numbers with Exact Parameters

### Author(s)

Mario Hasler

Maintainer: Mario Hasler <hasler@email.uni-kiel.de>

### References

Hasler, M. and Hothorn, L.A. (2011): A Dunnett-type procedure for multiple endpoints. *The International Journal of Biostatistics* 7, Article 3.

Hasler, M. and Hothorn, L.A. (2008): Multiple contrast tests in the presence of heteroscedasticity. *Biometrical Journal* 50, 793-800.

Dilba, G. et al. (2006): Simultaneous confidence sets and confidence intervals for multiple ratios. *Journal of Statistical Planning and Inference* 136, 2640-2658.

### See Also

[mratios](#)

### Examples

```
# Example 1:
# A Dunnett-test for the groups B and H against the standard S, on
# the (single) endpoint Thromb.count, assuming unequal variances for
# the groups. This is the well-known Dunnett-test but in the
# presence of heteroscedasticity.

data(coagulation)

comp1 <- SimTestDiff(data=coagulation, grp="Group", resp="Thromb.count", type="Dunnett",
  base=3, alternative="greater", covar.equal=FALSE)
comp1

# Example 2:
# A Dunnett-test for the groups B and H against the standard S,
# simultaneously on all endpoints, assuming unequal covariance
# matrices for the groups.

data(coagulation)

comp2 <- SimTestDiff(data=coagulation, grp="Group", resp=c("Thromb.count","ADP","TRAP"), type="Dunnett",
  base=3, alternative="greater", covar.equal=FALSE)
summary(comp2)
```

---

coagulation

*Data from a clinical study of three sets of extracorporeal circulation in heart-lung machines*

---

### Description

Three sets of extracorporeal circulation in heart-lung machines: treatments H and B, and standard S. Twelve (S and H each) and eleven (B) male adult patients. The analysis is based on a set of laboratory parameters restricted to the blood coagulation system, characterized by three primary endpoints (each as quotient from post- and pre-surgery values). Higher values indicate a better treatment effect. For more details, see Kropf et. al, 2000.

### Usage

```
data(coagulation)
```

### Format

A data frame with 35 observations on the following 5 variables.

Patient a numeric vector, the patients' number

Thromb.count a numeric vector

ADP a numeric vector

TRAP a numeric vector

Group a factor with levels B H S specifying the treatments, where S is the standard

### Source

Kropf, S. et al. (2000): Multiple comparisons of treatments with stable multivariate tests in a two-stage adaptive design, including a test for non-inferiority. *Biometrical Journal* 42, 951-965.

### References

Hasler, M. and Hothorn, L.A. (2011): A Dunnett-type procedure for multiple endpoints. *The International Journal of Biostatistics* 7, Article 3.

### Examples

```
data(coagulation)
str(coagulation)
```

**Description**

Random numbers of the multivariate normal distribution with EXACT mean vector, EXACT variance vector and approximate correlation matrix. This function is based on the function `rmvnorm` of the package `mvtnorm`.

**Usage**

```
ermvnorm(n, mean, sd, corr = diag(rep(1, length(mean))), mnt = 10000)
```

**Arguments**

|                   |   |
|-------------------|---|
| <code>n</code>    | number of observations                      |
| <code>mean</code> | mean vector                                 |
| <code>sd</code>   | vector of standard deviations               |
| <code>corr</code> | correlation matrix                          |
| <code>mnt</code>  | maximum number of tries for the computation |

**Details**

Unfortunately, it's very common to present only summary statistics in the literature when evaluating real data. This makes it hard to retrace or to verify the related statistical evaluation. Also, the use of such data as an example for other statistical tests is not possible. For that reason, `ermvnorm` allows to reproduce data by simulation. In contrast to `rmvnorm` of the package `mvtnorm`, the function `ermvnorm` produces random numbers that have EXACTLY the same parameter values as specified by `mean` and `sd`. The correlation matrix `corr` is met only approximately.

The simple idea behind `ermvnorm` is to apply `rmvnorm` of the package `mvtnorm`, but only for the first  $n-2$  random numbers. The remaining 2 numbers are obtained by solving a quadratic equation to achieve the specified values for the mean vector and for the vector of standard deviations. Depending on the  $n-2$  random numbers, the underlying quadratic equation can possibly have no solution. In this case, `ermvnorm` creates a new set of  $n-2$  random numbers until a valid data set is obtained, or until the maximum number of tries `mnt` is reached.

**Value**

A matrix of random numbers with dimension  $n * \text{length}(\text{mean})$ .

