Package 'DACT'

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Version 1.0.0

Title Design and Analysis for Clinical Trials

Author Ping Gao [aut, cre]

Maintainer Ping Gao <support@innovatiostat.com>

Description The applications and evaluation of the operating characteristics of many statistical methodologies require the use of
sophisticated software or extensive simulations. 'DACT' is designed to serve a wide range of innovative statistical designs and analyses.
The primary objective of the 'DACT' software is to promote the understanding and application of cutting-edge statistical solutions in
clinical trials. For this reason, the software is free for non-
commercial scientific research, including but not limited to academic
researchers and research/teaching institutions. Computing codes are available upon request.
For more details see P. Gao (2024) <doi:10.1080/10543406.2024.2341673>.
Gao, P., Zhang, W. (2024) <doi:10.1080/10543406.2024.2358796>.
P. Gao & Y. Li (2024) <doi:10.1080/10543406.2023.2233590>.
P. Gao, Y. Li (2024) <doi:10.1080/10543406.2024.2342518>.
Gao, P., L. Liu, and C. Mehta. (2013) <doi:10.1002/sim.5847>.

Depends clinfun, mvtnorm, doParallel

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Encoding UTF-8

Imports foreach, dplyr, jsonlite, MASS, survival

Config/roxygen2/version 8.0.0

URL https://github.com/innovatiostat/rcode

BugReports https://github.com/innovatiostat/rcode/issues

NeedsCompilation no

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Contents

`asd_ci_est_back` *Group sequential designs / Adaptive sequential designs: Final analysis, With one sample size change*

Description

Group sequential designs / Adaptive sequential designs: Final analysis, With one sample size change

Usage

```
asd_ci_est_back(
  s,
  c_bry,
  snew,
  c_bry_new,
  theta_hat_inter,
  theta_hat_inter_sd,
  inter_vt,
  theta_hat_last_ad,
  theta_hat_last_ad_sd,
  last_vt_ad,
  alpha_2
)
```

Arguments

s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
c_bry	Vector of critical boundaries for each analysis
snew	Vector of new information fractions after the sample size is changed
c_bry_new	Critical boundaries after the sample size is changed
theta_hat_inter	Treatment effect estimate observed at the interim analysis
theta_hat_inter_sd	Standard error of 'theta_hat_inter'
inter_vt	Index of the interim analysis at which the sample size is re-estimated (1-based)
theta_hat_last_ad	Treatment effect estimate observed at the last analysis after the sample size change
theta_hat_last_ad_sd	Standard error of 'theta_hat_last_ad'
last_vt_ad	Index of the last analysis after the sample size change
alpha_2	Type I error for the two-sided test

Value

A named list containing the following elements: 'p-value', 'confidence interval'.

References

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796.

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Gao, P., L. Liu, and C. Mehta. 2013 Oct 15. Exact inference for adaptive group sequential designs. Statistics in Medicine 32(23):3991–4005. doi:10.1002/sim.5847.

Examples

```
asd_ci_est_back(s = c(0.3,0.7,1), c_bry = c(4.347011, 2.845787, 2.380956), snew = c(0.5,1),
c_bry_new = c(3.310743, 2.781890), theta_hat_inter = 1.2, theta_hat_inter_sd = 1, inter_vt = 1,
theta_hat_last_ad = 2.2, theta_hat_last_ad_sd = 1, last_vt_ad = 2, alpha_2 = 0.05)
```

`asd_ci_est_one_arm_2_stage` *Final analysis: two stage design, with sample size change*

Description

Final analysis: two stage design, with sample size change

Usage

```
asd_ci_est_one_arm_2_stage(p_0, n_1, n_2, r_1_e, r_2, n_new, x_1, x_new, alpha)
```

Arguments

`p_0`	Response rate indicating low activity with insufficient clinical benefit.
`n_1`	Number of patients at first look.
`n_2`	Number of patients at second look.
`r_1_e`	The trial would be stopped for superiority if at least r_1_e responses are observed at the first look.
`r_2`	If no more than r_2 responses are observed at the second look, then the null hypothesis will not be rejected.
`n_new`	New sample size after the interim analysis.
`x_1`	Number of responses at the first look.
`x_new`	Number of responses at the final visit.
`alpha`	One-sided type I error.

Value

UL: upper limit of confidence interval.

LL: lower limit of confidence interval.

The results with continuity correction are not necessarily different from those with continuity correction.

The need for continuity correction can be determined through simulations on type I error (see Gao, Zhang, 2004).

References

P. Gao & W. Zhang (15 Apr 2024): Adaptive sequential design for phase II single-arm oncology trials: an expansion of Simon's design, Journal of Biopharmaceutical Statistics, DOI: 10.1080/10543406.2024.2341673. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2341673.

Gao, P., L. Liu, and C. Mehta. 2013 Oct 15. Exact inference for adaptive group sequential designs. Statistics in Medicine 32(23):3991–4005. doi:10.1002/sim.5847.

Examples

```
asd_ci_est_one_arm_2_stage( p_0=0.2,n_1=100,n_2=105,r_1_e=33,r_2=29,n_new=115,
x_1=28,x_new=34,alpha=0.025)
```

`asd_ci_est_one_arm_3_stage` *Final analysis: three stage design, with sample size change*

Description

Final analysis: three stage design, with sample size change

Usage

```
asd_ci_est_one_arm_3_stage(
  p_0,
  n_2,
  n_3,
  r_2_e,
  r_2,
  r_3,
  n_new,
  x_2,
  x_new,
  alpha
)
```

Arguments

`p_0`	Response rate indicating low activity with insufficient clinical benefit.
`n_2`	Number of patients at second look.
`n_3`	Number of patients at third look.
`r_2_e`	The trial would be stopped for superiority if at least r_2_e responses are observed at the second look. If r_2_e was not used in the design, enter NA.
`r_2`	If no more than r_2 responses are observed at the second look, then the trial would be stopped for futility.
`r_3`	If no more than r_3 responses are observed at the third look, then the null hypothesis will not be rejected.
`n_new`	New sample size after the interim analysis (at the second look).
`x_2`	Number of responses at the second look.
`x_new`	Number of responses at the final visit.
`alpha`	One-sided type I error.

Value

UL: upper limit of confidence interval.

LL: lower limit of confidence interval.

The results with continuity correction are not necessarily different from those with continuity correction.

The need for continuity correction can be determined through simulations on type I error (see Gao, Zhang, 2004).

References

P. Gao & W. Zhang (15 Apr 2024): Adaptive sequential design for phase II single-arm oncology trials: an expansion of Simon's design, Journal of Biopharmaceutical Statistics, DOI: 10.1080/10543406.2024.2341673. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2341673.

Gao, P., L. Liu, and C. Mehta. 2013 Oct 15. Exact inference for adaptive group sequential designs. Statistics in Medicine 32(23):3991–4005. doi:10.1002/sim.5847.

Examples

```
asd_ci_est_one_arm_3_stage( p_0=0.2,n_2=105,n_3=110,r_2_e=33,r_3=29,n_new=115,
x_2=28,x_new=34,alpha=0.025)
```

`asd_new_design` *Group sequential designs / Adaptive sequential designs: Interim analysis, Non-survival analysis, Use theta_interim*

Description

Group sequential designs / Adaptive sequential designs: Interim analysis, Non-survival analysis, Use theta_interim

Usage

```
asd_new_design(
  s,
  c_bry,
  inter_vt,
  snew,
  theta_hat_inter,
  theta_hat_inter_sd,
  n_control_inter,
  beta
)
```

Arguments

s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
c_bry	Vector of critical boundaries for each analysis
inter_vt	Index of the interim analysis at which the sample size is re-estimated (1-based)
snew	Vector of new information fractions after the sample size is changed
theta_hat_inter	Treatment effect estimate observed at the interim analysis
theta_hat_inter_sd	Standard error of 'theta_hat_inter'
n_control_inter	Sample size of the control arm at the interim analysis
beta	Type II error rate, i.e. 1 - power

Value

A named list containing the following elements: 'Interim analysis hypothesis test', 'Wald statistics', 'Critical boundary', 'Estimated effect size: theta', 'c_alpha', 'c_power_theta', 'N_control_new', 'new information fraction', 'New critical boundary'.

Examples

```
asd_new_design(s = c(1/3, 2/3, 1), c_bry = c(3.984298, 3.961146, 2.349682), inter_vt = 1,
snew = c(0.5, 1), theta_hat_inter = 0.3, theta_hat_inter_sd = 0.5,
n_control_inter = 100, beta = 0.1)
```

---

asd_new_design_survival

Group sequential designs / Adaptive sequential designs: Interim analysis, Survival analysis, Use theta_interim

---

Description

Group sequential designs / Adaptive sequential designs: Interim analysis, Survival analysis, Use theta_interim

Usage

```
asd_new_design_survival(
  s,
  c_bry,
  inter_vt,
  snew,
  theta_hat_inter,
```

```
  theta_hat_inter_sd,
  events_inter,
  beta
)
```

Arguments

s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
c_bry	Vector of critical boundaries for each analysis
inter_vt	Index of the interim analysis at which the sample size is re-estimated (1-based)
snew	Vector of new information fractions after the sample size is changed
theta_hat_inter	Treatment effect estimate observed at the interim analysis
theta_hat_inter_sd	Standard error of 'theta_hat_inter'
events_inter	Number of events observed at the interim analysis
beta	Type II error rate, i.e. 1 - power

Value

A named list containing the following elements: 'Interim analysis hypothesis test', 'Wald statistics', 'Critical boundary', 'Estimated effect size: theta', 'c_alpha', 'c_power_theta', ' events_new', 'New information fraction', 'New critical boundary'.

