

Package ‘triggerstrategy’

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Title Trigger Strategy in Clinical Trials

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Description The trigger strategy is a general framework for a multistage statistical design with multiple hypotheses, allowing an adaptive selection of interim analyses. The selection of interim stages can be associated with some prespecified endpoints which serve as the trigger. This selection allows us to refine the critical boundaries in hypotheses testing procedures, and potentially increase the statistical power. This package includes several trial designs using the trigger strategy.

See Gou, J. (2023), “Trigger strategy in repeated tests on multiple hypotheses”, *Statistics in Biopharmaceutical Research*, 15(1), 133-140, and Gou, J. (2022), “Sample size optimization and initial allocation of the significance levels in group sequential trials with multiple endpoints”, *Biometrical Journal*, 64(2), 301-311.

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alpha2boundary	<i>Convert cumulative alpha levels to normal critical boundaries</i>
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Description

This function converts cumulative alpha levels into normal critical boundaries.

Usage

```
alpha2boundary(
  alphas,
  t,
  initIntvl = c(1, 2 * stats::qnorm(p = alphas[1], lower.tail = FALSE))
)
```

Arguments

alphas	a list of cumulative errors from some error spending functions
t	a vector of information times
initIntvl	a pair of numbers as the lower and upper bounds of critical boundaries, used for stats::uniroot function

Details

The current version of `ldbounds::ldBounds` may not work for Hwang-Shih-DeCani boundaries.

Value

a vector of critical boundaries

Author(s)

Jiangtao Gou

Examples

```
library(ldbounds)
tvec <- c(0.5,1)
result <- ldbounds::ldBounds(t=tvec, iuse=1, alpha=0.05, sides=1)
print(result$upper.bounds)
bd <- alpha2boundary(alphas = result$exit.pr, t=tvec)
print(bd)
```

boundary2alpha

Convert normal critical boundaries to cumulative alpha levels.

Description

This function converts normal critical boundaries to cumulative alpha levels.

Usage

```
boundary2alpha(cvec, t)
```

Arguments

cvec	a vector of critical boundaries
t	a vector of information times

Value

alphas, a vector of cumulative errors

Author(s)

Jiangtao Gou
Fengqing Zhang

Examples

```
t <- c(0.5,0.8,1)
iuse <- 4
result <- gbounds(t=t, iuse=iuse)
print(result)
boundary2alpha(cvec=result$bd, t=t)
```

corrMatGenerator *Correlation matrix generator*

Description

This function generate the correlation matrix for group sequential trials with two endpoints.

Usage

```
corrMatGenerator(tp, ts, rhops)
```

Arguments

tp	an information fraction vector of Hp
ts	an information fraction vector of Hs
rhops	a number that shows the correlation coefficient between the test statistics of the primary endpoint and that of the secondary endpoint

Value

the correlation matrix, Hp goes first, and Hs goes second.

Author(s)

Jiangtao Gou

Examples

```
corrMatGenerator(tp=c(0.64,1),
  ts=c(0.25,0.49,1),
  rhops=1)
```

gbounds *Critical boundary in group sequential trials*

Description

This function computes the critical boundaries and the error spent until each stage in group sequential trials

Usage

```
gbounds(t, iuse = 1, alpha = 0.05, phi = rep(1, length(alpha)))
```

Arguments

t	a vector of information times
iuse	a number of the type of the error spending function, from -2, -1, 1, 2, 3, 4
alpha	a number of type I error rate
phi	a parameter for the power family or the HSD gamma family

Details

If the original Pocock is implemented, we specify `iuse=-2`. If the original O'Brien-Flemming is implemented, we specify `iuse=-1`.

Value

a list of two vectors: `bd` critical boundaries, `er` error spent until each stage

Author(s)

Jiangtao Gou

Examples

```
t<-c(0.5,0.8,1)
iuse <- 4
gbounds(t=t, iuse=iuse)
gbounds(t=(1:5)/5, iuse=4, alpha=0.01, phi=-4)
gbounds(t=(1:5)/5, iuse=-2, alpha=0.01)
```

marginalPwR

Marginal Power Rate

Description

This function computes the marginal powers.