**Note**

This function is to be used only with caution. Normally, random numbers with exact mean and standard deviation are not intended to be used. For example, simulations concerning type I error or power of statistical tests cannot be based on `ermvnorm`.

**Author(s)**

Mario Hasler and Gemechis Djira Dilba

**References**

Hothorn, T. et al. (2001): On Multivariate t and Gauss Probabilities in R. *R News* 1, 27-29.

**See Also**

[rmvnorm](#)

**Examples**

```
# Example 1:
# A dataset representing two correlated endpoints.

set.seed(1234)
dataset1 <- ermvnorm(n=10,mean=c(10,120),sd=c(1,10),corr=rbind(c(1,0.7),c(0.7,1)))
dataset1
mean(dataset1[,1]); mean(dataset1[,2])
sd(dataset1[,1]); sd(dataset1[,2])
round(cor(dataset1),3)
pairs(dataset1)

# Example 2:
# A dataset representing three uncorrelated endpoints.

set.seed(5678)
dataset2 <- ermvnorm(n=20,mean=c(1,12,150),sd=c(0.5,2,20))
dataset2
mean(dataset2[,1]); mean(dataset2[,2]); mean(dataset2[,3])
sd(dataset2[,1]); sd(dataset2[,2]); sd(dataset2[,3])
pairs(dataset2)
```

---

print.SimCi

*Print function for SimCi-objects*

---

**Description**

A short print out of the results of SimCiDiff and SimCiRat, respectively.

**Usage**

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

**Arguments**

x                    an object of class "SimCi" as obtained by calling SimCiDiff or SimCiRat  
 digits                digits for rounding the results  
 ...                    arguments to be passed to print

**Value**

A print out containing the estimates, raw and simultaneous confidence intervals computed by SimCiDiff or SimCiRat, respectively.

**Author(s)**

Mario Hasler

**See Also**

[print.SimTest](#)

---

print.SimTest                    *Print function for SimTest-objects*

---

**Description**

A short print out of the results of SimTestDiff and SimTestRat, respectively.

**Usage**

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

**Arguments**

x                    an object of class "SimTest" as obtained by calling SimTestDiff or SimTestRat  
 digits                digits for rounding the results  
 ...                    arguments to be passed to print

**Value**

A print out containing the margins, estimates, test statistics, raw and adjusted  $p$ -values computed by SimTestDiff or SimTestRat, respectively.

**Author(s)**

Mario Hasler

**See Also**

[print.SimCi](#)

---

 SimCiDiff

*Simultaneous Confidence Intervals for Differences of Means of Multiple Endpoints*


---

## Description

Simultaneous confidence intervals for general contrasts (linear functions) of normal means (e.g., "Dunnett", "Tukey", "Williams" ect.) when there is more than one primary response variable (endpoint). The procedure of Hasler and Hothorn (2011) is applied for differences of means of normally distributed data. The covariance matrices (containing the covariances between the endpoints) may be assumed to be equal or possibly unequal for the different groups. For the case of only a single endpoint and unequal covariance matrices (variances), the procedure coincides with the PI procedure of Hasler and Hothorn (2008).

## Usage

```
SimCiDiff(data, grp, resp = NULL, type = "Dunnett", base = 1, ContrastMat = NULL,
          alternative = "two.sided", covar.equal = FALSE, conf.level = 0.95)
```

## Arguments

|             |  |
|-------------|--|
| data        | a data frame containing a grouping variable and the endpoints as columns   |
| grp         | a character string with the name of the grouping variable  |
| resp        | a vector of character strings with the names of the endpoints; if resp=NULL (default), all column names of the data frame without the grouping variable are chosen automatically   |
| type        | a character string, defining the type of contrast, with the following options: <ul style="list-style-type: none"> <li>• "Dunnett": many-to-one comparisons</li> <li>• "Tukey": all-pair comparisons</li> <li>• "Sequen": comparisons of consecutive groups</li> <li>• "AVE": comparison of each group with average of all others</li> <li>• "GrandMean": comparison of each group with grand mean of all groups</li> <li>• "Changepoint": differences of averages of groups of higher order to averages of groups of lower order</li> <li>• "Marcus": Marcus contrasts</li> <li>• "McDermott": McDermott contrasts</li> <li>• "Williams": Williams trend tests</li> <li>• "UmbrellaWilliams": Umbrella-protected Williams trend tests</li> </ul> note that type is ignored if ContrastMat is specified by the user (see below) |
| base        | a single integer specifying the control group for Dunnett contrasts, ignored otherwise   |
| ContrastMat | a contrast matrix, where columns correspond to groups and rows correspond to contrasts   |

|                          |  |
|--------------------------|--|
| <code>alternative</code> | a character string specifying the alternative hypothesis, must be one of "two.sided" (default), "greater" or "less"  |
| <code>covar.equal</code> | a logical variable indicating whether to treat the covariance matrices (containing the covariances between the endpoints) for the different groups as being equal; if TRUE then the pooled covariance matrix is used, otherwise the Satterthwaite approximation to the degrees of freedom is used according to Hasler and Hothorn (2008) |
| <code>conf.level</code>  | a numeric value defining the simultaneous confidence level   |