Examples

```
asd_new_design_survival(s = c(1/3, 2/3, 1), c_bry = c(3.984298, 3.961146, 2.349682),
inter_vt = 1, snew = c(0.5, 1), theta_hat_inter = 0.3, theta_hat_inter_sd = 0.5,
events_inter = 100, beta = 0.1)
```

---

asd_new_design_theta *Group sequential designs / Adaptive sequential designs: Interim analysis, Non-survival analysis, Input theta*

Description

Group sequential designs / Adaptive sequential designs: Interim analysis, Non-survival analysis, Input theta

Usage

```
asd_new_design_theta(
  theta,
  s,
  c_bry,
  inter_vt,
  snew,
  theta_hat_inter,
  theta_hat_inter_sd,
  n_control_inter,
  beta
)
```

Arguments

theta	Assumed effect size
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
c_bry	Vector of critical boundaries for each analysis
inter_vt	Index of the interim analysis at which the sample size is re-estimated (1-based)
snew	Vector of new information fractions after the sample size is changed
theta_hat_inter	Treatment effect estimate observed at the interim analysis
theta_hat_inter_sd	Standard error of 'theta_hat_inter'
n_control_inter	Sample size of the control arm at the interim analysis
beta	Type II error rate, i.e. 1 - power

Value

A named list containing the following elements: 'Interim analysis hypothesis test', 'Wald statistics', 'Critical boundary', 'Assumed effect size: theta', 'c_alpha', 'c_power_theta', 'N_control_new', 'new information fraction', 'New critical boundary'.

Examples

```
asd_new_design_theta(theta = 0.2, s = c(1/3, 2/3, 1), c_bry = c(3.984298, 3.961146, 2.349682),
inter_vt = 1, snew = c(0.5, 1), theta_hat_inter = 0.3, theta_hat_inter_sd = 0.5,
n_control_inter = 100, beta = 0.1)
```

asd_new_design_theta_survival

Group sequential designs / Adaptive sequential designs: Interim analysis, Survival analysis, Input theta

Description

Group sequential designs / Adaptive sequential designs: Interim analysis, Survival analysis, Input theta

Usage

```
asd_new_design_theta_survival(
  theta,
  s,
  c_bry,
  inter_vt,
  snew,
  theta_hat_inter,
  theta_hat_inter_sd,
  events_inter,
  beta
)
```

Arguments

theta	Assumed effect size
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
c_bry	Vector of critical boundaries for each analysis
inter_vt	Index of the interim analysis at which the sample size is re-estimated (1-based)
snew	Vector of new information fractions after the sample size is changed
theta_hat_inter	Treatment effect estimate observed at the interim analysis
theta_hat_inter_sd	Standard error of 'theta_hat_inter'
events_inter	Number of events observed at the interim analysis
beta	Type II error rate, i.e. 1 - power

Value

A named list containing the following elements: 'Interim analysis hypothesis test', 'Wald statistics', 'Critical boundary', 'Assumed effect size: theta', 'c_alpha', 'c_power_theta', ' events_new', 'New information fraction', 'New critical boundary'.

Examples

```
asd_new_design_theta_survival(theta = 0.2, s = c(1/3, 2/3, 1),
c_bry = c(3.984298, 3.961146, 2.349682), inter_vt = 1, snew = c(0.5, 1), theta_hat_inter = 0.3,
theta_hat_inter_sd = 0.5, events_inter = 100, beta = 0.1)
```

---

asd_power_simu_binary *Group sequential designs / Adaptive sequential designs: Simulations, Binary distribution, Operating characteristics*

Description

Group sequential designs / Adaptive sequential designs: Simulations, Binary distribution, Operating characteristics

Usage

```
asd_power_simu_binary(
  p_t,
  p_c,
  direction,
  s,
  bry_type,
  alpha_2,
  samsz,
  N_max,
  theta_cut,
  beta,
  sim_num
)
```

Arguments

p_t	Event (response) proportion in the test arm
p_c	Event (response) proportion in the control arm
direction	Test direction: 1 = larger p is better, 0 = smaller p is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
bry_type	Critical boundary type: 1 = O'Brien-Fleming, 2 = Pocock, 3 = alpha-spending
alpha_2	Type I error for the two-sided test
samsz	Planned sample size of the control arm used in the simulation
N_max	Maximum allowed sample size (control arm)
theta_cut	Efficacy cut-off on the effect-size scale applied at the interim analysis
beta	Type II error rate, i.e. 1 - power
sim_num	Number of simulation replicates

Value

A matrix in which each row corresponds to one simulation replicate and the columns hold the simulated operating characteristics (e.g. rejection indicators, sample sizes and stopping stages).

References

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796.

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Gao, P., L. Liu, and C. Mehta. 2013 Oct 15. Exact inference for adaptive group sequential designs. Statistics in Medicine 32(23):3991–4005. doi:10.1002/sim.5847.

Examples

```
asd_power_simu_binary(p_t = 0.4, p_c = 0.2, direction = 1, s = c(1/3,2/3,1), bry_type = 1,
alpha_2 = 0.05, samsz = 107, N_max = 500, theta_cut = 0.05, beta = 0.1, sim_num = 20)
```

---

asd_power_simu_neg_binomial

Group sequential designs / Adaptive sequential designs: Simulations, Negative binomial distribution, Operating characteristics

---

Description

Group sequential designs / Adaptive sequential designs: Simulations, Negative binomial distribution, Operating characteristics

Usage

```
asd_power_simu_neg_binomial(
  r_t,
  r_c,
  kappa,
  direction,
  s,
  bry_type,
  alpha_2,
```

```
  samsz,
  N_max,
  theta_cut,
  beta,
  sim_num
)
```

Arguments

r_t	Rate parameter of the test arm (negative binomial endpoint)
r_c	Rate parameter of the control arm (negative binomial endpoint)
kappa	Dispersion (size) parameter of the negative binomial distribution
direction	Test direction: 1 = larger r is better, 0 = smaller r is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
bry_type	Critical boundary type: 1 = O'Brien-Fleming, 2 = Pocock, 3 = alpha-spending
alpha_2	Type I error for the two-sided test
samsz	Planned sample size of the control arm used in the simulation
N_max	Maximum allowed sample size (control arm)
theta_cut	Efficacy cut-off on the effect-size scale applied at the interim analysis
beta	Type II error rate, i.e. 1 - power
sim_num	Number of simulation replicates

Value

A matrix in which each row corresponds to one simulation replicate and the columns hold the simulated operating characteristics (e.g. rejection indicators, sample sizes and stopping stages).

References

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796.

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Gao, P., L. Liu, and C. Mehta. 2013 Oct 15. Exact inference for adaptive group sequential designs. Statistics in Medicine 32(23):3991–4005. doi:10.1002/sim.5847.

Examples

```
asd_power_simu_neg_binomial(r_t = 1.1, r_c = 1.1, kappa = 1, direction = 1, s = c(1/3,2/3,1),
bry_type = 1, alpha_2 = 0.05, samsz = 100, N_max = 200, theta_cut = 0.01,
beta = 0.1, sim_num = 20)
```

`asd_power_simu_normal` *Group sequential designs / Adaptive sequential designs: Simulations, Normal distribution, Operating characteristics*

Description

Group sequential designs / Adaptive sequential designs: Simulations, Normal distribution, Operating characteristics

Usage

```
asd_power_simu_normal(
  mu_t,
  mu_c,
  sigma_t,
  sigma_c,
  direction,
  s,
  bry_type,
  alpha_2,
  samsz,
  N_max,
  theta_cut,
  beta,
  sim_num
)
```

Arguments

`mu_t`	Mean of the test arm
`mu_c`	Mean of the control arm
`sigma_t`	Standard deviation of the test arm
`sigma_c`	Standard deviation of the control arm
`direction`	Test direction: 1 = larger mu is better, 0 = smaller mu is better
`s`	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
`bry_type`	Critical boundary type: 1 = O'Brien-Fleming, 2 = Pocock, 3 = alpha-spending
`alpha_2`	Type I error for the two-sided test

samsz	Planned sample size of the control arm used in the simulation
N_max	Maximum allowed sample size (control arm)
theta_cut	Efficacy cut-off on the effect-size scale applied at the interim analysis
beta	Type II error rate, i.e. 1 - power
sim_num	Number of simulation replicates

Value

A named list containing the following elements: 'Power at planned sample size', 'names(unlist(simu_out[[2]]'.

References

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796.

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Gao, P., L. Liu, and C. Mehta. 2013 Oct 15. Exact inference for adaptive group sequential designs. Statistics in Medicine 32(23):3991–4005. doi:10.1002/sim.5847.