Usage

```
marginalPwR(cvec, t, delta = 0)
```

Arguments

cvec	a vector of critical boundaries
t	a vector of information times
delta	a number shows the drift paramter

Value

a number shows the marginal power (delta isn't equal to zero) or type I error (delta is zero)

Author(s)

Jiangtao Gou

Examples

```
marginalPwR(c(2.218,2.218),c(0.1,0.5,1),delta=3)
marginalPwR(1.96,t=1,delta=3)
```

psPwRbhmb

Powers of testing the primary and secondary hypotheses

Description

This function computes the powers of testing the primary and secondary hypotheses using the holm, maurer-bretz, bonferroni methods.

Usage

```
psPwRbhmb(
  alpha,
  alpha0,
  t0,
  t1,
  tc0 = t0,
  tc1 = t1,
  rho = 0,
  iuse0 = 1,
  iuse1 = 1,
  phi0 = rep(1, length(alpha)),
  phi1 = rep(1, length(alpha)),
  usingRhoForBoundary = FALSE,
  groupsize,
  szratio = 1,
  effsz0,
  effsz1,
  method = "bonferroni"
)
```

Arguments

alpha	a number shows the overall error rate
alpha0	a number shows the error rate assigned to the primary endpoint initially
t0	a vector shows the information times of the primary endpoint
t1	a vector shows the information times of the secondary endpoint
tc0	a vector shows the calendar times of the primary endpoint

tc1	a vector shows the calendar times of the secondary endpoint
rho	a number shows the correlation between the primary and secondary endpoints
iuse0	an integer shows the type of group sequential boundaries used for the primary endpoint
iuse1	an integer shows the type of group sequential boundaries used for the secondary endpoint
phi0	a parameter for the power family or the HSD gamma family for the primary endpoint
phi1	a parameter for the power family or the HSD gamma family for the secondary endpoint
usingRhoForBoundary	an indicator whether using the information of rho to calculate the boundary, default is FALSE (not using)
groupsize	a value of sample size in group 1
szratio	a value of the sample size ratio, n_2/n_1
effsz0	a value of effect size for hypothesis H0
effsz1	a value of effect size for hypothesis H1
method	a text of method, including holm, maurer-bretz, bonferroni

Details

The methods include holm, maurer-bretz, and bonferroni. Users can decide whether the correlation information is used or not.

Value

a vector of two values of the probability that H0 is rejected, the probability that H1 is rejected, the power, using holm, maurer-bretz, or bonferroni.

Author(s)

Jiangtao Gou

References

Gou, J. (2023). Trigger strategy in repeated tests on multiple hypotheses. *Statistics in Biopharmaceutical Research*, 15(1), 133-140. Gou, J. (2022). Sample size optimization and initial allocation of the significance levels in group sequential trials with multiple endpoints. *Biometrical Journal*, 64(2), 301-311. Tamhane, A. C., Gou, J., Jennison, C., Mehta, C. R., and Curto, T. (2018). A gatekeeping procedure to test a primary and a secondary endpoint in a group sequential design with multiple interim looks. *Biometrics*, 74(1), 40-48. Tamhane, A. C., & Gou, J. (2022). Chapter 2 - Multiple test procedures based on p-values. In X. Cui, T. Dickhaus, Y. Ding, & J. C. Hsu (Eds.), *Handbook of multiple comparisons* (Vol. 45, pp. 11-34).

Examples

```

alpha <- 0.025
alpha0 <- 0.0136
iuse0 <- 1
iuse1 <- 2
phi0 <- -4
phi1 <- 1
tc0 <- c(1,2)
tc1 <- c(1,2,3)
t0 <- c(0.6,1)
t1 <- c(0.5,0.9,1)
rho <- 0
effsz0 <- 0.33
effsz1 <- 0.30
groupsize=226
szratio=1
method="bonferroni"
method = "holm"
method="maurer-bretz"
psPwRbmb(alpha=alpha, alpha0=alpha0,
  t0=t0, t1=t1, tc0=tc0, tc1=tc1,
  rho=rho, iuse0=1, iuse1=iuse1,
  phi0=phi0, phi1=phi1,
  usingRhoForBoundary=usingRhoForBoundary,
  groupsize=groupsize, szratio=szratio,
  effsz0=effsz0, effsz1=effsz1,
  method=method)

```

psPwRtrigger

Powers of testing the primary and secondary hypotheses using trigger strategy

Description

This function computes the powers of testing the primary and secondary hypotheses using trigger strategy.