### Details

The interest is in simultaneous confidence intervals for several linear combinations (contrasts) of treatment means in a one-way ANOVA model, and simultaneously for multiple endpoints. For example, corresponding intervals for the all-pair comparison of Tukey (1953) and the many-to-one comparison of Dunnett (1955) are implemented, but allowing for multiple endpoints. Also, the user is free to create other interesting problem-specific contrasts. An approximate multivariate  $t$ -distribution is used to calculate lower and upper limits (see Hasler and Hothorn, 2011). Simultaneous tests based on these intervals control the familywise error rate in an admissible range and in the strong sense. The covariance matrices of the treatment groups (containing the covariances between the endpoints) can be assumed to be equal (`covar.equal=TRUE`) or unequal (`covar.equal=FALSE`). If being equal, the pooled covariance matrix is used, otherwise Satterthwaite approximations to the degrees of freedom are used according to Hasler and Hothorn (2008). Unequal covariance matrices occur if variances or correlations of some endpoints differ depending on the treatment groups.

### Value

An object of class `SimCi` containing:

|                          |  |
|--------------------------|--|
| <code>estimate</code>    | a matrix of estimated differences  |
| <code>lower.raw</code>   | a matrix of raw (unadjusted) lower limits  |
| <code>upper.raw</code>   | a matrix of raw (unadjusted) upper limits  |
| <code>lower</code>       | a matrix of lower limits adjusted for multiplicity   |
| <code>upper</code>       | a matrix of upper limits adjusted for multiplicity   |
| <code>CorrMatDat</code>  | either the estimated common correlation matrix of the data ( <code>covar.equal=TRUE</code> ) or the list of the different (one for each treatment) estimated correlation matrices of the data ( <code>covar.equal=FALSE</code> ) |
| <code>CorrMatComp</code> | the estimated correlation matrix to be used for the multivariate $t$ -distribution   |
| <code>degr.fr</code>     | either a single degree of freedom ( <code>covar.equal=TRUE</code> ) or a vector of degrees of freedom ( <code>covar.equal=FALSE</code> ) related to the comparisons  |

### Note

All measurement objects of each treatment group must have values for each endpoint. If there are missing values then the procedure stops. If `covar.equal=TRUE`, then the number of endpoints must not be greater than the total sample size minus the number of treatment groups. If `covar.equal=FALSE`, the number of endpoints must not be greater than the minimal sample size minus 1. Otherwise the procedure stops.

All the intervals have the same direction for all comparisons and endpoints (`alternative="..."`). In case of doubt, use `"two.sided"`.

### Author(s)

Mario Hasler

### References

Hasler, M. and Hothorn, L.A. (2011): A Dunnett-type procedure for multiple endpoints. *The International Journal of Biostatistics* 7, Article 3.

Hasler, M. and Hothorn, L.A. (2008): Multiple contrast tests in the presence of heteroscedasticity. *Biometrical Journal* 50, 793-800.

### See Also

[SimCiRat](#), [SimTestDiff](#), [SimTestRat](#)

### Examples

```
# Example 1:
# Simultaneous confidence intervals related to a Dunnett-test for the groups
# B and H against the standard S, on the (single) endpoint Thromb.count,
# assuming unequal variances for the groups. These are the well-known
# Dunnett-intervals but in the presence of heteroscedasticity.

data(coagulation)

interv1 <- SimCiDiff(data=coagulation, grp="Group", resp="Thromb.count", type="Dunnett",
  base=3, alternative="greater", covar.equal=FALSE)
interv1

# Example 2:
# Simultaneous confidence intervals related to a Dunnett-test for the groups
# B and H against the standard S, simultaneously on all endpoints, assuming
# unequal covariance matrices for the groups.

data(coagulation)

interv2 <- SimCiDiff(data=coagulation, grp="Group", resp=c("Thromb.count","ADP","TRAP"), type="Dunnett",
  base=3, alternative="greater", covar.equal=FALSE)
summary(interv2)
```

## Description

Simultaneous confidence intervals for ratios of contrasts (linear functions) of normal means (e.g., "Dunnett", "Tukey", "Williams" ect.) when there is more than one primary response variable (endpoint). The procedure of Hasler and Hothorn (2011) is applied for ratios of means of normally distributed data. The covariance matrices (containing the covariances between the endpoints) may be assumed to be equal or possibly unequal for the different groups. For the case of only a single endpoint and unequal covariance matrices (variances), the procedure coincides with the PI procedure of Hasler and Hothorn (2008).

