Package 'cTOST'

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Type Package

Title Finite Sample Correction of the Two One-Sided Tests in the
Univariate Framework

Version 1.0.0

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Description A system containing easy-to-use tools to compute the bioequivalence assess-
ment in the univariate framework using the methods pro-
posed in Boulaguiem et al. (2023) <doi:10.1101/2023.03.11.532179>.

Depends PowerTOST, cli, knitr, R (>= 4.0)

Imports OwenQ, rmarkdown

Suggests asciicast

License AGPL-3

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LazyData true

RoxygenNote 7.2.3

VignetteBuilder knitr

URL https://github.com/yboulag/cTOST

BugReports https://github.com/yboulag/cTOST/issues

NeedsCompilation no

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R **topics documented:**

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atost   *The alpha-TOST Corrective Procedure for (Bio)Equivalence Testing*

Description

This functions is used to compute the alpha-TOST, a corrective procedure of the significance level applied to the Two One-Sided Test (TOST) for (bio)equivalence testing in the univariate framework.

Usage

```
atost(theta, sigma, nu, alpha, delta)
```

Arguments

theta	A numeric value corresponding to the difference of means.
sigma	A numeric value corresponding to the standard error.
nu	A numeric value corresponding to the number of degrees of freedom.
alpha	A numeric value specifying the significance level.
delta	A numeric value corresponding to (bio)equivalence limit. We assume symmetry, i.e, the (bio)equivalence interval corresponds to (-delta,delta)

Value

A tost object with the structure:

- decision: A boolean variable indicating whether (bio)equivalence is accepted or not.
- ci: Confidence interval at the 1 - 2*alpha level.
- theta: The difference of means used for the test.
- sigma: The standard error used for the test.
- nu: The number of degrees of freedom used for the test.
- alpha: The significance level used for the test.
- delta: The (bio)equivalence limits used for the test.
- method: The method used for the test (here the "alpha-TOST").

Author(s)

Younes Boulaguiem, Stéphane Guerrier, Dominique-Laurent Couturier

Examples

```
data(skin)

theta_hat = diff(apply(skin,2,mean))
nu = nrow(skin) - 1
sig_hat = sd(apply(skin,1,diff))/sqrt(nu)
res_atost = atost(theta = theta_hat, sigma = sig_hat, nu = nu,
            alpha = 0.05, delta = log(1.25))
res_atost
compare_to_tost(res_atost)
```

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compare_to_tost	*Comparison of a Corrective Procedure to the results of the Two One-Sided Tests (TOST)*

Description

This function renders a comparison of the alpha-TOST or the delta-TOST outputs obtained with the functions 'atost' or 'dtost', respectively, to the TOST output obtained with 'tost'.

Usage

```
compare_to_tost(x, ticks = 30, rn = 5)
```

Arguments

x	A tost object, which is the output of one of the following functions: 'atost' or 'dtost'.
ticks	an integer indicating the number of segments that will be printed to represent the confidence intervals.
rn	integer indicating the number of decimals places to be used (see function 'round') for the printed results.

Value

Pints a comparison between the TOST results (i.e., output of 'tost') and either the alpha-TOST or the delta-TOST results (i.e., outputs of 'atost' or 'dtost', respectively).

---

dtost   *The delta-TOST Corrective Procedure for (Bio)Equivalence Testing*

Description

This functions is used to compute the delta-TOST, a corrective procedure of the (bio)equivalence bounds applied to the Two One-Sided Test (TOST) for (bio)equivalence testing in the univariate framework.

Usage

```
dtost(theta, sigma, nu, alpha, delta)
```

Arguments

theta   A numeric value corresponding to the difference of means.

sigma   A numeric value corresponding to the standard error.

nu   A numeric value corresponding to the number of degrees of freedom.

alpha   A numeric value specifying the significance level.

delta   A numeric value corresponding to (bio)equivalence limit. We assume symmetry, i.e, the (bio)equivalence interval corresponds to (-delta,delta)

Value

A tost object with the structure:

- decision: A boolean variable indicating whether (bio)equivalence is accepted or not.
- ci: Confidence interval at the 1 - 2*alpha level.
- theta: The difference of means used for the test.
- sigma: The standard error used for the test.
- nu: The number of degrees of freedom used for the test.
- alpha: The significance level used for the test.
- delta: The (bio)equivalence limits used for the test.
- method: The method used for the test (here the "delta-TOST").