Usage

```

psPwRtrigger(
  alpha,
  alpha0,
  t0,
  t1,
  tc0 = t0,
  tc1 = t1,
  rho = 0,
  iuse0 = 1,
  iuse1 = 1,

```

```

    phi0 = rep(1, length(alpha)),
    phi1 = rep(1, length(alpha)),
    usingRhoForBoundary = FALSE,
    groupsize,
    szratio = 1,
    effsz0,
    effsz1
  )

```

Arguments

alpha	a number shows the overall error rate
alpha0	a number shows the error rate assigned to the primary endpoint initially
t0	a vector shows the information times of the primary endpoint
t1	a vector shows the information times of the secondary endpoint
tc0	a vector shows the calendar times of the primary endpoint
tc1	a vector shows the calendar times of the secondary endpoint
rho	a number shows the correlation between the primary and secondary endpoints
iuse0	an integer shows the type of group sequential boundaries used for the primary endpoint
iuse1	an integer shows the type of group sequential boundaries used for the secondary endpoint
phi0	a parameter for the power family or the HSD gamma family for the primary endpoint
phi1	a parameter for the power family or the HSD gamma family for the secondary endpoint
usingRhoForBoundary	an indicator whether using the information of rho to calculate the boundary, default is FALSE (not using)
groupsize	a value of sample size in group 1
szratio	a value of the sample size ratio, n_2/n_1
effsz0	a value of effect size for hypothesis H0
effsz1	a value of effect size for hypothesis H1

Value

a vector of two values of the probability that H0 is rejected, and the probability that H1 is rejected, using the trigger strategy

References

Gou, J. (2023). Trigger strategy in repeated tests on multiple hypotheses. *Statistics in Biopharmaceutical Research*, 15(1), 133-140. Gou, J. (2022). Sample size optimization and initial allocation of the significance levels in group sequential trials with multiple endpoints. *Biometrical Journal*, 64(2), 301-311.

Examples

```

alpha <- 0.0250
alpha0 <- 0.0136
iuse0 <- 1
iuse1 <- 2
phi0 <- -4
phi1 <- 1
tc0 <- c(1,2)
tc1 <- c(1,2,3)
t0 <- c(0.6,1)
t1 <- c(0.5,0.9,1)
rho <- 0
effsz0 <- 0.33
effsz1 <- 0.30
groupsize=226
sratio=1
psPwRtrigger(alpha=alpha, alpha0=alpha0,
  t0=t0, t1=t1, tc0=tc0, tc1=tc1,
  rho=rho, iuse0=1, iuse1=iuse1,
  phi0=phi0, phi1=phi1,
  usingRhoForBoundary=FALSE,
  groupsize=groupsize, sratio=sratio,
  effsz0=effsz0, effsz1=effsz1)

```

sBoundsPh2

Critical boundaries for the secondary endpoint in the partially hierarchical group sequential design

Description

This function computes the critical boundaries for the secondary endpoint in the partially hierarchical group sequential design.

Usage

```

sBoundsPh2(
  alpha,
  alpha0,
  t0,
  t1,
  tc0 = t0,
  tc1 = t1,
  rho = 0,
  iuse0 = 1,
  iuse1h = 1,
  iuse1t = 1,
  phi0 = rep(1, length(alpha)),
  phi1h = rep(1, length(alpha)),

```

```

    phi1t = rep(1, length(alpha))
  )

```

Arguments

alpha	a value of overall type I error rate
alpha0	a value of the type I error rate for testing H0
t0	a vector of information times for H0
t1	a vector of information times for H1
tc0	a vector of calendar times for H0
tc1	a vector of calendar times for H1
rho	a value of the correlation between the test statistics for H0 and H1.
iuse0	a value of the type of error spending function for H0, ranging from 1 to 4
iuse1h	a value of the type of error spending function for H1 first half, ranging from 1 to 4
iuse1t	a value of the type of error spending function for H1 second half, ranging from 1 to 4
phi0	a value of the parameter of error spending function for H0
phi1h	a value of the parameter of error spending function for H1 first half
phi1t	a value of the parameter of error spending function for H1 second half

Value

a list of two vectors: bd critical boundaries, er error spent until each stage

Author(s)

Jiangtao Gou

References

Gou, J. (2023). Trigger strategy in repeated tests on multiple hypotheses. *Statistics in Biopharmaceutical Research*, 15(1), 133-140. Gou, J. (2022). Sample size optimization and initial allocation of the significance levels in group sequential trials with multiple endpoints. *Biometrical Journal*, 64(2), 301-311.