## Usage

```
SimCiRat(data, grp, resp = NULL, type = "Dunnett", base = 1, Num.Contrast = NULL,
          Den.Contrast = NULL, alternative = "two.sided", covar.equal = FALSE,
          conf.level = 0.95)
```

## Arguments

|              |  |
|--------------|--|
| data         | a data frame containing a grouping variable and the endpoints as columns   |
| grp          | a character string with the name of the grouping variable  |
| resp         | a vector of character strings with the names of the endpoints; if resp=NULL (default), all column names of the data frame without the grouping variable are chosen automatically   |
| type         | a character string, defining the type of contrast, with the following options: <ul style="list-style-type: none"> <li>• "Dunnett": many-to-one comparisons, with control in the denominator</li> <li>• "Tukey": all-pair comparisons</li> <li>• "Sequen": comparisons of consecutive groups, where the group with lower order is the denominator</li> <li>• "AVE": comparison of each group with average of all others, where the average is taken as denominator</li> <li>• "GrandMean": comparison of each group with grand mean of all groups, where the grand mean is taken as denominator</li> <li>• "Changepoint": ratios of averages of groups of higher order divided by averages of groups of lower order</li> <li>• "Marcus": Marcus contrasts as ratios</li> <li>• "McDermott": McDermott contrasts as ratios</li> <li>• "Williams": Williams contrasts as ratios</li> <li>• "UmbrellaWilliams": Umbrella-protected Williams contrasts as ratios</li> </ul> <p>note that type is ignored if Num.Contrast and Den.Contrast are specified by the user (see below)</p> |
| base         | a single integer specifying the control (i.e. denominator) group for Dunnett contrasts, ignored otherwise  |
| Num.Contrast | a numerator contrast matrix, where columns correspond to groups and rows correspond to contrasts   |
| Den.Contrast | a denominator contrast matrix, where columns correspond to groups and rows correspond to contrasts   |

|                          |  |
|--------------------------|--|
| <code>alternative</code> | a character string specifying the alternative hypothesis, must be one of "two.sided" (default), "greater" or "less"  |
| <code>covar.equal</code> | a logical variable indicating whether to treat the covariance matrices (containing the covariances between the endpoints) for the different groups as being equal; if TRUE then the pooled covariance matrix is used, otherwise the Satterthwaite approximation to the degrees of freedom is used according to Hasler and Hothorn (2008) |
| <code>conf.level</code>  | a numeric value defining the simultaneous confidence level   |

### Details

The interest is in simultaneous confidence intervals for several ratios of linear combinations (contrasts) of treatment means in a one-way ANOVA model, and simultaneously for multiple endpoints. For example, corresponding intervals for the all-pair comparison of Tukey (1953) and the many-to-one comparison of Dunnett (1955) for ratios of means are implemented, but allowing for multiple endpoints. Also, the user is free to create other interesting problem-specific contrasts. An approximate multivariate  $t$ -distribution is used to calculate lower and upper limits (see Hasler and Hothorn, 2011). Simultaneous tests based on these intervals control the familywise error rate in an admissible range and in the strong sense. The covariance matrices of the treatment groups (containing the covariances between the endpoints) can be assumed to be equal (`covar.equal=TRUE`) or unequal (`covar.equal=FALSE`). If being equal, the pooled covariance matrix is used, otherwise Satterthwaite approximations to the degrees of freedom are used according to Hasler and Hothorn (2008). Unequal covariance matrices occur if variances or correlations of some endpoints differ depending on the treatment groups.

