Package 'frequentistSSD'

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Type Package

Title Screened Selection Design with Survival Endpoints

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Description A study based on the screened selection design (SSD) is an exploratory phase II randomized trial with two or more arms but without concurrent control. The primary aim of the SSD trial is to pick a desirable treatment arm (e.g., in terms of the median survival time) to recommend to the subsequent randomized phase IIb (with the concurrent control) or phase III. Though The survival endpoint is often encountered in phase II trials, the existing SSD methods cannot deal with the survival endpoint. Furthermore, the existing SSD won't control the type I error rate. The proposed designs can "partially" control or provide the empirical type I error/false positive rate by an optimal algorithm (implemented by the optimal() function) for each arm. All the design needed components (sample size, operating characteristics) are supported.

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Depends survival

NeedsCompilation no

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R topics documented:

`get_oc` *Generate operating characteristics for Two-Stage Screened Selection Design for Randomized Phase II Trials with Time-to-Event Endpoints*

Description

Obtain the operating characteristics of Two-Stage Screened Selection Design for Randomized Phase II Trials with Time-to-Event Endpoints. The arguments for this function are from outputs of the functions of `optimal()` and `sample_size()`

Usage

```
get_oc(shape, m0, mA, hr, frac, ta, tf, c1, c,
       diff, n, nsim, seed = 2483)
```

Arguments

`shape`	the shape parameter of weibull distribution
`m0`	the median survival time of historical data
`mA`	the median survival time of arm A
`hr`	the hazard ratio of arm B to arm A
`frac`	the ratio of sample size in stage 1 compared to total sample size (e.g., n1/n)
`ta`	the accrual duration
`tf`	the follow-up duration
`c1`	the critical value at stage 1
`c`	the critical value at stage 2
`diff`	the equivalence margin
`n`	the total sample size for each arm
`nsim`	the number of simulated trials
`seed`	the seed. The default value is seed = 2483

Value

`get_oc()` returns: (1) n: total sample size for each arm (2) SSD.Arm.A: selection probability of Arm A (3) SSD.Arm.B: selection probability of Arm B (4) SSD.No.Arm: the probability of no arms selected (5) diff: the equivalence margin (6) Mean.N.Arm.A: the average number of patients allocated to Arm A (7) Mean.N.Arm.B: the average number of patients allocated to Arm B

Author(s)

Chia-Wei Hsu, Haitao Pan, Jianrong Wu

References

Jianrong Wu, Haitao Pan, Chia-Wei Hsu (2021). "Two-Stage Screened Selection Designs for Randomized Phase II Trials with Time-to-Event Endpoints." Submitted

Examples

```
## c1, n, c they all come from optimal function. Details are shown as follows:
## Not run: optimal(shape = 1, m0 = 1, ms = 2.4, tf = 3,
                  ta = 24, tot_size = 19, dist = "WB")
| alpha | beta | n1 |   c1   |  n |    c   |   t1    | MTSL |   ESS   |   PS
|  0.05 | 0.08 | 15 | 0.0508 | 19 | 1.6434 | 17.9751 |  27  | 16.5183 | 0.5203

## End(Not run)

get_oc(shape = 1, m0 = 1, mA = 2.4, hr = 0.6, frac = 15/19,
       ta = 24, tf = 3, c1 = 0.0508, c = 1.6434,
       diff = 0.25, n = 19, nsim = 10000)
```

`get_oc_3arm` *Generate operating characteristics for Two-Stage Screened Selection Design for Randomized Phase II Trials with Time-to-Event Endpoints for 3 arms*

Description

Obtain the operating characteristics of Two-Stage Screened Selection Design for Randomized Phase II Trials with Time-to-Event Endpoints for 3 arms. The arguments for this function are from outputs of the functions of `optimal()` and `sample_size_3arm()`

Usage

```
get_oc_3arm(shape, m0, mA, hr2, hr3, frac, ta, tf, c1, c,
            diff, n, nsim, seed = 2483)
```

