

Package ‘strata.MaxCombo’

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Title Stratified Max-Combo Test

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Description Non-proportional hazard (NPH) is commonly observed in immuno-oncology studies, where the survival curves of the treatment and control groups show delayed separation. To properly account for NPH, several statistical methods have been developed. One such method is Max-Combo test, which is a straightforward and flexible hypothesis testing method that can simultaneously test for constant, early, middle, and late treatment effects. However, the majority of the Max-Combo test performed in clinical studies are unstratified, ignoring the important prognostic stratification factors. To fill this gap, we have developed an R package for stratified Max-Combo testing that accounts for stratified baseline factors. Our package explores various methods for calculating combined test statistics, estimating joint distributions, and determining the p-values.

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Encoding UTF-8

Imports mvtnorm

RoxygenNote 7.2.3

NeedsCompilation no

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sim_data	<i>simulated survival data with two stratum</i>
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Description

Simulated survival data for demonstrating the usage of WLRtest and SMCTest.

Usage

```
data(sim_data)
```

Format

The data file consists of four components: event_time, event_status, group and strata. Data contains different event_times, two event_status (0: censored and 1: event), two groups (control and experimental) and two stratum (first and second).

See Also

[SMCTest](#), [WLRtest](#)

SMCTest	<i>This function performs stratified Max-Combo test.</i>
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Description

This function performs stratified Max-Combo test.

Usage

```
SMCTest(  
  time,  
  event,  
  group,  
  stratum,  
  alternative = c("two.sided", "less", "greater"),  
  rho = c(0, 1, 1, 0),  
  gamma = c(0, 0, 1, 1)  
)
```

Arguments

time	a vector of event or censored times.
event	a vector with entries 0 or 1, indicating event occurrence (1) or time being censored (0).
group	a vector indicating treatment groups.
stratum	a vector of stratification factor.
alternative	choose from "two.sided", "less" or "greater" to determine which type of tests to conduct and calculate the corresponding p-values.
rho	a vector indicating different values of rho in Fleming-Harrington weight.
gamma	a vector indicating different values of gamma in Fleming-Harrington weight.

Value

A list with components:

z.list	a vector of z values calculated from all stratified weighted log-rank tests under stratification method 1.
z.max	the z value that is the furthest away from 0 under stratification method 1.
cov	the covariance matrix of different stratified weighted log-rank tests under stratification method 1.
pval	p-value of desired alternative test under stratification method 1.
z.list2	a vector of z values calculated from all stratified weighted log-rank tests under stratification method 2.
z.max2	the z value that is the furthest away from 0 under stratification method 2.
cov2	the covariance matrix of different stratified weighted log-rank tests under stratification method 2.
pval2	p-value of desired alternative test under stratification method 2.
z.list3	a vector of z values calculated from all stratified weighted log-rank tests under stratification method 3.
z.max3	the z value that is the furthest away from 0 under stratification method 3.
cov3	the covariance matrix of different stratified weighted log-rank tests under stratification method 3.
pval3	p-value of desired alternative test under stratification method 3.

References

Magirr, D. and Jiménez, J. (2023). Stratified modestly-weighted log-rank tests in settings with an anticipated delayed separation of survival curves. *Biometrical Journal.*, 2023;65:2200126 doi: [10.1002/bimj.202200126](https://doi.org/10.1002/bimj.202200126)

See Also

[WLRtest](#)

Examples

```
data(sim_data)
##load survival data
time <- sim_data$event_time
event <- sim_data$event_status
group <- sim_data$group
stratum <- sim_data$strata

##perform stratified max-combo test
SMCTest(time,event,group,stratum,alternative="two.sided",rho=c(0,1,1,0),gamma=c(0,0,1,1))
```

WLRtest

This function performs weighted log-rank test.

Description

This function performs weighted log-rank test.

Usage

```
WLRtest(time, event, group, rho = 0, gamma = 0)
```

Arguments

time	time a vector of event or censored times.
event	a vector with entries 0 or 1, indicating event occurrence (1) or time being censored (0).
group	a vector indicating treatment groups.
rho	a value of rho in Fleming-Harrington weight
gamma	a value of gamma in Fleming-Harrington weight

Value

A list with components:

z	z value of weighted log-rank test.
pvalue.two.sided	p-value for two-sided test.
pvalue.less	p-value for one-sided test (less).
pvalue.greater	p-value for one-sided test (greater).
D	a matrix containing components that can be used in stratified max-combo test.

References

Ristl, R., Ballarini, N., Götte, H., Schöler, A., Posch, M. and König, F. (2021). Delayed treatment effects, treatment switching and heterogeneous patient populations: How to design and analyze RCTs in oncology. *Pharmaceutical Statistics.*, 20:129-145 doi: [10.1002/pst.2062](https://doi.org/10.1002/pst.2062)

See Also

[SMCTest](#)

Examples

```
data(sim_data)
##load survival data
time <- sim_data$event_time
event <- sim_data$event_status
group <- sim_data$group

##perform weighted log-rank test
WLRtest(time,event,group,rho=0,gamma=0)
```

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* **datasets**

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