### Value

An object of class `SimCi` containing:

|                          |  |
|--------------------------|--|
| <code>estimate</code>    | a matrix of estimated differences  |
| <code>lower.raw</code>   | a matrix of raw (unadjusted) lower limits  |
| <code>upper.raw</code>   | a matrix of raw (unadjusted) upper limits  |
| <code>lower</code>       | a matrix of lower limits adjusted for multiplicity   |
| <code>upper</code>       | a matrix of upper limits adjusted for multiplicity   |
| <code>CorrMatDat</code>  | either the estimated common correlation matrix of the data ( <code>covar.equal=TRUE</code> ) or the list of the different (one for each treatment) estimated correlation matrices of the data ( <code>covar.equal=FALSE</code> ) |
| <code>CorrMatComp</code> | the estimated correlation matrix to be used for the multivariate $t$ -distribution   |
| <code>degr.fr</code>     | either a single degree of freedom ( <code>covar.equal=TRUE</code> ) or a vector of degrees of freedom ( <code>covar.equal=FALSE</code> ) related to the comparisons  |

### Note

All measurement objects of each treatment group must have values for each endpoint. If there are missing values then the procedure stops. If `covar.equal=TRUE`, then the number of endpoints must not be greater than the total sample size minus the number of treatment groups. If

`covar.equal=FALSE`, the number of endpoints must not be greater than the minimal sample size minus 1. Otherwise the procedure stops.

All the intervals have the same direction for all comparisons and endpoints (`alternative="..."`). In case of doubt, use `"two.sided"`.

In contrast to simultaneous confidence intervals for differences, the correlation matrix for the multivariate  $t$ -distribution depends on the unknown ratios. The same problem also arises for the degrees of freedom if the covariance matrices for the different groups are assumed to be unequal (`covar.equal=FALSE`). Both problems can be handled by a plug-in approach, see the references therefore.

### Author(s)

Mario Hasler

### References

Hasler, M. and Hothorn, L.A. (2011): A Dunnett-type procedure for multiple endpoints. *The International Journal of Biostatistics* 7, Article 3.

Hasler, M. and Hothorn, L.A. (2008): Multiple contrast tests in the presence of heteroscedasticity. *Biometrical Journal* 50, 793-800.

Dilba, G. et al. (2006): Simultaneous confidence sets and confidence intervals for multiple ratios. *Journal of Statistical Planning and Inference* 136, 2640-2658.

### See Also

[SimCiDiff](#), [SimTestRat](#), [SimTestDiff](#)

### Examples

```
# Example 1:
# Simultaneous confidence intervals for ratios of means, related to a
# Dunnett-test for the groups B and H against the standard S, on the (single)
# endpoint Thromb.count, assuming unequal variances for the groups. These are the
# well-known Dunnett-intervals but in the presence of heteroscedasticity and for
# ratios of means.

data(coagulation)

interv1 <- SimCiRat(data=coagulation, grp="Group", resp="Thromb.count", type="Dunnett",
  base=3, alternative="greater", covar.equal=FALSE)
interv1

# Example 2:
# Simultaneous confidence intervals for ratios of means, related to a
# Dunnett-test for the groups B and H against the standard S, simultaneously on
# all endpoints, assuming unequal covariance matrices for the groups.

data(coagulation)

interv2 <- SimCiRat(data=coagulation, grp="Group", resp=c("Thromb.count", "ADP", "TRAP"), type="Dunnett",
```

```
base=3, alternative="greater", covar.equal=FALSE)
summary(interv2)
```

---

 SimTestDiff

*Simultaneous Tests for Differences of Means of Multiple Endpoints*


---

## Description

Simultaneous tests for general contrasts (linear functions) of normal means (e.g., "Dunnett", "Tukey", "Williams" ect.) when there is more than one primary response variable (endpoint). The procedure of Hasler and Hothorn (2011) is applied for differences of means of normally distributed data. The covariance matrices (containing the covariances between the endpoints) may be assumed to be equal or possibly unequal for the different groups. For the case of only a single endpoint and unequal covariance matrices (variances), the procedure coincides with the PI procedure of Hasler and Hothorn (2008).

## Usage

```
SimTestDiff(data, grp, resp = NULL, type = "Dunnett", base = 1, ContrastMat = NULL,
  alternative = "two.sided", Margin = NULL, covar.equal = FALSE)
```

## Arguments

|      |  |
|------|--|
| data | a data frame containing a grouping variable and the endpoints as columns   |
| grp  | a character string with the name of the grouping variable  |
| resp | a vector of character strings with the names of the endpoints; if resp=NULL (default), all column names of the data frame without the grouping variable are chosen automatically   |
| type | a character string, defining the type of contrast, with the following options: <ul style="list-style-type: none"> <li>• "Dunnett": many-to-one comparisons</li> <li>• "Tukey": all-pair comparisons</li> <li>• "Sequen": comparisons of consecutive groups</li> <li>• "AVE": comparison of each group with average of all others</li> <li>• "GrandMean": comparison of each group with grand mean of all groups</li> <li>• "Changepoint": differences of averages of groups of higher order to averages of groups of lower order</li> <li>• "Marcus": Marcus contrasts</li> <li>• "McDermott": McDermott contrasts</li> <li>• "Williams": Williams trend tests</li> <li>• "UmbrellaWilliams": Umbrella-protected Williams trend tests</li> </ul> note that type is ignored if ContrastMat is specified by the user (see below) |
| base | a single integer specifying the control group for Dunnett contrasts, ignored otherwise   |