Arguments

`shape`	the shape parameter of weibull distribution
`m0`	the median survival time of historical data
`mA`	the median survival time of arm A
`hr2`	the hazard ratio of arm B to arm A
`hr3`	the hazard ratio of arm C to arm A
`frac`	the ratio of sample size in stage 1 compared to total sample size (e.g., n1/n)
`ta`	the accrual duration
`tf`	the follow-up duration
`c1`	the critical value at stage 1

c	the critical value at stage 2
diff	the equivalence margin
n	the total sample size for each arm
nsim	the number of simulated trials
seed	the seed. The default value is seed = 2483

Value

get_oc_3arm() returns: (1) n: total sample size for each arm (2) SSD.Arm.A: selection probability of Arm A (3) SSD.Arm.B: selection probability of Arm B (4) SSD.Arm.C: selection probability of Arm C (5) SSD.No.Arm: the probability of no arms selected (6) diff: the equivalence margin (7) Mean.N.Arm.A: the average number of patients allocated to Arm A (8) Mean.N.Arm.B: the average number of patients allocated to Arm B (9) Mean.N.Arm.C: the average number of patients allocated to Arm C

Author(s)

Chia-Wei Hsu, Haitao Pan, Jianrong Wu

References

Jianrong Wu, Haitao Pan, Chia-Wei Hsu (2021). "Two-Stage Screened Selection Designs for Randomized Phase II Trials with Time-to-Event Endpoints." Submitted

Examples

```
## c1, n, c they all come from optimal function. Details are shown as follows:
## Not run: optimal(shape = 1, m0 = 1, ms = 2, tf = 3,
                 ta = 24, tot_size = 21, dist = "WB")
| alpha | beta | n1 |    c1   |  n |   c   |   t1    | MTSL |   ESS   |   PS
|  0.05 | 0.14 | 16 | -0.0463 | 21 | 1.644 | 17.8248 |  27  | 18.3983 | 0.4815

## End(Not run)

get_oc_3arm(shape = 1, m0 = 1, mA = 2, hr2 = 1, hr3 = 0.6,
            frac = 16/21, ta = 24, tf = 3, c1 = -0.0463,
            c = 1.644, diff = 0, n = 21, nsim = 10000,
            seed = 2483)
```

---

optimal *Find optimal parameters*

Description

Find the optimal parameters used in the get_oc() function

Usage

```
optimal(shape, m0, ms, tf, ta,
        tot_size, dist)
```

Arguments

shape	the shape parameter of weibull distribution
m0	the median survival time of historical data
ms	the minimal clinical meaningful median survival time
tf	the follow-up duration
ta	the accrual duration
tot_size	the required sample size for each arm
dist	the distribution

Value

`optimal()` returns a list containing two blocks:

`$param`: (1) S0: historical survival probability at the landmark time point x0 (2) hr: hazard ratio of the hypothetical arm with "minimal clinical meaningful median survival time" to the historical arm (3) rate: accrual rate (calculated as tot_size/ta)

`$Two_stage`: (1) alpha: type I error (2) beta: type II error (3) n1: the required sample size for the first stage (4) c1: the cutoff point at the first stage (5) n: the required sample size for each arm (is equal to tot_size) (6) c: the cutoff point at the final stage (7) t1: the expected time of interim analysis (first stage) (8) MTSL: the maximum total study length (ta + tf) (9) ESS: the expected sample size for each arm (10) PS: the probability of early stopping

Note

(1) For `optimal()` function, if the ms is set to be equal to the less effective arm (e.g., say, the arm A is less effective than the arm B), with the rationale, by this way, the computed boundaries, c1, n1, c, would control the pre-specified type I (since both arms A and B are all under the same null case) while the power for the better arm B, would have at least pre-specified power 1-beta

(2) `optimal()` funcition will be applied to either two or three-arm cases to find the optimal cutoff bounaries, c1, n1, c

Author(s)

Chia-Wei Hsu, Haitao Pan, Jianrong Wu

References

Jianrong Wu, Haitao Pan, Chia-Wei Hsu (2021). "Two-Stage Screened Selection Designs for Randomized Phase II Trials with Time-to-Event Endpoints." Submitted