Examples

```
asd_power_simu_normal(mu_t = 0, mu_c = 0, sigma_t = 1, sigma_c = 1, direction = 1,
s = c(1/3,2/3,1), bry_type = 1, alpha_2 = 0.05, samsz = 100, N_max = 500, theta_cut = 0.05,
beta = 0.1, sim_num = 20)
```

---

asd_power_simu_poisson

Group sequential designs / Adaptive sequential designs: Simulations, Poisson distribution, Operating characteristics

---

Description

Group sequential designs / Adaptive sequential designs: Simulations, Poisson distribution, Operating characteristics

Usage

```
asd_power_simu_poisson(
  lambda_t,
  lambda_c,
  direction,
  s,
  bry_type,
  alpha_2,
  samsz,
  N_max,
  theta_cut,
  beta,
  sim_num
)
```

Arguments

lambda_t	Event rate in the test arm (Poisson / negative binomial endpoint)
lambda_c	Event rate in the control arm (Poisson / negative binomial endpoint)
direction	Test direction: 1 = larger lambda is better, 0 = smaller lambda is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
bry_type	Critical boundary type: 1 = O'Brien-Fleming, 2 = Pocock, 3 = alpha-spending
alpha_2	Type I error for the two-sided test
samsz	Planned sample size of the control arm used in the simulation
N_max	Maximum allowed sample size (control arm)
theta_cut	Efficacy cut-off on the effect-size scale applied at the interim analysis
beta	Type II error rate, i.e. 1 - power
sim_num	Number of simulation replicates

Value

A named list containing the following elements: 'Sequential design', 'Simulation results'.

References

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796.

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Gao, P., L. Liu, and C. Mehta. 2013 Oct 15. Exact inference for adaptive group sequential designs. Statistics in Medicine 32(23):3991–4005. doi:10.1002/sim.5847.

Examples

```
asd_power_simu_poisson(lambda_t = 1.1, lambda_c = 0.8, direction = 1, s = c(1/3,2/3,1),
bry_type = 1, alpha_2 = 0.05, samsz = 100, N_max = 200, theta_cut = 0.01,
beta = 0.1, sim_num = 20)
```

---

asd_power_simu_survival

Group sequential designs / Adaptive sequential designs: Simulations, Survival analysis, Operating characteristics

---

Description

Group sequential designs / Adaptive sequential designs: Simulations, Survival analysis, Operating characteristics

Usage

```
asd_power_simu_survival(
  HR,
  s,
  bry_type,
  alpha_2,
  evt_num,
  evt_max,
  HR_cut,
  surv_rate,
  beta,
  sim_num
)
```

Arguments

HR	Hazard ratio (test vs control)
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
bry_type	Critical boundary type: 1 = O'Brien-Fleming, 2 = Pocock, 3 = alpha-spending
alpha_2	Type I error for the two-sided test
evt_num	Total number of events at the final analysis

evt_max	Maximum number of events
HR_cut	Hazard-ratio cut-off for early stopping at the interim analysis
surv_rate	Survival rate used to translate the number of events into a sample size
beta	Type II error rate, i.e. 1 - power
sim_num	Number of simulation replicates

Value

A matrix in which each row corresponds to one simulation replicate and the columns hold the simulated operating characteristics (e.g. rejection indicators, sample sizes and stopping stages).

References

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796.

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Gao, P., L. Liu, and C. Mehta. 2013 Oct 15. Exact inference for adaptive group sequential designs. Statistics in Medicine 32(23):3991–4005. doi:10.1002/sim.5847.

Examples

```
asd_power_simu_survival(HR = 0.8, s = c(1/3,2/3,1), bry_type = 1, alpha_2 = 0.05, evt_num = 845,
evt_max = 1500, HR_cut = 0.95, surv_rate = 0.5, beta = 0.1, sim_num = 20)
```

---

asd_simu_OC_binary *Group sequential designs / Adaptive sequential designs: Simulations, Binary distribution, Optimizing adaptive sequential design*

Description

Group sequential designs / Adaptive sequential designs: Simulations, Binary distribution, Optimizing adaptive sequential design

Usage

```
asd_simu_OC_binary(
  p_t,
  p_c,
  direction,
  s1,
  s2,
  alpha_2,
  alpha_2_alps_s1,
  alpha_2_alps_s2,
  theta_cut,
  samsz_1,
  samsz_2,
  N_max_1,
  N_max_2,
  beta,
  sim_num
)
```

Arguments

p_t	Event (response) proportion in the test arm
p_c	Event (response) proportion in the control arm
direction	Test direction: 1 = larger p is better, 0 = smaller p is better
s1	Information fractions for the first stage / first group
s2	Information fractions for the second stage / second group
alpha_2	Type I error for the two-sided test
alpha_2_alps_s1	Type I error spent up to the interim analysis (stage 1 / group 1)
alpha_2_alps_s2	Cumulative type I error spent at the final analysis (stage 2 / group 2)
theta_cut	Efficacy cut-off on the effect-size scale applied at the interim analysis
samsz_1	Planned sample size (control arm) of the first stage / group
samsz_2	Planned sample size (control arm) of the second stage / group
N_max_1	Maximum allowed sample size (control arm) of the first stage / group
N_max_2	Maximum allowed sample size (control arm) of the second stage / group
beta	Type II error rate, i.e. 1 - power
sim_num	Number of simulation replicates

Value

A named list containing the following elements: 'Looks', 'Information fractions', 'O'Brien-Fleming boundaries'.

References

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796.

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Gao, P., L. Liu, and C. Mehta. 2013 Oct 15. Exact inference for adaptive group sequential designs. Statistics in Medicine 32(23):3991–4005. doi:10.1002/sim.5847.

Examples

```
asd_simu_OC_binary(p_t = c(0.3,0.4,0.5), p_c = 0.2, direction = 1, s1 = c(1/3,2/3,1),
s2 = c(0.5,1), alpha_2 = 0.05, alpha_2_alps_s1 = c(0.001,0.001,0.048),
alpha_2_alps_s2 = c(0.001,0.049), theta_cut = 0.01, samsz_1 = 100, samsz_2 = 150,
N_max_1 = 200, N_max_2 = 300, beta = 0.1, sim_num = 20)
```

---

asd_simu_OC_neg_binomial

Group sequential designs / Adaptive sequential designs: Simulations, Negative binomial distribution, Optimizing adaptive sequential design

---

Description

Group sequential designs / Adaptive sequential designs: Simulations, Negative binomial distribution, Optimizing adaptive sequential design

Usage

```
asd_simu_OC_neg_binomial(
  r_t,
  r_c,
  kappa,
  direction,
  s1,
  s2,
  alpha_2,
  alpha_2_alps_s1,
  alpha_2_alps_s2,
  theta_cut,
```

```
  samsz_1,
  samsz_2,
  N_max_1,
  N_max_2,
  beta,
  sim_num
)
```

Arguments

r_t	Rate parameter of the test arm (negative binomial endpoint)
r_c	Rate parameter of the control arm (negative binomial endpoint)
kappa	Dispersion (size) parameter of the negative binomial distribution
direction	Test direction: 1 = larger r is better, 0 = smaller r is better
s1	Information fractions for the first stage / first group
s2	Information fractions for the second stage / second group
alpha_2	Type I error for the two-sided test
alpha_2_alps_s1	Type I error spent up to the interim analysis (stage 1 / group 1)
alpha_2_alps_s2	Cumulative type I error spent at the final analysis (stage 2 / group 2)
theta_cut	Efficacy cut-off on the effect-size scale applied at the interim analysis
samsz_1	Planned sample size (control arm) of the first stage / group
samsz_2	Planned sample size (control arm) of the second stage / group
N_max_1	Maximum allowed sample size (control arm) of the first stage / group
N_max_2	Maximum allowed sample size (control arm) of the second stage / group
beta	Type II error rate, i.e. 1 - power
sim_num	Number of simulation replicates

Value

A named list containing the following elements: 'Looks', 'Information fractions', 'O'Brien-Fleming boundaries'.

References

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796.

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Gao, P., L. Liu, and C. Mehta. 2013 Oct 15. Exact inference for adaptive group sequential designs. Statistics in Medicine 32(23):3991–4005. doi:10.1002/sim.5847.