Examples

```

alpha <- 0.05
alpha0 <- 0.03
iuse0 <- 4
iuse1h <- 4
iuse1t <- 4
phi0 <- -4
phi1h <- 1
phi1t <- 1
tc0 <- c(3,6,9,12)

```

```

tc1 <- c(6,12,18,24)
t0 <- c(0.3,0.6,0.9,1)
t1 <- (1:4)/4
rho <- 0
sBoundsPh2(alpha, alpha0,
            t0, t1, tc0, tc1,
            rho, iuse0, iuse1h, iuse1t,
            phi0, phi1h, phi1t)
alpha <- 0.025
alpha0 <- 0.01
iuse0 <- 4
iuse1 <- 4
phi0 <- -4
phi1 <- -4
tc0 <- c(3,6,9,12,18)
tc1 <- c(6,12,18,36)
t0 <- (1:5)/5
t1 <- (1:4)/4
rho <- 0.0;
sBoundsPh2(alpha, alpha0,
            t0, t1, tc0, tc1,
            rho, iuse0, iuse1h=iuse1, iuse1t=iuse1,
            phi0, phi1h=phi1, phi1t=phi1)

```

sErrRphInt2

Type I error rate of the overall null hypothesis using the partial hierarchical design

Description

This function computes the type I error rate of the overall null hypothesis using the partial hierarchical group sequential design.

Usage

```
sErrRphInt2(cvec0, cvec1, t0, t1, tc0 = t0, tc1 = t1, rho = 0)
```

Arguments

cvec0	a vector of critical boundaries for testing H0
cvec1	a vector of critical boundaries for testing H1
t0	a vector of information times for H0
t1	a vector of information times for H1
tc0	a vector of calendar times for H0
tc1	a vector of calendar times for H1
rho	a value of the correlation between the test statistics for H0 and H1.

Value

a number shows the type I error rate of testing H_0 intersect H_1

Author(s)

Jiangtao Gou

References

Gou, J. (2023). Trigger strategy in repeated tests on multiple hypotheses. *Statistics in Biopharmaceutical Research*, 15(1), 133-140. Gou, J. (2022). Sample size optimization and initial allocation of the significance levels in group sequential trials with multiple endpoints. *Biometrical Journal*, 64(2), 301-311. Tamhane, A. C., Gou, J., Jennison, C., Mehta, C. R., and Curto, T. (2018). A gatekeeping procedure to test a primary and a secondary endpoint in a group sequential design with multiple interim looks. *Biometrics*, 74(1), 40-48. Tamhane, A. C., & Gou, J. (2022). Chapter 2 - Multiple test procedures based on p-values. In X. Cui, T. Dickhaus, Y. Ding, & J. C. Hsu (Eds.), *Handbook of multiple comparisons* (Vol. 45, pp. 11–34).

Examples

```
alpha0 <- 0.03
alpha1 <- 0.02
iuse0 <- 4
iuse1 <- 4
phi0 <- -4
phi1 <- 1
tc0 <- c(3,6,9,12)
tc1 <- c(6,12,18,24)
t0 <- c(0.3,0.6,0.9,1)
t1 <- (1:4)/4
rho <- 0
cvecList0 <- gbounds(t=t0,iuse=iuse0,
  alpha=alpha0,phi=phi0)
cvec0 <- cvecList0$bd
cvecList1 <- gbounds(t=t1,iuse=iuse1,
  alpha=alpha1,phi=phi1)
cvec1 <- cvecList1$bd
result <- sErrRphInt2(cvec0, cvec1,
  t0, t1, tc0, tc1, rho)
print(result)
```

solveAlphaXsampleSize *Sample size calculation*

Description

This function computes the sample size and the error rate pre-assigned to the primary endpoint using methods of trigger, holm, maurer-bretz, bonferroni.