|             |  |
|-------------|--|
| ContrastMat | a contrast matrix, where columns correspond to groups and rows correspond to contrasts   |
| alternative | a character string specifying the alternative hypothesis, must be one of "two.sided" (default), "greater" or "less"  |
| Margin      | a single numeric value, or a numeric vector corresponding to endpoints, or a matrix where columns correspond to endpoints and rows correspond to contrasts, default is 0   |
| covar.equal | a logical variable indicating whether to treat the covariance matrices (containing the covariances between the endpoints) for the different groups as being equal; if TRUE then the pooled covariance matrix is used, otherwise the Satterthwaite approximation to the degrees of freedom is used according to Hasler and Hothorn (2008) |

### Details

The interest is in simultaneous tests for several linear combinations (contrasts) of treatment means in a one-way ANOVA model, and simultaneously for multiple endpoints. For example, the all-pair comparison of Tukey (1953) and the many-to-one comparison of Dunnett (1955) are implemented, but allowing for multiple endpoints. Also, the user is free to create other interesting problem-specific contrasts. An approximate multivariate  $t$ -distribution is used to calculate (adjusted)  $p$ -values (see Hasler and Hothorn, 2011). This approach controls the familywise error rate in an admissible range and in the strong sense. The covariance matrices of the treatment groups (containing the covariances between the endpoints) can be assumed to be equal (`covar.equal=TRUE`) or unequal (`covar.equal=FALSE`). If being equal, the pooled covariance matrix is used, otherwise Satterthwaite approximations to the degrees of freedom are used according to Hasler and Hothorn (2008). Unequal covariance matrices occur if variances or correlations of some endpoints differ depending on the treatment groups.

### Value

An object of class `SimTest` containing:

|                          |  |
|--------------------------|--|
| <code>estimate</code>    | a matrix of estimated differences  |
| <code>statistic</code>   | a matrix of the calculated test statistics   |
| <code>p.val.raw</code>   | a matrix of raw $p$ -values  |
| <code>p.val.adj</code>   | a matrix of $p$ -values adjusted for multiplicity  |
| <code>CorrMatDat</code>  | either the estimated common correlation matrix of the data ( <code>covar.equal=TRUE</code> ) or the list of the different (one for each treatment) estimated correlation matrices of the data ( <code>covar.equal=FALSE</code> ) |
| <code>CorrMatComp</code> | the estimated correlation matrix to be used for the multivariate $t$ -distribution   |
| <code>degr.fr</code>     | either a single degree of freedom ( <code>covar.equal=TRUE</code> ) or a vector of degrees of freedom ( <code>covar.equal=FALSE</code> ) related to the comparisons  |

**Note**

All measurement objects of each treatment group must have values for each endpoint. If there are missing values then the procedure stops. If `covar.equal=TRUE`, then the number of endpoints must not be greater than the total sample size minus the number of treatment groups. If `covar.equal=FALSE`, the number of endpoints must not be greater than the minimal sample size minus 1. Otherwise the procedure stops.

All hypotheses are tested with the same test direction for all comparisons and endpoints (`alternative="..."`). In case of doubt, use `"two.sided"`.

If `Margin` is a single numeric value or a numeric vector, then the same value(s) are used for the remaining comparisons or endpoints. If `Margin` is not specified, the default is 0.

**Author(s)**

Mario Hasler

**References**

Hasler, M. and Hothorn, L.A. (2011): A Dunnett-type procedure for multiple endpoints. *The International Journal of Biostatistics* 7, Article 3.

Hasler, M. and Hothorn, L.A. (2008): Multiple contrast tests in the presence of heteroscedasticity. *Biometrical Journal* 50, 793-800.