Examples

```
asd_simu_OC_neg_binomial(r_t = c(0.3,0.4,0.5), r_c = 0.2, kappa = 1, direction = 1,
s1 = c(1/3,2/3,1), s2 = c(0.5,1), alpha_2 = 0.05, alpha_2_alps_s1 = c(0.001,0.001,0.048),
alpha_2_alps_s2 = c(0.001,0.049), theta_cut = 0.01, samsz_1 = 100,
samsz_2 = 150, N_max_1 = 200, N_max_2 = 300, beta = 0.1, sim_num = 20)
```

---

asd_simu_OC_normal *Group sequential designs / Adaptive sequential designs: Simulations, Normal distribution, Optimizing adaptive sequential design*

Description

Group sequential designs / Adaptive sequential designs: Simulations, Normal distribution, Optimizing adaptive sequential design

Usage

```
asd_simu_OC_normal(
  mu_t,
  mu_c,
  sigma_t,
  sigma_c,
  direction,
  s1,
  s2,
  alpha_2,
  alpha_2_alps_s1,
  alpha_2_alps_s2,
  theta_cut,
  samsz_1,
  samsz_2,
  N_max_1,
  N_max_2,
  beta,
  sim_num
)
```

Arguments

mu_t	Mean of the test arm
mu_c	Mean of the control arm
sigma_t	Standard deviation of the test arm
sigma_c	Standard deviation of the control arm
direction	Test direction: 1 = larger mu is better, 0 = smaller mu is better
s1	Information fractions for the first stage / first group
s2	Information fractions for the second stage / second group
alpha_2	Type I error for the two-sided test
alpha_2_alps_s1	Type I error spent up to the interim analysis (stage 1 / group 1)
alpha_2_alps_s2	Cumulative type I error spent at the final analysis (stage 2 / group 2)
theta_cut	Efficacy cut-off on the effect-size scale applied at the interim analysis
samsz_1	Planned sample size (control arm) of the first stage / group
samsz_2	Planned sample size (control arm) of the second stage / group
N_max_1	Maximum allowed sample size (control arm) of the first stage / group
N_max_2	Maximum allowed sample size (control arm) of the second stage / group
beta	Type II error rate, i.e. 1 - power
sim_num	Number of simulation replicates

Value

A named list containing the following elements: 'Looks', 'Information fractions', 'O'Brien-Fleming boundaries'.

References

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796.

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Gao, P., L. Liu, and C. Mehta. 2013 Oct 15. Exact inference for adaptive group sequential designs. Statistics in Medicine 32(23):3991–4005. doi:10.1002/sim.5847.

Examples

```
asd_simu_OC_normal(mu_t = c(0.3,0.4,0.5), mu_c = 0, sigma_t = 1, sigma_c = 1, direction = 1,
s1 = c(1/3,2/3,1), s2 = c(0.5,1), alpha_2 = 0.05, alpha_2_alps_s1 = c(0.001,0.001,0.048),
alpha_2_alps_s2 = c(0.001,0.049), theta_cut = 0.01, samsz_1 = 100,
samsz_2 = 150, N_max_1 = 200, N_max_2 = 300, beta = 0.1, sim_num = 20)
```

---

asd_simu_OC_poisson *Group sequential designs / Adaptive sequential designs: Simulations, Poisson distribution, Optimizing adaptive sequential design*

Description

Group sequential designs / Adaptive sequential designs: Simulations, Poisson distribution, Optimizing adaptive sequential design

Usage

```
asd_simu_OC_poisson(
  lambda_t,
  lambda_c,
  direction,
  s1,
  s2,
  alpha_2,
  alpha_2_alps_s1,
  alpha_2_alps_s2,
  theta_cut,
  samsz_1,
  samsz_2,
  N_max_1,
  N_max_2,
  beta,
  sim_num
)
```

Arguments

lambda_t	Event rate in the test arm (Poisson / negative binomial endpoint)
lambda_c	Event rate in the control arm (Poisson / negative binomial endpoint)
direction	Test direction: 1 = larger lambda is better, 0 = smaller lambda is better
s1	Information fractions for the first stage / first group
s2	Information fractions for the second stage / second group
alpha_2	Type I error for the two-sided test

`alpha_2_alps_s1`
: Type I error spent up to the interim analysis (stage 1 / group 1)

`alpha_2_alps_s2`
: Cumulative type I error spent at the final analysis (stage 2 / group 2)

`theta_cut`
: Efficacy cut-off on the effect-size scale applied at the interim analysis

`samsz_1`
: Planned sample size (control arm) of the first stage / group

`samsz_2`
: Planned sample size (control arm) of the second stage / group

`N_max_1`
: Maximum allowed sample size (control arm) of the first stage / group

`N_max_2`
: Maximum allowed sample size (control arm) of the second stage / group

`beta`
: Type II error rate, i.e. 1 - power

`sim_num`
: Number of simulation replicates

Value

A named list containing the following elements: 'Looks', 'Information fractions', 'O'Brien-Fleming boundaries'.

References

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796.

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Gao, P., L. Liu, and C. Mehta. 2013 Oct 15. Exact inference for adaptive group sequential designs. Statistics in Medicine 32(23):3991–4005. doi:10.1002/sim.5847.

Examples

```
asd_simu_OC_poisson(lambda_t = c(0.3,0.4,0.5), lambda_c = 0.2, direction = 1, s1 = c(1/3,2/3,1),
s2 = c(0.5,1), alpha_2 = 0.05, alpha_2_alps_s1 = c(0.001,0.001,0.048),
alpha_2_alps_s2 = c(0.001,0.049), theta_cut = 0.01, samsz_1 = 50, samsz_2 = 80,
N_max_1 = 120, N_max_2 = 150, beta = 0.1, sim_num = 20)
```

asd_simu_OC_survival *Group sequential designs / Adaptive sequential designs: Simulations, Survival analysis, Optimizing adaptive sequential design*

Description

Group sequential designs / Adaptive sequential designs: Simulations, Survival analysis, Optimizing adaptive sequential design

Usage

```
asd_simu_OC_survival(
  HR,
  s1,
  s2,
  alpha_2,
  alpha_2_alps_s1,
  alpha_2_alps_s2,
  surv_rate,
  evt_num_1,
  evt_num_2,
  evt_max_1,
  evt_max_2,
  HR_cut,
  beta,
  sim_num
)
```

Arguments

HR	Hazard ratio (test vs control)
s1	Information fractions for the first stage / first group
s2	Information fractions for the second stage / second group
alpha_2	Type I error for the two-sided test
alpha_2_alps_s1	Type I error spent up to the interim analysis (stage 1 / group 1)
alpha_2_alps_s2	Cumulative type I error spent at the final analysis (stage 2 / group 2)
surv_rate	Survival rate used to translate the number of events into a sample size
evt_num_1	Number of events for the first stage / group
evt_num_2	Number of events for the second stage / group
evt_max_1	Maximum number of events for the first stage / group
evt_max_2	Maximum number of events for the second stage / group
HR_cut	Hazard-ratio cut-off for early stopping at the interim analysis
beta	Type II error rate, i.e. 1 - power
sim_num	Number of simulation replicates

Value

A named list containing the following elements: 'Looks', 'Information fractions', 'O'Brien-Fleming boundaries'.

References

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796.

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Gao, P., L. Liu, and C. Mehta. 2013 Oct 15. Exact inference for adaptive group sequential designs. Statistics in Medicine 32(23):3991–4005. doi:10.1002/sim.5847.

Examples

```
asd_simu_OC_survival(HR = c(0.7,0.78,0.8), s1 = c(1/3,2/3,1), s2 = c(0.5,1), alpha_2 = 0.05,
alpha_2_alps_s1 = c(0.001,0.001,0.048), alpha_2_alps_s2 = c(0.001,0.049), surv_rate = 0.5,
evt_num_1 = 600, evt_num_2 = 800, evt_max_1 = 1000, evt_max_2 = 1500,
HR_cut = 0.95, beta = 0.1, sim_num = 20)
```

EXP_3_stg_sz *Three-stage design*

Description

Three-stage design

Usage

```
EXP_3_stg_sz(alpha, beta, p_0, p_low, p_1, d_23_cut)
```

Arguments

alpha	One-sided type I error.
beta	Type II error.
p_0	Response rate indicating low activity with insufficient clinical benefit.
p_low	Minimally clinically beneficial response rate.
p_1	Assumed response rate.
d_23_cut	Min(n3-n2) sets the minimal difference between n3 and n2 for the design.

Value

n1: Number of patients at first look. n1 for the three-stage design is the from Simon's design with p=p_1.

n_2: Number of patients at second look. n_2 for the three-stage design is the n1 from Simon's design with p=p_low.

r1: If no more than r1 responses are observed at the first look, then the trial would be stopped for futility.

r_2: The null hypothesis will be rejected if at least r_2 responses are observed at the end of the trial.

EN(p0) is the expected sample size under the null hypothesis.

PET(p0) is the probability of early termination under the null hypothesis.

PET_p is the probability of early termination under p=p_1.

PET_p_low is the probability of early termination under p=p_low.

power_p_1 is the power under p=p_1.

power_p_low is the power under p=p_low.

Type I error is the probability of rejecting the null hypothesis under p<=p_0.

The minimax design has the smallest n_2 among all possible choices of (n1,r1,n_2,r_2).

The optimal design has the smallest EN(p0) among all possible choices of (n1,r1,n_2,r_2).

The n1 and n_2 for the average design is the average of n1's and n_2's from the minimax and the optimal designs.

References

R. Simon. Optimal Two-Stage Designs for Phase II Clinical Trials. Controlled Clinical Trials 10:1-10 (1989).

P. Gao & W. Zhang (15 Apr 2024): Adaptive sequential design for phase II single-arm oncology trials: an expansion of Simon's design, Journal of Biopharmaceutical Statistics, DOI: 10.1080/10543406.2024.2341673. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2341673.