Author(s)

Younes Boulaguiem, Stéphane Guerrier, Dominique-Laurent Couturier

Examples

```
data(skin)

theta_hat = diff(apply(skin,2,mean))
nu = nrow(skin) - 1
sig_hat = sd(apply(skin,1,diff))/sqrt(nu)
res_dtost = dtost(theta = theta_hat, sigma = sig_hat, nu = nu,
            alpha = 0.05, delta = log(1.25))
res_dtost
compare_to_tost(res_dtost)
```

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print.tost   *Print Results of (Bio)Equivalence Assessment*

Description

Print Results of (Bio)Equivalence Assessment

Usage

```
## S3 method for class 'tost'
print(x, ticks = 30, rn = 5, ...)
```

Arguments

x	A `tost` object, which is the output of one of the following functions 'tost', 'atost' or 'dtost'.
ticks	Number of ticks to print the confidence interval in the console.
rn	Number of digits to consider when printing the results.
...	Further arguments to be passed to or from methods.

Value

Prints object.

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skin   *Log transformed cutaneous delivery of econazole (ECZ) from bioe-*
                                        quivalent products on porcine skin

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Description

Original data were collected in the same way as described in Quariter et. al. (2019), and represents cutaneous delivery of econazole nitrate (ECZ in ng/cm^2) on porcine skin from a reference medicinal product and an approved bioequivalent product. The dataset contains 17 pairs of comparable porcine skin samples on which measurement of ECZ deposition was gathered, and log transformed, using both creams.

Usage

```
data(skin)
```

Format

A 'data.frame' with 16 rows and 2 columns:

Reference Econazole nitrate delivery for the reference product.

Generic Econazole nitrate delivery for the generic bioequivalent product.

Obs. The observation corresponds to a given skin on which the log ECZ delivery was collected for each of the reference and generic cream.

References

Quartier, Julie, et al. "Cutaneous Biodistribution: A High-Resolution Methodology to Assess Bioequivalence in Topical Skin Delivery", Pharmaceutics, (2019). Boulaguiem, Younes, et al. "Finite Sample Adjustments for Average Equivalence Testing", bioRxiv, (2023)

Examples

```
data(skin)
theta <- diff(apply(skin,2,mean))
nu <- nrow(skin)-1
sigma_nu <- sd(apply(skin,1,diff))/sqrt(nu)
```

---

tost *Two One-Sided Test (TOST) for (Bio)Equivalence Testing*

Description

This function performs a Two One-Sided Test (TOST) for (bio)equivalence testing.

Usage

```
tost(theta, sigma, nu, alpha, delta)
```

Arguments

theta   A numeric value corresponding to the difference of means (e.g. between a generic and reference drug).

sigma   A numeric value corresponding to the standard error.

nu   A numeric value corresponding to the number of degrees of freedom.

alpha   A numeric value specifying the significance level.

delta   A numeric value corresponding to (bio)equivalence limit. We assume symmetry, i.e, the (bio)equivalence interval corresponds to (-delta,delta)

Value

A tost object with the structure:

- decision: A boolean variable indicating whether (bio)equivalence is accepted or not.

- ci: Confidence interval at the 1 - 2*alpha level.

- theta: The difference of means used for the test.

- sigma: The standard error used for the test.

- nu: The number of degrees of freedom used for the test.

- alpha: The significance level used for the test.

- delta: The (bio)equivalence limits used for the test.

- method: The method used for the test (here the "TOST").

Author(s)

Younes Boulaguiem, Stéphane Guerrier, Dominique-Laurent Couturier

Examples

```
data(skin)

theta_hat = diff(apply(skin,2,mean))
nu = nrow(skin) - 1
sig_hat = sd(apply(skin,1,diff))/sqrt(nu)
tost(theta = theta_hat, sigma = sig_hat, nu = nu,
     alpha = 0.05, delta = log(1.25))
```

Index