

Package ‘frequentistSSDBinary’

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Type Package

Title Screened Selection Design with Binary 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 response rate) to recommend to the subsequent randomized phase IIb (with the concurrent control) or phase III. The proposed designs can “partially” control or provide the empirical type I error/false positive rate by an optimal algorithm (implemented by the `optimal_2arm_binary()` or `optimal_3arm_binary()` function) for each arm. All the design needed components (sample size, operating characteristics) are supported.

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Encoding UTF-8

Depends mvtnorm, clinfun, ph2mult

NeedsCompilation no

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get_oc_2arm_binary	<i>Generate operating characteristics for Two-Stage Screened Selection Design for Randomized Phase II Trials with Binary Endpoints</i>
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Description

Obtain the operating characteristics of Two-Stage Screened Selection Design for Randomized Phase II Trials with Binary Endpoints. The arguments for this function are from outputs of the functions of `sample_size_2arm_binary()` and `optimal_2arm_binary()`

Usage

```
get_oc_2arm_binary(r1, r2, n1, n, p0, p1, p2, diff = 0, nsim, seed = 2483)
```

Arguments

r1	the maximum number of successes in stage 1 which will terminate trial
r2	the maximum number of successes in stage 2 not to warrant further investigation
n1	the number of subjects in stage 1
n	the total number of subjects (stage 1 + stage 2)
p0	the response rate of historical data
p1	the response rate of arm 1
p2	the response rate of arm 2
diff	the equivalence margin
nsim	the number of simulated trials
seed	the seed. The default value is seed = 2483

Value

`get_oc_2arm_binary()` 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, Zongheng Cai, Haitao Pan

References

Cai, Z., Pan, H., Wu, J., Hsu, C.W. (2024). Uncontrolled Randomized Screening Selection Design for Pediatric Oncology Trials. Accepted in Book Chapter of "Master Protocol Clinical Trial for Efficient Evidence Generation"

Wu, J., Pan, H., & Hsu, C. W. (2022). Two-stage screened selection designs for randomized phase II trials with time-to-event endpoints. Biometrical Journal, 64(7), 1207-1218

Yap, C., Pettitt, A. & Billingham, L. Screened selection design for randomised phase II oncology trials: an example in chronic lymphocytic leukaemia. BMC Med Res Methodol 13, 87 (2013)

Examples

```
get_oc_2arm_binary(r1 = 2, r2 = 6, n1 = 11, n = 21, p0 = 0.2,
                  p1 = 0.415, p2 = 0.615, nsim = 100)
```

get_oc_3arm_binary	<i>Generate operating characteristics for Two-Stage Screened Selection Design for Randomized Phase II Trials with Binary Endpoints for 3 arms</i>
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Description

Obtain the operating characteristics of Two-Stage Screened Selection Design for Randomized Phase II Trials with Binary Endpoints for 3 arms. The arguments for this function are from outputs of the functions of sample_size_3arm_binary() and optimal_3arm_binary()

Usage

```
get_oc_3arm_binary(r1, r2, n1, n, p0, p1, p2, p3, diff = 0, nsim, seed = 2483)
```

Arguments

r1	the maximum number of successes in stage 1 which will terminate trial
r2	the maximum number of successes in stage 2 not to warrant further investigation
n1	the number of subjects in stage 1
n	the total number of subjects (stage 1 + stage 2)
p0	the response rate of historical data
p1	the response rate of arm 1
p2	the response rate of arm 2
p3	the response rate of arm 3
diff	the equivalence margin. The default value is diff = 0
nsim	the number of simulated trials
seed	the seed. The default value is seed = 2483

Value

get_oc_3arm_binary() 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)

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References

Cai, Z., Pan, H., Wu, J., Hsu, C.W. (2024). Uncontrolled Randomized Screening Selection Design for Pediatric Oncology Trials. Accepted in Book Chapter of "Master Protocol Clinical Trial for Efficient Evidence Generation"

Wu, J., Pan, H., & Hsu, C. W. (2022). Two-stage screened selection designs for randomized phase II trials with time-to-event endpoints. *Biometrical Journal*, 64(7), 1207-1218

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Examples

```
get_oc_3arm_binary(r1 = 4, r2 = 25, n1 = 15, n = 82,
                  p0 = 0.2, p1 = 0.415, p2 = 0.515,
                  p3 = 0.615, nsim = 100)
```

optimal_2arm_binary *Find optimal design parameters*

Description

Find the optimal parameters used in the get_oc_2arm() function

Usage

```
optimal_2arm_binary(p0, p1, p2, alpha = 0.1, beta = 0.2, tot_sample)
```

Arguments

p0	the response rate of historical data
p1	the response rate of arm 1
p2	the response rate of arm 2
alpha	the type I error to be controlled. The default value is alpha = 0.1
beta	the type II error to be controlled. The default value is beta = 0.2
tot_sample	the required sample size for each arm from function sample_size_2arm_binary()

Value

optimal_2arm_binary() returns: (1) alpha: type I error (2) beta: typeII error (3) r1: the maximum number of successes in stage 1 which will terminate trial (4) n1: the number of subjects in stage 1 (5) r2: the maximum number of successes in stage 2 not to warrant further investigation (6) n: the total number of subjects (stage 1 + stage 2) (7) ESS: the expected sample size for each arm (8) PS:the probability of early stopping

Author(s)

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References

Cai, Z., Pan, H., Wu, J., Hsu, C.W. (2024). Uncontrolled Randomized Screening Selection Design for Pediatric Oncology Trials. Accepted in Book Chapter of "Master Protocol Clinical Trial for Efficient Evidence Generation"