Examples

```
## For 2 arms
## Not run:
shape <- 1
m0 <- 1
ms <- 2.4
tf <- 3
ta <- 24
tot_size <- 19
dist <- "WB"

optimal(shape = shape, m0 = m0, ms = ms, tf = tf,
        ta = ta, tot_size = tot_size, dist = dist)

## End(Not run)

## For 3 arms
## Not run:
shape <- 1
m0 <- 1
ms <- 2
tf <- 3
ta <- 24
tot_size <- 21
dist <- "WB"

optimal(shape = shape, m0 = m0, ms = ms, tf = tf,
        ta = ta, tot_size = tot_size, dist = dist)

## End(Not run)
```

---

sample_size *Calculate the sample size for each arm*

Description

Calculate the sample size for each arm in a two-arm trial

Usage

```
sample_size(kappa, mA, hr, ta, tf, diff, P)
```

Arguments

kappa	the shape parameter of weibull distribution
mA	the median survival time of arm A
hr	the hazard ratio of arm B to arm A
ta	the accrual duration

tf	the follow-up duration
diff	the equivalence margin
P	the chance of correctly selecting the superior arm

Value

sample_size() returns required sample size for each arm

Author(s)

Chia-Wei Hsu, Haitao Pan, Jianrong Wu

References

Jianrong Wu, Haitao Pan, Chia-Wei Hsu (2021). "Two-Stage Screened Selection Designs for Randomized Phase II Trials with Time-to-Event Endpoints." Submitted

Examples

```
sample_size(kappa = 1, mA = 2.4, hr = 0.60, ta = 24,
            tf = 3, diff = 0.25, P = 0.9)
```

---

sample_size_3arm *Calculate the sample size for each arm*

Description

Calculate the sample size for each arm in a three-arm trial

Usage

```
sample_size_3arm(kappa, m0, mA, mB, delta, ta, tf, P, diff)
```

Arguments

kappa	the shape parameter of weibull distribution
m0	the median survival time of historical control with respect to both arm A, B and C
mA	the median survival time of arm A
mB	the median survival time of arm B
delta	the hazard ratio of arm C to arm A
ta	the accrual duration
tf	the follow-up duration
P	the chance of correctly selecting the superior arm
diff	the equivalence margin

Value

`sample_size_3arm()` returns required sample size for each arm

Author(s)

Chia-Wei Hsu, Haitao Pan, Jianrong Wu

References

Jianrong Wu, Haitao Pan, Chia-Wei Hsu (2021). "Two-Stage Screened Selection Designs for Randomized Phase II Trials with Time-to-Event Endpoints." Submitted

Examples

```
sample_size_3arm(kappa = 1, m0 = 1, mA = 2, mB = 2, delta = 0.6,
                 ta = 24, tf = 3, P = 0.90, diff = 0)

sample_size_3arm(kappa = 1, m0 = 1, mA = 2, mB = 2, delta = 0.6,
                 ta = 24, tf = 3, P = 0.90, diff = 0.25)
```

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sampsize_1stage_2arm *Calculate the sample size for each arm*

Description

Provide the required sample size (per arm) based on the one-stage selection design given the type I error rate and power. Details see the reference paper

Usage

```
sampsize_1stage_2arm(kappa, alpha, beta, m0, m1, ta, tf, delta)
```

Arguments

`kappa`	the shape parameter of weibull distribution
`alpha`	type I error rate
`beta`	type II error rate
`m0`	the median survival time of historical control with respect to both arm A and B
`m1`	the median survival time of arm A
`ta`	the accrual duration
`tf`	the follow-up duration
`delta`	the hazard ratio of arm B to arm A

Value

`sampsize_1stage_2arm()` returns required sample size for each arm

Author(s)

Chia-Wei Hsu, Haitao Pan, Jianrong Wu

References

Jianrong Wu, Haitao Pan, Chia-Wei Hsu (2021). "Two-Stage Screened Selection Designs for Randomized Phase II Trials with Time-to-Event Endpoints." Submitted

Examples

```
sampsize_1stage_2arm(kappa = 1, alpha = 0.05, beta = 0.1, m0 = 1,
                     m1 = 2.5, delta = 0.65, ta = 24, tf = 9)
```

Index