Usage

```

solveAlphaXsampleSize(
  alpha,
  beta0,
  beta1,
  effsz0,
  effsz1,
  szratio = 1,
  t0 = 1,
  t1 = 1,
  tc0 = t0,
  tc1 = t1,
  rho = 0,
  iuse0 = 1,
  iuse1 = 1,
  phi0 = rep(1, length(alpha)),
  phi1 = rep(1, length(alpha)),
  usingRhoForBoundary = FALSE,
  method = "trigger",
  myinit
)

```

Arguments

alpha	a number of overall type I error rate
beta0	a number of type II error rate for H0
beta1	a number of type II error rate for H1
effsz0	a number of the effect size of testing H0
effsz1	a number of the effect size of testing H1
szratio	a number of the ratio of sample size of testing H0 to that of testing H1
t0	a vector of information times for H0
t1	a vector of information times for H1
tc0	a vector of calendar times for H0
tc1	a vector of calendar times for H1
rho	a value of correlation coefficient between H0 and H1
iuse0	an integer shows the type of group sequential boundaries used for the primary endpoint
iuse1	an integer shows the type of group sequential boundaries used for the secondary endpoint
phi0	a parameter for the power family or the HSD gamma family for the primary endpoint
phi1	a parameter for the power family or the HSD gamma family for the secondary endpoint

usingRhoForBoundary
 an indicator whether using the information of rho to calculate the boundary, default is FALSE (not using)

method
 a text of method, including trigger, holm, maurer-bretz, bonferroni

myinit
 a vector of two starting points for alpha0 and sample size.

Value

a list of two values, alpha0 and groupsize

References

Gou, J. (2023). Trigger strategy in repeated tests on multiple hypotheses. *Statistics in Biopharmaceutical Research*, 15(1), 133-140. Gou, J. (2022). Sample size optimization and initial allocation of the significance levels in group sequential trials with multiple endpoints. *Biometrical Journal*, 64(2), 301-311.

Examples

```
# Single Stage Example
alpha <- 0.025
effsz0 <- 0.4
effsz1 <- 0.30
szratio <- 1
beta0 <- 0.10
beta1 <- 0.20
solveAlphaXsampleSize(alpha, beta0, beta1,
  effsz0, effsz1, szratio)
# Multi-stage example
alpha <- 0.025
beta0 <- 0.10
beta1 <- 0.20
effsz0 <- 0.33
effsz1 <- 0.30
szratio <- 1
t0 <- c(0.5,0.9,1)
t1 <- c(0.6,1)
tc0 <- c(1,2)
tc1 <- c(1,2,3)
rho <- 0
iuse0 <- 1
iuse1 <- 2
phi0 <- -4
phi1 <- 1
usingRhoForBoundary <- FALSE
myinit <- c(300,alpha/2)
myinit <- c(200,alpha/10)
method="trigger"
method="bonferroni"
method="holm"
method="maurer-bretz"
```

```

solveAlphaXsampleSize(alpha=alpha,
  beta0=beta0, beta1=beta1,
  effsz0=effsz0, effsz1=effsz1,
  szratio=szratio,
  t0=t0, t1=t1, tc0=tc0, tc1=tc1,
  rho=rho, iuse0=iuse0, iuse1=iuse1,
  phi0=phi0, phi1=phi1,
  usingRhoForBoundary=usingRhoForBoundary,
  method=method,
  myinit=myinit)

```

```

solveAlphaXsampleSizeGA

```

Sample size calculation using Genetic Algorithms

Description

This function computes the sample size and the error rate pre-assigned to the primary endpoint using methods of trigger, holm, maurer-bretz, bonferroni, with Genetic Algorithms.

Usage

```

solveAlphaXsampleSizeGA(
  alpha,
  beta0,
  beta1,
  effsz0,
  effsz1,
  szratio = 1,
  t0 = 1,
  t1 = 1,
  tc0 = t0,
  tc1 = t1,
  rho = 0,
  iuse0 = 1,
  iuse1 = 1,
  phi0 = rep(1, length(alpha)),
  phi1 = rep(1, length(alpha)),
  usingRhoForBoundary = FALSE,
  method = "trigger",
  lower = c(1, 1e-04),
  upper = c(10000, alpha - 1e-04),
  maxiter = 20,
  run = 200,
  seed = 1949
)