Examples

```
EXP_3_stg_sz(alpha=c(0.001,0.024),beta=0.1,p_0=0.2,p_low=0.33,p_1=0.4,d_23_cut=5)
```

fixed_rej_nbglm_simu *Fixed sample designs: Negative binomial distribution, Simulations*

Description

Fixed sample designs: Negative binomial distribution, Simulations

Usage

```
fixed_rej_nbglm_simu(alpha_2, r_c, r_t, rand_ratio, kappa, samsz, sim_num)
```

Arguments

alpha_2	The type I error for the two-sided test
r_c	The event rate of the test arm
r_t	The event rate of the control arm
rand_ratio	The ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
kappa	Dispersion (size) parameter of the negative binomial distribution
samsz	Planned sample size of the control arm used in the simulation
sim_num	Number of simulation replicates

Value

The output is the simulated power, which can be used to verify if the calculated sample size provided intended power

Examples

```
fixed_rej_nbglm_simu(alpha_2 = 0.05, r_c = 1, r_t = 1*0.6, rand_ratio = 1, kappa = 1,
samsz = 188, sim_num = 20)
```

fixed_rej_rate_binary *Fixed sample designs: Binary distribution, Simulations*

Description

Fixed sample designs: Binary distribution, Simulations

Usage

```
fixed_rej_rate_binary(p_t, p_c, rand_ratio, alpha_2, samsz, sim_num)
```

Arguments

p_t	The event rate of the test arm
p_c	The event rate of the control arm
rand_ratio	The ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
alpha_2	The type I error for the two-sided test
samsz	Planned sample size of the control arm used in the simulation
sim_num	Number of simulation replicates

Value

The output is the simulated power, which can be used to verify if the calculated sample size provided intended power

Examples

```
fixed_rej_rate_binary(p_t = 0.4, p_c = 0.2, rand_ratio = 1, alpha_2 = 0.05,
samsz = 106, sim_num = 20)
```

---

fixed_rej_rate_normal *Fixed sample designs: Normal distribution, Simulations*

Description

Fixed sample designs: Normal distribution, Simulations

Usage

```
fixed_rej_rate_normal(
  mu_t,
  mu_c,
  sigma_t,
  sigma_c,
  alpha_2,
  rand_ratio,
  samsz,
  sim_num
)
```

Arguments

mu_t	Mean of the test arm
mu_c	Mean of the control arm
sigma_t	Standard deviation of the test arm
sigma_c	Standard deviation of the control arm
alpha_2	The type I error for the two-sided test
rand_ratio	The ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
samsz	Planned sample size of the control arm used in the simulation
sim_num	Number of simulation replicates

Value

The output is the simulated power, which can be used to verify if the calculated sample size provided intended power

Examples

```
fixed_rej_rate_normal(mu_t = 0, mu_c = 0, sigma_t = 1, sigma_c = 1, alpha_2 = 0.05,
rand_ratio = 1, samsz = 82, sim_num = 20)
```

---

fixed_rej_rate_poisson

Fixed sample designs: Poisson distribution, Simulations

Description

Fixed sample designs: Poisson distribution, Simulations

Usage

```
fixed_rej_rate_poisson(lambda_t, lambda_c, rand_ratio, alpha_2, samsz, sim_num)
```

Arguments

lambda_t	The event rate of the test arm
lambda_c	The event rate of the control arm
rand_ratio	The ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
alpha_2	The type I error for the two-sided test
samsz	Planned sample size of the control arm used in the simulation
sim_num	Number of simulation replicates

Value

The output is the simulated power, which can be used to verify if the calculated sample size provided intended power

Examples

```
fixed_rej_rate_poisson(lambda_t = 11, lambda_c = 10, rand_ratio = 2, alpha_2 = 0.05,
samsz = 163, sim_num = 20)
```

---

fixed_rej_rate_surv_cox

Fixed sample designs: Survival analysis, Simulations

Description

Fixed sample designs: Survival analysis, Simulations

Usage

```
fixed_rej_rate_surv_cox(HR, evt_num, alpha_2, sim_num)
```

Arguments

HR	The hazards ratio of test arm vs. the control arm
evt_num	Total number of events at the final analysis
alpha_2	The type I error for the two-sided test
sim_num	Number of simulation replicates

Value

The output is the simulated power, which can be used to verify if the calculated sample size provided intended power

Examples

```
fixed_rej_rate_surv_cox(HR = 0.8, evt_num = 845, alpha_2 = 0.05, sim_num = 20)
```

gsd_ci_est — *Group sequential designs / Adaptive sequential designs: Final analysis, Without sample size change*

Description

Group sequential designs / Adaptive sequential designs: Final analysis, Without sample size change

Usage

```
gsd_ci_est(s, c_bry, theta_hat_last, theta_hat_last_sd, last_vt, alpha_2)
```

Arguments

s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
c_bry	Vector of critical boundaries for each analysis
theta_hat_last	Treatment effect estimate observed at the final analysis
theta_hat_last_sd	Standard error of 'theta_hat_last'
last_vt	Index of the analysis at which the trial stopped
alpha_2	Type I error for the two-sided test

Value

A named list containing the following elements: 'p-value', 'confidence interval'.

Examples

```
gsd_ci_est(s = c(1/3,2/3,1), c_bry = c(3.471095, 2.454434,2.004037), theta_hat_last = 2.004,
theta_hat_last_sd = 1, last_vt = 3, alpha_2 = 0.05)
```

gsd_ci_est_2_stage — *Final analysis: two stage design, no sample size change*

Description

Final analysis: two stage design, no sample size change

Usage

```
gsd_ci_est_2_stage(p_0, n_1, n_2, r_1_e, r_2, x_last, last_vt, alpha)
```

Arguments

p_0	Response rate indicating low activity with insufficient clinical benefit.
n_1	Number of patients at first look.
n_2	Number of patients at second look.
r_1_e	The trial would be stopped for superiority if at least r2e responses are observed at the second look.
r_2	If no more than r_2 responses are observed at the second look, then the null hypothesis will not be rejected.
x_last	Number of responses at the final visit.
last_vt	1.
alpha	One-sided type I error.

Value

UL: upper limit of confidence interval.

LL: lower limit of confidence interval.

The results with continuity correction are not necessarily different from those with continuity correction.

The need for continuity correction can be determined through simulations on type I error (see Gao, Zhang, 2004).

References

P. Gao & W. Zhang (15 Apr 2024): Adaptive sequential design for phase II single-arm oncology trials: an expansion of Simon's design, Journal of Biopharmaceutical Statistics, DOI: 10.1080/10543406.2024.2341673. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2341673.

Gao, P., L. Liu, and C. Mehta. 2013 Oct 15. Exact inference for adaptive group sequential designs. Statistics in Medicine 32(23):3991–4005. doi:10.1002/sim.5847.

Examples

```
gsd_ci_est_2_stage(p_0=0.2,n_1=100,n_2=105,r_1_e=NA,r_2=29,x_last=31,last_vt=1,alpha=0.025)
```

---

gsd_ci_est_3_stage *Final analysis: three stage design, no sample size change*

Description

Final analysis: three stage design, no sample size change

Usage

```
gsd_ci_est_3_stage(p_0, n_2, n_3, r_2_e, r_3, x_last, last_vt, alpha)
```

Arguments

p_0	Response rate indicating low activity with insufficient clinical benefit.
n_2	Number of patients at second look.
n_3	Number of patients at third look.
r_2_e	The trial would be stopped for superiority if at least r_2_e responses are observed at the second look. If r_2_e was not used in the design, enter NA.
r_3	If no more than r_3 responses are observed at the third look, then the null hypothesis will not be rejected.
x_last	Number of responses at the final visit.
last_vt	1.
alpha	One-sided type I error.

Value

UL: upper limit of confidence interval.

LL: lower limit of confidence interval.

The results with continuity correction are not necessarily different from those with continuity correction.

The need for continuity correction can be determined through simulations on type I error (see Gao, Zhang, 2004).

References

P. Gao & W. Zhang (15 Apr 2024): Adaptive sequential design for phase II single-arm oncology trials: an expansion of Simon's design, Journal of Biopharmaceutical Statistics, DOI: 10.1080/10543406.2024.2341673. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2341673.

Gao, P., L. Liu, and C. Mehta. 2013 Oct 15. Exact inference for adaptive group sequential designs. Statistics in Medicine 32(23):3991–4005. doi:10.1002/sim.5847.

Examples

```
gsd_ci_est_3_stage(p_0=0.2,n_2=100,n_3=105,r_2_e=31,r_3=29,x_last=31,last_vt=3,alpha=0.025)
```

---

gsd_power_simu_binary *Group sequential designs / Adaptive sequential designs: Simulations, Binary distribution, Type I error and power*

Description

Group sequential designs / Adaptive sequential designs: Simulations, Binary distribution, Type I error and power

Usage

```
gsd_power_simu_binary(
  p_t,
  p_c,
  direction,
  s,
  bry_type,
  alpha_2,
  samsz,
  sim_num
)
```

Arguments

p_t	Event (response) proportion in the test arm
p_c	Event (response) proportion in the control arm
direction	Test direction: 1 = larger p is better, 0 = smaller p is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
bry_type	Critical boundary type: 1 = O'Brien-Fleming, 2 = Pocock, 3 = alpha-spending
alpha_2	Type I error for the two-sided test
samsz	Planned sample size of the control arm used in the simulation
sim_num	Number of simulation replicates

Value

A named list containing the following elements: 'Planned sample size', 'rejection rate', 'Mean sample size'.