**See Also**

[SimTestRat](#), [SimCiDiff](#), [SimCiRat](#),

**Examples**

```
# Example 1:
# A Dunnett-test for the groups B and H against the standard S, on
# the (single) endpoint Thromb.count, assuming unequal variances for
# the groups. This is the well-known Dunnett-test but in the
# presence of heteroscedasticity.

data(coagulation)

comp1 <- SimTestDiff(data=coagulation, grp="Group", resp="Thromb.count", type="Dunnett",
  base=3, alternative="greater", covar.equal=FALSE)
comp1

# Example 2:
# A Dunnett-test for the groups B and H against the standard S,
# simultaneously on all endpoints, assuming unequal covariance
# matrices for the groups.

data(coagulation)

comp2 <- SimTestDiff(data=coagulation, grp="Group", resp=c("Thromb.count","ADP","TRAP"), type="Dunnett",
  base=3, alternative="greater", covar.equal=FALSE)
summary(comp2)
```

**Description**

Simultaneous tests for ratios of contrasts (linear functions) of normal means (e.g., "Dunnett", "Tukey", "Williams" ect.) when there is more than one primary response variable (endpoint). The procedure of Hasler and Hothorn (2011) is applied for ratios of means of normally distributed data. The covariance matrices (containing the covariances between the endpoints) may be assumed to be equal or possibly unequal for the different groups. For the case of only a single endpoint and unequal covariance matrices (variances), the procedure coincides with the PI procedure of Hasler and Hothorn (2008).

**Usage**

```
SimTestRat(data, grp, resp = NULL, type = "Dunnett", base = 1, Num.Contrast = NULL,
           Den.Contrast = NULL, alternative = "two.sided", Margin = NULL,
           covar.equal = FALSE)
```

**Arguments**

|      |  |
|------|--|
| data | a data frame containing a grouping variable and the endpoints as columns   |
| grp  | a character string with the name of the grouping variable  |
| resp | a vector of character strings with the names of the endpoints; if resp=NULL (default), all column names of the data frame without the grouping variable are chosen automatically   |
| type | a character string, defining the type of contrast, with the following options: <ul style="list-style-type: none"> <li>• "Dunnett": many-to-one comparisons, with control in the denominator</li> <li>• "Tukey": all-pair comparisons</li> <li>• "Sequen": comparisons of consecutive groups, where the group with lower order is the denominator</li> <li>• "AVE": comparison of each group with average of all others, where the average is taken as denominator</li> <li>• "GrandMean": comparison of each group with grand mean of all groups, where the grand mean is taken as denominator</li> <li>• "Changepoint": ratios of averages of groups of higher order divided by averages of groups of lower order</li> <li>• "Marcus": Marcus contrasts as ratios</li> <li>• "McDermott": McDermott contrasts as ratios</li> <li>• "Williams": Williams contrasts as ratios</li> <li>• "UmbrellaWilliams": Umbrella-protected Williams contrasts as ratios</li> </ul> |

note that type is ignored if Num.Contrast and Den.Contrast are specified by the user (see below)

|              |  |
|--------------|--|
| base         | a single integer specifying the control (i.e. denominator) group for Dunnett contrasts, ignored otherwise  |
| Num.Contrast | a numerator contrast matrix, where columns correspond to groups and rows correspond to contrasts   |
| Den.Contrast | a denominator contrast matrix, where columns correspond to groups and rows correspond to contrasts   |
| alternative  | a character string specifying the alternative hypothesis, must be one of "two.sided" (default), "greater" or "less"  |
| Margin       | a single numeric value, or a numeric vector corresponding to endpoints, or a matrix where columns correspond to endpoints and rows correspond to contrasts, default is 1   |
| covar.equal  | a logical variable indicating whether to treat the covariance matrices (containing the covariances between the endpoints) for the different groups as being equal; if TRUE then the pooled covariance matrix is used, otherwise the Satterthwaite approximation to the degrees of freedom is used according to Hasler and Hothorn (2008) |

### Details

The interest is in simultaneous tests for several ratios of linear combinations (contrasts) of treatment means in a one-way ANOVA model, and simultaneously for multiple endpoints. For example, the all-pair comparison of Tukey (1953) and the many-to-one comparison of Dunnett (1955) for ratios of means are implemented, but allowing for multiple endpoints. Also, the user is free to create other interesting problem-specific contrasts. An approximate multivariate  $t$ -distribution is used to calculate (adjusted)  $p$ -values (see Hasler and Hothorn, 2011). This approach controls the familywise error rate in an admissible range and in the strong sense. The covariance matrices of the treatment groups (containing the covariances between the endpoints) can be assumed to be equal (`covar.equal=TRUE`) or unequal (`covar.equal=FALSE`). If being equal, the pooled covariance matrix is used, otherwise Satterthwaite approximations to the degrees of freedom are used according to Hasler and Hothorn (2008). Unequal covariance matrices occur if variances or correlations of some endpoints differ depending on the treatment groups.