```

Arguments

alpha	a number of overall type I error rate
beta0	a number of type II error rate for H0
beta1	a number of type II error rate for H1
effsz0	a number of the effect size of testing H0
effsz1	a number of the effect size of testing H1
sratio	a number of the ratio of sample size of testing H0 to that of testing H1
t0	a vector of information times for H0
t1	a vector of information times for H1
tc0	a vector of calendar times for H0
tc1	a vector of calendar times for H1
rho	a value of correlation coefficient between H0 and H1
iuse0	an integer shows the type of group sequential boundaries used for the primary endpoint
iuse1	an integer shows the type of group sequential boundaries used for the secondary endpoint
phi0	a parameter for the power family or the HSD gamma family for the primary endpoint
phi1	a parameter for the power family or the HSD gamma family for the secondary endpoint
usingRhoForBoundary	an indicator whether using the information of rho to calculate the boundary, default is FALSE (not using)
method	a text of method, including trigger, holm, maurer-bretz, bonferroni
lower	a vector of two lower limits for alpha0 and sample size
upper	a vector of two upper limits for alpha0 and sample size.
maxiter	a number of maximum number of iterations
run	a number of maximum number of consecutive generations without any improvement in the best fitness value before the GA is stopped
seed	a number of seed of random number generator

Details

R package GA is used for Genetic Algorithms.

Value

a list of two values, alpha0 and groupsize

References

Gou, J. (2023). Trigger strategy in repeated tests on multiple hypotheses. *Statistics in Biopharmaceutical Research*, 15(1), 133-140. Gou, J. (2022). Sample size optimization and initial allocation of the significance levels in group sequential trials with multiple endpoints. *Biometrical Journal*, 64(2), 301-311.

Examples

```
alpha=0.025
beta0=0.10
beta1=0.20
effsz0=0.33
effsz1=0.30
szratio=1
t0=c(0.5,0.9,1)
t1=c(0.6,1)
tc0=c(1,2)
tc1=c(1,2,3)
rho=0
iuse0=1
iuse1=2
phi0=-4
phi1=1
usingRhoForBoundary=FALSE
method="trigger"
method="bonferroni"
method="holm"
method="maurer-bretz"
lower = c(180,0.005)
upper = c(240, alpha-0.005)
maxiter = 1 # Increase this number for more precise results
run = 1 # Increase this number for more precise results
seed = 123
result <- solveAlphaXsampleSizeGA(alpha=alpha,
  beta0=beta0, beta1=beta1,
  effsz0=effsz0, effsz1=effsz1,
  szratio=szratio,
  t0=t0, t1=t1, tc0=tc0, tc1=tc1,
  rho=rho, iuse0=iuse0, iuse1=iuse1,
  phi0=phi0, phi1=phi1,
  usingRhoForBoundary=usingRhoForBoundary,
  method=method,
  lower = lower, upper = upper,
  maxiter = maxiter,
  run = run,
  seed = seed)
print(result)
```

sPwRholm

Power of testing the secondary hypothesis using Holm

Description

This function computes the power of testing the secondary hypothesis using Holm

Usage

```
sPwRholm(
  alpha,
  alpha0,
  t0,
  t1,
  delta0,
  delta1,
  rho = 0,
  iuse0 = 1,
  iuse1 = 1,
  phi0 = rep(1, length(alpha)),
  phi1 = rep(1, length(alpha))
)
```

Arguments

alpha	a number shows the overall error rate
alpha0	a number shows the error rate assigned to the primary endpoint initially
t0	a vector shows the information times of the primary endpoint
t1	a vector shows the information times of the secondary endpoint
delta0	a value of delta for hypothesis H0
delta1	a value of delta for hypothesis H1
rho	a number shows the correlation between the primary and secondary endpoints
iuse0	an integer shows the type of group sequential boundaries used for the primary endpoint
iuse1	an integer shows the type of group sequential boundaries used for the secondary endpoint
phi0	a parameter for the power family or the HSD gamma family for the primary endpoint
phi1	a parameter for the power family or the HSD gamma family for the secondary endpoint