References

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796.

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Gao, P., L. Liu, and C. Mehta. 2013 Oct 15. Exact inference for adaptive group sequential designs. Statistics in Medicine 32(23):3991–4005. doi:10.1002/sim.5847.

Examples

```
gsd_power_simu_binary(p_t = 0.4, p_c = 0.4, direction = 1, s = c(1/3,2/3,1), bry_type = 1,
alpha_2 = 0.05, samsz = 100, sim_num = 20)
```

`gsd_power_simu_negbinom` *Group sequential designs / Adaptive sequential designs: Simulations, Negative binomial distribution, Type I error and power*

Description

Group sequential designs / Adaptive sequential designs: Simulations, Negative binomial distribution, Type I error and power

Usage

```
gsd_power_simu_negbinom(
  r_t,
  r_c,
  kappa,
  direction,
  s,
  bry_type,
  alpha_2,
  samsz,
  sim_num
)
```

Arguments

`r_t`	Rate parameter of the test arm (negative binomial endpoint)
`r_c`	Rate parameter of the control arm (negative binomial endpoint)
`kappa`	Dispersion (size) parameter of the negative binomial distribution
`direction`	Test direction: 1 = larger r is better, 0 = smaller r is better
`s`	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
`bry_type`	Critical boundary type: 1 = O'Brien-Fleming, 2 = Pocock, 3 = alpha-spending
`alpha_2`	Type I error for the two-sided test
`samsz`	Planned sample size of the control arm used in the simulation
`sim_num`	Number of simulation replicates

Value

A named list containing the following elements: 'Planned sample size', 'rejection rate', 'Mean sample size'.

References

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796.

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Gao, P., L. Liu, and C. Mehta. 2013 Oct 15. Exact inference for adaptive group sequential designs. Statistics in Medicine 32(23):3991–4005. doi:10.1002/sim.5847.

Examples

```
gsd_power_simu_negbinom(r_t = 1.1, r_c = 1.1, kappa = 1, direction = 1, s = c(1/3,2/3,1),
bry_type = 1, alpha_2 = 0.05, samsz = 100, sim_num = 20)
```

---

gsd_power_simu_normal *Group sequential designs / Adaptive sequential designs: Simulations, Normal distribution, Type I error and power*

Description

Group sequential designs / Adaptive sequential designs: Simulations, Normal distribution, Type I error and power

Usage

```
gsd_power_simu_normal(
  mu_t,
  mu_c,
  sigma_t,
  sigma_c,
  direction,
  s,
  bry_type,
  alpha_2,
```

```
  samsz,
  sim_num
)
```

Arguments

mu_t	Mean of the test arm
mu_c	Mean of the control arm
sigma_t	Standard deviation of the test arm
sigma_c	Standard deviation of the control arm
direction	Test direction: 1 = larger mu is better, 0 = smaller mu is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
bry_type	Critical boundary type: 1 = O'Brien-Fleming, 2 = Pocock, 3 = alpha-spending
alpha_2	Type I error for the two-sided test
samsz	Planned sample size of the control arm used in the simulation
sim_num	Number of simulation replicates

Value

A named list containing the following elements: 'Planned control sample size', 'rejection rate', 'Mean control sample size'.

References

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796.

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Gao, P., L. Liu, and C. Mehta. 2013 Oct 15. Exact inference for adaptive group sequential designs. Statistics in Medicine 32(23):3991–4005. doi:10.1002/sim.5847.

Examples

```
gsd_power_simu_normal(mu_t = 0.4, mu_c = 0, sigma_t = 1, sigma_c = 1, direction = 1,
s = c(1/4,1/3,2/3,1), bry_type = 1, alpha_2 = 0.05, samsz = 100, sim_num = 20)
```

gsd_power_simu_poisson *Group sequential designs / Adaptive sequential designs: Simulations, Poisson distribution, Type I error and power*

Description

Group sequential designs / Adaptive sequential designs: Simulations, Poisson distribution, Type I error and power

Usage

```
gsd_power_simu_poisson(
  lambda_c,
  lambda_t,
  direction,
  s,
  bry_type,
  alpha_2,
  samsz,
  sim_num
)
```

Arguments

lambda_c	Event rate in the control arm (Poisson / negative binomial endpoint)
lambda_t	Event rate in the test arm (Poisson / negative binomial endpoint)
direction	Test direction: 1 = larger lambda is better, 0 = smaller lambda is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
bry_type	Critical boundary type: 1 = O'Brien-Fleming, 2 = Pocock, 3 = alpha-spending
alpha_2	Type I error for the two-sided test
samsz	Planned sample size of the control arm used in the simulation
sim_num	Number of simulation replicates

Value

A named list containing the following elements: 'Planned sample size', 'rejection rate', 'Mean sample size'.

References

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796.

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Gao, P., L. Liu, and C. Mehta. 2013 Oct 15. Exact inference for adaptive group sequential designs. Statistics in Medicine 32(23):3991–4005. doi:10.1002/sim.5847.

Examples

```
gsd_power_simu_poisson(lambda_c = 0.5, lambda_t = 0.8, direction = 1, s = c(1/3,2/3,1),
bry_type = 1, alpha_2 = 0.05, samsz = 100, sim_num = 20)
```

`gsd_power_simu_survival`

Group sequential designs / Adaptive sequential designs: Simulations, Survival analysis, Type I error and power

---

Description

Group sequential designs / Adaptive sequential designs: Simulations, Survival analysis, Type I error and power

Usage

```
gsd_power_simu_survival(HR, s, bry_type, alpha_2, surv_rate, evt_num, sim_num)
```

Arguments

`HR`	Hazard ratio (test vs control)
`s`	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
`bry_type`	Critical boundary type: 1 = O'Brien-Fleming, 2 = Pocock, 3 = alpha-spending
`alpha_2`	Type I error for the two-sided test
`surv_rate`	Survival rate used to translate the number of events into a sample size
`evt_num`	Total number of events at the final analysis
`sim_num`	Number of simulation replicates

Value

A named list containing the following elements: 'Planned sample size', 'Rejection rate', 'Mean sample size'.

References

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796.

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Gao, P., L. Liu, and C. Mehta. 2013 Oct 15. Exact inference for adaptive group sequential designs. Statistics in Medicine 32(23):3991–4005. doi:10.1002/sim.5847.

Examples

```
gsd_power_simu_survival(HR = 0.8, s = c(1/3,2/3,1), bry_type = 1, alpha_2 = 0.05,
surv_rate = 0.5, evt_num = 845, sim_num = 20)
```

---

hybrid_fixed_prior_rej_binary_simu

Hybrid: Simulations, Binary distribution, Using given estimates of informative prior

---

Description

Hybrid: Simulations, Binary distribution, Using given estimates of informative prior

Usage

```
hybrid_fixed_prior_rej_binary_simu(
  t_prior,
  theta_prior,
  p_t,
  p_c,
  s,
  sampsz,
  N_max,
  theta_cut,
```

```
  cp_min,
  gamma,
  alpha_2,
  beta,
  sim_num
)
```

Arguments

t_prior	The prior is assumed to have a normal distribution. This is the mean of the prior distribution
theta_prior	The prior distribution of theta is assumed to have a normal distribution. The Fisher's information time is the reciprocal of the variance from the prior distribution
p_t	Event (response) proportion in the test arm
p_c	Event (response) proportion in the control arm
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
sampsz	Planned sample size: the planned sample size at the final analysis
N_max	Maximum sample size: a user chosen , maximum allowable sample size for sample size modification
theta_cut	Efficacy cut-off on the effect-size scale applied at the interim analysis
cp_min	Promising zone cp_min
gamma	Parameter chosen for the credible interval modified predictive power (CI_MPP)
alpha_2	Type I error for the two-sided test
beta	Type II error rate, i.e. 1 - power
sim_num	Number of simulation replicates

Value

The simulations are conducted with both non-informative prior and informative prior

References

Gao, P. Improving the effectiveness of sample size re-estimation: an operating characteristic focused, hybrid frequentist-Bayesian approach, Statistics in Medicine, 2025; 44:e10310. To link to this article: https://onlinelibrary.wiley.com/doi/10.1002/sim.10310.

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796.