Wu, J., Pan, H., & Hsu, C. W. (2022). Two-stage screened selection designs for randomized phase II trials with time-to-event endpoints. *Biometrical Journal*, 64(7), 1207-1218

Yap, C., Pettitt, A. & Billingham, L. Screened selection design for randomised phase II oncology trials: an example in chronic lymphocytic leukaemia. *BMC Med Res Methodol* 13, 87 (2013)

Examples

```
optimal_2arm_binary(p0 = 0.2, p1 = 0.415, p2 = 0.615, tot_sample = 21)
```

```
optimal_3arm_binary      Find optimal design parameters
```

Description

Find the optimal parameters used in the get_oc_3arm_binary() function

Usage

```
optimal_3arm_binary(p0, p1, p2, p3, alpha = 0.1, beta = 0.2, tot_sample)
```

Arguments

p0	the response rate of historical data
p1	the response rate of arm 1
p2	the response rate of arm 2
p3	the response rate of arm 3
alpha	the type I error to be controlled. The default value is alpha = 0.1
beta	the type II error to be controlled. The default value is beta = 0.2
tot_sample	the required sample size for each arm from function sample_size_3arm_binary()

Value

optimal_3arm_binary() returns: (1) alpha: type I error (2) beta: typeII error (3) r1: the maximum number of successes in stage 1 which will terminate trial (4) n1: the number of subjects in stage 1 (5) r2: the maximum number of successes in stage 2 not to warrant further investigation (6) n: the total number of subjects (stage 1 + stage 2) (7) ESS: the expected sample size for each arm (8) PS:the probability of early stopping

Author(s)

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References

Cai, Z., Pan, H., Wu, J., Hsu, C.W. (2024). Uncontrolled Randomized Screening Selection Design for Pediatric Oncology Trials. Accepted in Book Chapter of "Master Protocol Clinical Trial for Efficient Evidence Generation"

Wu, J., Pan, H., & Hsu, C. W. (2022). Two-stage screened selection designs for randomized phase II trials with time-to-event endpoints. Biometrical Journal, 64(7), 1207-1218

Yap, C., Pettitt, A. & Billingham, L. Screened selection design for randomised phase II oncology trials: an example in chronic lymphocytic leukaemia. BMC Med Res Methodol 13, 87 (2013)

Examples

```
optimal_3arm_binary(p0 = 0.2, p1 = 0.415, p2 = 0.515, p3 = 0.615,
                    alpha = 0.1, beta = 0.2, tot_sample = 82)
```

```
sample_size_2arm_binary
```

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

Description

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

Usage

```
sample_size_2arm_binary(p0, p1, p2, diff = 0, selection.prob = 0.9,
                        alpha = 0.1, beta = 0.2)
```

Arguments

p0	the successful probability of historical data
p1	the response rate of arm 1
p2	the response rate of arm 2
diff	the equivalence margin

selection.prob the probability of selection of a superior arm. The default value is selection.prob = 0.9

alpha the type I error to be controlled. The default value is alpha = 0.1

beta the type II error to be controlled. The default value is beta = 0.2

Value

sample_size_2arm_binary() returns required sample size for each arm

Author(s)

Chia-Wei Hsu, Zongheng Cai, Haitao Pan

References

Cai, Z., Pan, H., Wu, J., Hsu, C.W. (2024). Uncontrolled Randomized Screening Selection Design for Pediatric Oncology Trials. Accepted in Book Chapter of "Master Protocol Clinical Trial for Efficient Evidence Generation"

Wu, J., Pan, H., & Hsu, C. W. (2022). Two-stage screened selection designs for randomized phase II trials with time-to-event endpoints. *Biometrical Journal*, 64(7), 1207-1218

Yap, C., Pettitt, A. & Billingham, L. Screened selection design for randomised phase II oncology trials: an example in chronic lymphocytic leukaemia. *BMC Med Res Methodol* 13, 87 (2013)

Examples

```
sample_size_2arm_binary(p0 = 0.2, p1 = 0.415, p2 = 0.615)
```

```
sample_size_3arm_binary
```

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

Description

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

Usage

```
sample_size_3arm_binary(p0, p1, p2, p3, diff = 0, selection.prob = 0.9, alpha = 0.1,
  beta = 0.2)
```

Arguments

p0	the response rate of historical control arm
p1	the response rate of arm 1
p2	the response rate of arm 2
p3	the response rate of arm 3
diff	the equivalence margin. The default value is $\text{diff} = 0$
selection.prob	the probability of selection of a superior arm. The default value is $\text{selection.prob} = 0.9$
alpha	the type I error to be controlled. The default value is $\alpha = 0.1$
beta	the type II error to be controlled. The default value is $\beta = 0.2$

Value

sample_size_3arm_binary() returns required sample size for each arm

Author(s)

Chia-Wei Hsu, Zongheng Cai, Haitao Pan

References

- Cai, Z., Pan, H., Wu, J., Hsu, C.W. (2024). Uncontrolled Randomized Screening Selection Design for Pediatric Oncology Trials. Accepted in Book Chapter of "Master Protocol Clinical Trial for Efficient Evidence Generation"
- Wu, J., Pan, H., & Hsu, C. W. (2022). Two-stage screened selection designs for randomized phase II trials with time-to-event endpoints. *Biometrical Journal*, 64(7), 1207-1218
- Yap, C., Pettitt, A. & Billingham, L. Screened selection design for randomised phase II oncology trials: an example in chronic lymphocytic leukaemia. *BMC Med Res Methodol* 13, 87 (2013)

Examples

```
sample_size_3arm_binary(p0 = 0.2, p1 = 0.415, p2 = 0.515, p3 = 0.615)
```


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