### Value

An object of class `SimTest` containing:

|             |  |
|-------------|--|
| estimate    | a matrix of estimated ratios   |
| statistic   | a matrix of the calculated test statistics   |
| p.val.raw   | a matrix of raw $p$ -values  |
| p.val.adj   | a matrix of $p$ -values adjusted for multiplicity  |
| CorrMatDat  | either the estimated common correlation matrix of the data ( <code>covar.equal=TRUE</code> ) or the list of the different (one for each treatment) estimated correlation matrices of the data ( <code>covar.equal=FALSE</code> ) |
| CorrMatComp | the estimated correlation matrix to be used for the multivariate $t$ -distribution   |
| degr.fr     | either a single degree of freedom ( <code>covar.equal=TRUE</code> ) or a vector of degrees of freedom ( <code>covar.equal=FALSE</code> ) related to the comparisons  |

**Note**

All measurement objects of each treatment group must have values for each endpoint. If there are missing values then the procedure stops. If `covar.equal=TRUE`, then the number of endpoints must not be greater than the total sample size minus the number of treatment groups. If `covar.equal=FALSE`, the number of endpoints must not be greater than the minimal sample size minus 1. Otherwise the procedure stops.

All hypotheses are tested with the same test direction for all comparisons and endpoints (`alternative="..."`). In case of doubt, use `"two.sided"`.

If `Margin` is a single numeric value or a numeric vector, then the same value(s) are used for the remaining comparisons or endpoints. If `Margin` is not specified, the default is 1.

**Author(s)**

Mario Hasler

**References**

Hasler, M. and Hothorn, L.A. (2011): A Dunnett-type procedure for multiple endpoints. *The International Journal of Biostatistics* 7, Article 3.

Hasler, M. and Hothorn, L.A. (2008): Multiple contrast tests in the presence of heteroscedasticity. *Biometrical Journal* 50, 793-800.

Dilba, G. et al. (2006): Simultaneous confidence sets and confidence intervals for multiple ratios. *Journal of Statistical Planning and Inference* 136, 2640-2658.

**See Also**

[SimTestDiff](#), [SimCiRat](#), [SimCiDiff](#),

**Examples**

```
# Example 1:
# A Dunnett-test for the groups B and H against the standard S, on the (single)
# endpoint Thromb.count, assuming unequal variances for the groups, and in terms of
# ratios. This is the well-known Dunnett-test but in the presence of
# heteroscedasticity and for ratios of means.

data(coagulation)

comp1 <- SimTestRat(data=coagulation, grp="Group", resp="Thromb.count", type="Dunnett",
  base=3, alternative="greater", covar.equal=FALSE)
comp1

# Example 2:
# A Dunnett-test for the groups B and H against the standard S, simultaneously on
# all endpoints, assuming unequal covariance matrices for the groups, and in terms
# of ratios.

data(coagulation)
```

```
comp2 <- SimTestRat(data=coagulation, grp="Group", resp=c("Thromb.count", "ADP", "TRAP"), type="Dunnett",
  base=3, alternative="greater", covar.equal=FALSE)
summary(comp2)
```

---

summary.SimCi

*Summary function for SimCi-objects*

---

## Description

A detailed print out of the results of SimCiDiff and SimCiRat, respectively.

## Usage

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

## Arguments

|        |   |
|--------|---|
| object | an object of class "SimCi" as obtained by calling SimCiDiff or SimCiRat |
| digits | digits for rounding the results   |
| ...    | arguments to be passed to print   |

## Value

A print out containing the estimates, raw and simultaneous confidence intervals, estimated covariance and correlation matrices of the data and of the comparisons computed by SimCiDiff or SimCiRat, respectively.

## Author(s)

Mario Hasler

## See Also

[summary.SimTest](#)

---

|                 |   |
|-----------------|---|
| summary.SimTest | <i>Summary function for SimTest-objects</i> |
|-----------------|---|

---

**Description**

A detailed print out of the results of SimTestDiff and SimTestRat, respectively.

**Usage**

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

**Arguments**

|        |   |
|--------|---|
| object | an object of class "SimTest" as obtained by calling SimTestDiff or SimTestRat |
| digits | digits for rounding the results   |
| ...    | arguments to be passed to print   |

**Value**

A print out containing the estimates, test statistics, raw and adjusted  $p$ -values, estimated covariance correlation matrices of the data and of the comparisons computed by SimTestDiff or SimTestRat, respectively.

**Author(s)**

Mario Hasler

**See Also**

[summary.SimCi](#)

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