C. R. Mehta, S. J. Pocock. Adaptive increase in sample size when interim results are promising: A practical guide with examples. Statistics in Medicine. Volume30, Issue28, 10 December 2011, Pages 3267-3284

Examples

```
hybrid_fixed_prior_rej_binary_simu(t_prior = 5, theta_prior = 0.2, p_t = 0.3, p_c = 0.3,
s = c(0.5,1), sampsz = 100, N_max = 150, theta_cut = 0.001, cp_min = 0.27, gamma = 0.5,
alpha_2 = 0.05, beta = 0.1, sim_num = 20)
```

`hybrid_fixed_prior_rej_negbinom_simu`

Hybrid: Simulations, Negative binomial distribution, Using given estimates of informative prior

---

Description

Hybrid: Simulations, Negative binomial distribution, Using given estimates of informative prior

Usage

```
hybrid_fixed_prior_rej_negbinom_simu(
  t_prior,
  theta_prior,
  r_t,
  r_c,
  kappa,
  nu_t,
  rand_ratio,
  s,
  sampsz,
  N_max,
  theta_cut,
  cp_min,
  gamma,
  alpha_2,
  beta,
  sim_num
)
```

Arguments

`t_prior`	The prior is assumed to have a normal distribution. This is the mean of the prior distribution
`theta_prior`	The prior distribution of theta is assumed to have a normal distribution. The Fisher's information time is the reciprocal of the variance from the prior distribution
`r_t`	Event rate for test arm
`r_c`	Event rate for control arm

kappa	dispersion parameter
nu_t	exposure time
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
sampsz	Planned sample size: the planned sample size at the final analysis
N_max	Maximum sample size: a user chosen , maximum allowable sample size for sample size modification
theta_cut	Efficacy cut-off on the effect-size scale applied at the interim analysis
cp_min	Promising zone cp_min
gamma	Parameter chosen for the credible interval modified predictive power (CI_MPP)
alpha_2	Type I error for the two-sided test
beta	Type II error rate, i.e. 1 - power
sim_num	Number of simulation replicates

Value

The simulations are conducted with both non-informative prior and informative prior.

References

Gao, P. Improving the effectiveness of sample size re-estimation: an operating characteristic focused, hybrid frequentist-Bayesian approach, Statistics in Medicine, 2025; 44:e10310. To link to this article: https://onlinelibrary.wiley.com/doi/10.1002/sim.10310.

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796.

C. R. Mehta, S. J. Pocock. Adaptive increase in sample size when interim results are promising: A practical guide with examples. Statistics in Medicine. Volume30, Issue28, 10 December 2011, Pages 3267-3284

Examples

```
hybrid_fixed_prior_rej_negbinom_simu(t_prior = 5, theta_prior = 0.2, r_t = 1, r_c = 1,
kappa = 1, nu_t = 1, rand_ratio = 1, s = c(0.5,1), sampsz = 100, N_max = 150,
theta_cut = 0.001, cp_min = 0.27, gamma = 0.5, alpha_2 = 0.05, beta = 0.1, sim_num = 20)
```

`hybrid_fixed_prior_rej_normal_simu` *Hybrid: Simulations, Normal distribution, Using given estimates of informative prior*

Description

Hybrid: Simulations, Normal distribution, Using given estimates of informative prior

Usage

```
hybrid_fixed_prior_rej_normal_simu(
  t_prior,
  theta_prior,
  mu,
  sigma,
  s,
  sampsz,
  N_max,
  theta_cut,
  cp_min,
  gamma,
  alpha_2,
  beta,
  sim_num
)
```

Arguments

`t_prior`	The prior is assumed to have a normal distribution. This is the mean of the prior distribution
`theta_prior`	The prior distribution of theta is assumed to have a normal distribution. The Fisher's information time is the reciprocal of the variance from the prior distribution
`mu`	Effect size used when calibrating the boundaries
`sigma`	Futility threshold
`s`	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
`sampsz`	Planned sample size: the planned sample size at the final analysis
`N_max`	Maximum sample size: a user chosen , maximum allowable sample size for sample size modification
`theta_cut`	Efficacy cut-off on the effect-size scale applied at the interim analysis
`cp_min`	Promising zone cp_min
`gamma`	Parameter chosen for the credible interval modified predictive power (CI_MPP)

alpha_2	Type I error for the two-sided test
beta	Type II error rate, i.e. 1 - power
sim_num	Number of simulation replicates

Value

The simulations are conducted with both non-informative prior and informative prior

References

Gao, P. Improving the effectiveness of sample size re-estimation: an operating characteristic focused, hybrid frequentist-Bayesian approach, Statistics in Medicine, 2025; 44:e10310. To link to this article: https://onlinelibrary.wiley.com/doi/10.1002/sim.10310.

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796.

C. R. Mehta, S. J. Pocock. Adaptive increase in sample size when interim results are promising: A practical guide with examples. Statistics in Medicine. Volume30, Issue28, 10 December 2011, Pages 3267-3284

Examples

```
hybrid_fixed_prior_rej_normal_simu(t_prior = 5, theta_prior = 0.2, mu = 0, sigma = 1,
s = c(0.5,1), sampsz = 100, N_max = 150, theta_cut = 0.001, cp_min = 0.27, gamma = 0.5,
alpha_2 = 0.05, beta = 0.1, sim_num = 20)
```

---

hybrid_fixed_prior_rej_poisson_simu

Hybrid: Simulations, Poisson distribution, Using given estimates of informative prior

---

Description

Hybrid: Simulations, Poisson distribution, Using given estimates of informative prior

Usage

```
hybrid_fixed_prior_rej_poisson_simu(
  t_prior,
  theta_prior,
  lambda_t,
  lambda_c,
  s,
```

```
  sampsz,
  N_max,
  theta_cut,
  cp_min,
  gamma,
  alpha_2,
  beta,
  sim_num
)
```

Arguments

t_prior	The prior is assumed to have a normal distribution. This is the mean of the prior distribution
theta_prior	The prior distribution of theta is assumed to have a normal distribution. The Fisher's information time is the reciprocal of the variance from the prior distribution
lambda_t	Event rate in the test arm (Poisson / negative binomial endpoint)
lambda_c	Event rate in the control arm (Poisson / negative binomial endpoint)
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
sampsz	Planned sample size: the planned sample size at the final analysis
N_max	Maximum sample size: a user chosen , maximum allowable sample size for sample size modification
theta_cut	Efficacy cut-off on the effect-size scale applied at the interim analysis
cp_min	Promising zone cp_min
gamma	Parameter chosen for the credible interval modified predictive power (CI_MPP)
alpha_2	Type I error for the two-sided test
beta	Type II error rate, i.e. 1 - power
sim_num	Number of simulation replicates

Value

The simulations are conducted with both non-informative prior and informative prior

References

Gao, P. Improving the effectiveness of sample size re-estimation: an operating characteristic focused, hybrid frequentist-Bayesian approach, Statistics in Medicine, 2025; 44:e10310. To link to this article: https://onlinelibrary.wiley.com/doi/10.1002/sim.10310.

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796.

C. R. Mehta, S. J. Pocock. Adaptive increase in sample size when interim results are promising: A practical guide with examples. Statistics in Medicine. Volume30, Issue28, 10 December 2011, Pages 3267-3284

Examples

```
hybrid_fixed_prior_rej_poisson_simu(t_prior = 5, theta_prior = 0.2, lambda_t = 0.5,
lambda_c = 0.5, s = c(0.5,1), sampsz = 100, N_max = 150, theta_cut = 0.001, cp_min = 0.27,
gamma = 0.5, alpha_2 = 0.05, beta = 0.1, sim_num = 20)
```

---

hybrid_fixed_prior_rej_survival_simu

Hybrid: Simulations, Survival analysis, Using given estimates of informative prior

---

Description

Hybrid: Simulations, Survival analysis, Using given estimates of informative prior

Usage

```
hybrid_fixed_prior_rej_survival_simu(
  t_prior,
  theta_prior,
  HR,
  lambda,
  s,
  alpha_2,
  surv_rate,
  evt_num,
  evt_max,
  HR_cut,
  cp_min,
  gamma,
  samp_multip,
  sim_num,
  beta
)
```

Arguments

t_prior	The prior is assumed to have a normal distribution. This is the mean of the prior distribution
theta_prior	The prior distribution of theta is assumed to have a normal distribution. The Fisher's information time is the reciprocal of the variance from the prior distribution

HR	Hazard ratio (test vs control)
lambda	'lambda' as used by this function; see Examples.
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha_2	Type I error for the two-sided test
surv_rate	Survival rate used to translate the number of events into a sample size
evt_num	Total number of events at the final analysis
evt_max	Maximum number of events
HR_cut	Hazard-ratio cut-off for early stopping at the interim analysis
cp_min	Promising zone cp_min
gamma	Parameter chosen for the credible interval modified predictive power (CI_MPP)
samp_multip	Multiplication factor applied to the sample size when it is increased
sim_num	Number of simulation replicates
beta	Type II error rate, i.e. 1 - power

Value

The simulations are conducted with both non-informative prior and informative prior

References

Gao, P. Improving the effectiveness of sample size re-estimation: an operating characteristic focused, hybrid frequentist-Bayesian approach, Statistics in Medicine, 2025; 44:e10310. To link to this article: https://onlinelibrary.wiley.com/doi/10.1002/sim.10310.

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796.