Value

a number shows the statistical power of rejecting H1

Examples

```

alpha <- 0.025
alpha0 <- 0.01
iuse0 <- 4
iuse1 <- 4
phi0 <- -4
phi1 <- -4
t0 <- (1:5)/5
t1 <- (1:4)/4
rho <- 0.5
delta0 <- 1
delta1 <- 3
sPwRholm(alpha=alpha, alpha0=alpha0,
          t0=t0, t1=t1,
          delta0=delta0, delta1=delta1,
          rho=rho, iuse0=iuse0, iuse1=iuse1,
          phi0=phi0, phi1=phi1)

```

sPwRholmye

Power of testing the secondary hypothesis using Holm-Ye

Description

This function computes the power of testing the secondary hypothesis using Holm-Ye

Usage

```

sPwRholmye(
  alpha,
  alpha0,
  t0,
  t1,
  tc0 = t0,
  tc1 = t1,
  delta0,
  delta1,
  rho = 0,
  iuse0 = 1,
  iuse1 = 1,
  phi0 = rep(1, length(alpha)),
  phi1 = rep(1, length(alpha))
)

```

Arguments

alpha	a number shows the overall error rate
alpha0	a number shows the error rate assigned to the primary endpoint initially

t0	a vector shows the information times of the primary endpoint
t1	a vector shows the information times of the secondary endpoint
tc0	a vector shows the calendar times of the primary endpoint
tc1	a vector shows the calendar times of the secondary endpoint
delta0	a value of delta for hypothesis H0
delta1	a value of delta for hypothesis H1
rho	a number shows the correlation between the primary and secondary endpoints
iuse0	an integer shows the type of group sequential boundaries used for the primary endpoint
iuse1	an integer shows the type of group sequential boundaries used for the secondary endpoint
phi0	a parameter for the power family or the HSD gamma family for the primary endpoint
phi1	a parameter for the power family or the HSD gamma family for the secondary endpoint

Value

a number shows the statistical power of rejecting H1

Examples

```
alpha <- 0.025
alpha0 <- 0.01
iuse0 <- 4
iuse1 <- 4
phi0 <- -4
phi1 <- -4
tc0 <- c(3,6,9,12,18)
tc1 <- c(6,12,18,36)
t0 <- (1:5)/5
t1 <- (1:4)/4
rho <- 0.5
delta0 <- 1
delta1 <- 3
sPwRholmye(alpha=alpha, alpha0=alpha0,
  t0=t0, t1=t1, tc0=tc0, tc1=tc1,
  delta0=delta0, delta1=delta1,
  rho=rho, iuse0=iuse0, iuse1=iuse1,
  phi0=phi0, phi1=phi1)
```

sPwRnaiveBonf

Power of testing the secondary hypothesis using Bonferroni

Description

This function computes the power of testing the secondary hypothesis using Bonferroni

Usage

```
sPwRnaiveBonf(
  alpha,
  alpha0 = alpha/2,
  t1,
  delta1,
  iuse1,
  phi1 = rep(1, length(alpha))
)
```

Arguments

alpha	a number shows the overall error rate
alpha0	a number shows the error rate assigned to the primary endpoint initially
t1	a vector shows the information times of the secondary endpoint
delta1	a value of delta for hypothesis H1
iuse1	an integer shows the type of group sequential boundaries used for the secondary endpoint
phi1	a parameter for the power family or the HSD gamma family for the secondary endpoint

Value

a value of the probability that H1 is rejected, the power, using the naive Bonferroni method

Examples

```
alpha <- 0.025
alpha0 <- 0.01
iuse0 <- 4
iuse1 <- 4
phi0 <- -4
phi1 <- -4
tc0 <- c(3,6,9,12,18)
tc1 <- c(6,12,18,36)
t0 <- (1:5)/5
t1 <- (1:4)/4
rho <- 0.5
delta0 <- 1
```

```

delta1 <- 3
sPwRnaiveBonf(alpha=alpha,
  alpha0=alpha0,
  t1=t1,
  delta1=delta1,
  iuse1=iuse1,
  phi1=phi1)

```

sPwRph2

Power of testing the secondary hypothesis in partially hierarchical design

Description

This function computes the power of testing the secondary hypothesis in partially hierarchical design.

Usage

```
sPwRph2(cvec0, cvec1, delta0, delta1, t0, t1, tc0 = t0, tc1 = t1, rho = 0)
```

Arguments

cvec0	a vector of critical boundaries for testing H0
cvec1	a vector of critical boundaries for testing H1
delta0	a value of drift parameter for testing H0
delta1	a value of drift parameter for testing H1
t0	a vector of information times for H0
t1	a vector of information times for H1
tc0	a vector of calendar times for H0
tc1	a vector of calendar times for H1
rho	a value of correlation coefficient between H0 and H1

Value

a value of the probability that H1 is rejected, the power

References

Gou, J. (2023). Trigger strategy in repeated tests on multiple hypotheses. *Statistics in Biopharmaceutical Research*, 15(1), 133-140. Gou, J. (2022). Sample size optimization and initial allocation of the significance levels in group sequential trials with multiple endpoints. *Biometrical Journal*, 64(2), 301-311.

Examples

```

alpha <- 0.05
alpha0 <- 0.03
iuse0 <- 4
iuse1h <- 4
iuse1t <- 4
phi0 <- -4
phi1h <- 1
phi1t <- 1
tc0 <- c(3,6,9,12)
tc1 <- c(6,12,18,24)
t0 <- c(0.3,0.6,0.9,1)
t1 <- (1:4)/4
rho <- 0
cveclst0 <- gbounds(t=t0, iuse=iuse0,
  alpha=alpha0, phi=phi0)
cvec0 <- cveclst0$bd
cveclst1 <- sBoundsPh2(alpha, alpha0,
  t0, t1, tc0, tc1,
  rho, iuse0, iuse1h, iuse1t,
  phi0, phi1h, phi1t)
cvec1 <- cveclst1$bd
sPwRph2(cvec0, cvec1,
  delta0=2, delta1=3,
  t0, t1, tc0, tc1,
  rho=0)

```

sPwRtrigger

Power of testing the secondary hypothesis using Trigger strategy

Description

This function computes the power of testing the secondary hypothesis using Trigger strategy

Usage

```

sPwRtrigger(
  alpha,
  alpha0,
  t0,
  t1,
  tc0 = t0,
  tc1 = t1,
  delta0,
  delta1,
  rho = 0,
  iuse0 = 1,
  iuse1 = 1,

```

```

    phi0 = rep(1, length(alpha)),
    phi1 = rep(1, length(alpha)),
    usingRhoForBoundary = FALSE
  )

```

Arguments

alpha	a number shows the overall error rate
alpha0	a number shows the error rate assigned to the primary endpoint initially
t0	a vector shows the information times of the primary endpoint
t1	a vector shows the information times of the secondary endpoint
tc0	a vector shows the calendar times of the primary endpoint
tc1	a vector shows the calendar times of the secondary endpoint
delta0	a value of delta for hypothesis H0
delta1	a value of delta for hypothesis H1
rho	a number shows the correlation between the primary and secondary endpoints
iuse0	an integer shows the type of group sequential boundaries used for the primary endpoint
iuse1	an integer shows the type of group sequential boundaries used for the secondary endpoint
phi0	a parameter for the power family or the HSD gamma family for the primary endpoint
phi1	a parameter for the power family or the HSD gamma family for the secondary endpoint
usingRhoForBoundary	an indicator whether using the information of rho to calculate the boundary, default is FALSE (not using)

Value

a value of the probability that H1 is rejected, the power, using the trigger strategy

References

Gou, J. (2023). Trigger strategy in repeated tests on multiple hypotheses. *Statistics in Biopharmaceutical Research*, 15(1), 133-140. Gou, J. (2022). Sample size optimization and initial allocation of the significance levels in group sequential trials with multiple endpoints. *Biometrical Journal*, 64(2), 301-311.

Examples

```

alpha <- 0.025
alpha0 <- 0.01
iuse0 <- 4
iuse1 <- 4
phi0 <- -4

```

```
phi1 <- -4
tc0 <- c(3,6,9,12,18)
tc1 <- c(6,12,18,36)
t0 <- (1:5)/5
t1 <- (1:4)/4
rho <- 0.5
delta0 <- 1
delta1 <- 3
sPwRtrigger(alpha=alpha, alpha0=alpha0,
  t0=t0, t1=t1, tc0=tc0, tc1=tc1,
  delta0=delta0, delta1=delta1,
  rho=rho, iuse0=1, iuse1=iuse1,
  phi0=phi0, phi1=phi1,
  usingRhoForBoundary=FALSE)
```

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