C. R. Mehta, S. J. Pocock. Adaptive increase in sample size when interim results are promising: A practical guide with examples. Statistics in Medicine. Volume30, Issue28, 10 December 2011, Pages 3267-3284

Examples

```
hybrid_fixed_prior_rej_survival_simu(t_prior = 10, theta_prior = 0.8, HR = 1, lambda = 1,
s = c(0.5,1), alpha_2 = 0.05, surv_rate = 0.5, evt_num = 88, evt_max = 331, HR_cut = 0.95,
cp_min = 0.27, gamma = 0.5, samp_multip = 5, beta = 0.1, sim_num = 20)
```

`hybrid_random_prior_rej_binary_simu` *Hybrid: Simulations, Binary distribution, Using random informative prior from previous trial*

Description

Hybrid: Simulations, Binary distribution, Using random informative prior from previous trial

Usage

```
hybrid_random_prior_rej_binary_simu(
  p_t_0,
  p_c_0,
  sampsz_0,
  p_t,
  p_c,
  s,
  sampsz,
  N_max,
  theta_cut,
  cp_min,
  gamma,
  alpha_2,
  beta,
  sim_num
)
```

Arguments

`p_t_0`	Event rate for test arm - previous trial
`p_c_0`	Event rate for control arm - previous trial
`sampsz_0`	Sample size from previous trial
`p_t`	Event rate for test arm
`p_c`	Event rate for control arm
`s`	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
`sampsz`	Planned sample size: the planned sample size at the final analysis
`N_max`	Maximum sample size: a user chosen , maximum allowable sample size for sample size modification
`theta_cut`	Efficacy cut-off on the effect-size scale applied at the interim analysis
`cp_min`	Promising zone cp_min
`gamma`	Parameter chosen for the credible interval modified predictive power (CI_MPP)
`alpha_2`	Type I error for the two-sided test

beta	Type II error rate, i.e. 1 - power
sim_num	Number of simulation replicates

Value

The simulations are conducted with both non-informative prior and informative prior

References

Gao, P. Improving the effectiveness of sample size re-estimation: an operating characteristic focused, hybrid frequentist-Bayesian approach, Statistics in Medicine, 2025; 44:e10310. To link to this article: https://onlinelibrary.wiley.com/doi/10.1002/sim.10310.

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796.

C. R. Mehta, S. J. Pocock. Adaptive increase in sample size when interim results are promising: A practical guide with examples. Statistics in Medicine. Volume30, Issue28, 10 December 2011, Pages 3267-3284

Examples

```
hybrid_random_prior_rej_binary_simu(p_t_0 = 0.4, p_c_0 = 0.3, sampsz_0 = 60, p_t = 0.3,
p_c = 0.3, s = c(0.5,1), sampsz = 100, N_max = 150, theta_cut = 0.001, cp_min = 0.27,
gamma = 0.5, alpha_2 = 0.05, beta = 0.1, sim_num = 20)
```

---

hybrid_random_prior_rej_negbinom_simu

Hybrid: Simulations, Negative binomial distribution, Using random informative prior from previous trial

---

Description

Hybrid: Simulations, Negative binomial distribution, Using random informative prior from previous trial

Usage

```
hybrid_random_prior_rej_negbinom_simu(
  r_t_0,
  r_c_0,
  sampsz_0,
  r_t,
  r_c,
```

```
  kappa,
  nu_t,
  rand_ratio,
  s,
  sampsz,
  N_max,
  theta_cut,
  cp_min,
  gamma,
  alpha_2,
  beta,
  sim_num
)
```

Arguments

r_t_0	Event rate for test arm - previous trial
r_c_0	Event rate for control arm - previous trial
sampsz_0	Sample size from previous trial
r_t	Event rate for test arm - current trial
r_c	Event rate for control arm - current trial
kappa	dispersion parameter
nu_t	exposure time
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
sampsz	Planned sample size: the planned sample size at the final analysis
N_max	Maximum sample size: a user chosen , maximum allowable sample size for sample size modification
theta_cut	Efficacy cut-off on the effect-size scale applied at the interim analysis
cp_min	Promising zone cp_min
gamma	Parameter chosen for the credible interval modified predictive power (CI_MPP)
alpha_2	Type I error for the two-sided test
beta	Type II error rate, i.e. 1 - power
sim_num	Number of simulation replicates

Value

The simulations are conducted with both non-informative prior and informative prior

References

Gao, P. Improving the effectiveness of sample size re-estimation: an operating characteristic focused, hybrid frequentist-Bayesian approach, Statistics in Medicine, 2025; 44:e10310. To link to this article: https://onlinelibrary.wiley.com/doi/10.1002/sim.10310.

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796.

C. R. Mehta, S. J. Pocock. Adaptive increase in sample size when interim results are promising: A practical guide with examples. Statistics in Medicine. Volume30, Issue28, 10 December 2011, Pages 3267-3284

Examples

```
hybrid_random_prior_rej_negbinom_simu(r_t_0 = 1.2, r_c_0 = 1, sampsz_0 = 50, r_t = 1, r_c = 1,
kappa = 1, nu_t = 1, rand_ratio = 1, s = c(0.5,1), sampsz = 100, N_max = 150,
theta_cut = 0.001, cp_min = 0.27, gamma = 0.5, alpha_2 = 0.05, beta = 0.1, sim_num = 20)
```

---

hybrid_random_prior_rej_normal_simu

Hybrid: Simulations, Normal distribution, Using random informative prior from previous trial

---

Description

Hybrid: Simulations, Normal distribution, Using random informative prior from previous trial

Usage

```
hybrid_random_prior_rej_normal_simu(
  mu_0,
  sigma_0,
  sampsz_0,
  mu,
  sigma,
  s,
  sampsz,
  N_max,
  theta_cut,
  cp_min,
  gamma,
  alpha_2,
  beta,
  sim_num
)
```

Arguments

mu_0	Effect size from previous trial
sigma_0	Common standard deviation from previous trial
sampsz_0	Sample size from previous trial
mu	Effect size used when calibrating the boundaries
sigma	Futility threshold
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
sampsz	Planned sample size: the planned sample size at the final analysis
N_max	Maximum sample size: a user chosen , maximum allowable sample size for sample size modification
theta_cut	Efficacy cut-off on the effect-size scale applied at the interim analysis
cp_min	Promising zone cp_min
gamma	Parameter chosen for the credible interval modified predictive power (CI_MPP)
alpha_2	Type I error for the two-sided test
beta	Type II error rate, i.e. 1 - power
sim_num	Number of simulation replicates

Value

The simulations are conducted with both non-informative prior and informative prior

References

Gao, P. Improving the effectiveness of sample size re-estimation: an operating characteristic focused, hybrid frequentist-Bayesian approach, Statistics in Medicine, 2025; 44:e10310. To link to this article: https://onlinelibrary.wiley.com/doi/10.1002/sim.10310.

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796.

C. R. Mehta, S. J. Pocock. Adaptive increase in sample size when interim results are promising: A practical guide with examples. Statistics in Medicine. Volume30, Issue28, 10 December 2011, Pages 3267-3284

Examples

```
hybrid_random_prior_rej_normal_simu(mu_0 = 0.3, sigma_0 = 1, sampsz_0 = 60, mu = 0, sigma = 1,
s = c(0.5,1), sampsz = 100, N_max = 250, theta_cut = 0.01, cp_min = 0.27, gamma = 0.5,
alpha_2 = 0.05, beta = 0.1, sim_num = 20)
```

`hybrid_random_prior_rej_poisson_simu` *Hybrid: Simulations, Poisson distribution, Using random informative prior from previous trial*

Description

Hybrid: Simulations, Poisson distribution, Using random informative prior from previous trial

Usage

```
hybrid_random_prior_rej_poisson_simu(
  lambda_t_0,
  lambda_c_0,
  sampsz_0,
  lambda_t,
  lambda_c,
  s,
  sampsz,
  N_max,
  theta_cut,
  cp_min,
  gamma,
  alpha_2,
  beta,
  sim_num
)
```

Arguments

`lambda_t_0`	Event rate for test arm - previous trial
`lambda_c_0`	Event rate for control arm - previous trial
`sampsz_0`	Sample size from previous trial
`lambda_t`	Event rate for test arm - current trial
`lambda_c`	Event rate for control arm - current trial
`s`	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
`sampsz`	Planned sample size: the planned sample size at the final analysis
`N_max`	Maximum sample size: a user chosen , maximum allowable sample size for sample size modification
`theta_cut`	Efficacy cut-off on the effect-size scale applied at the interim analysis
`cp_min`	Promising zone cp_min
`gamma`	Parameter chosen for the credible interval modified predictive power (CI_MPP)
`alpha_2`	Type I error for the two-sided test

beta	Type II error rate, i.e. 1 - power
sim_num	Number of simulation replicates

Value

The simulations are conducted with both non-informative prior and informative prior

References

Gao, P. Improving the effectiveness of sample size re-estimation: an operating characteristic focused, hybrid frequentist-Bayesian approach, Statistics in Medicine, 2025; 44:e10310. To link to this article: https://onlinelibrary.wiley.com/doi/10.1002/sim.10310.

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796.

C. R. Mehta, S. J. Pocock. Adaptive increase in sample size when interim results are promising: A practical guide with examples. Statistics in Medicine. Volume30, Issue28, 10 December 2011, Pages 3267-3284

Examples

```
hybrid_random_prior_rej_poisson_simu(lambda_t_0 = 0.5, lambda_c_0 = 0.3, sampsz_0 = 60,
lambda_t = 0.5, lambda_c = 0.5, s = c(0.5,1), sampsz = 100, N_max = 150, theta_cut = 0.001,
cp_min = 0.27, gamma = 0.5, alpha_2 = 0.05, beta = 0.1, sim_num = 20)
```

---

hybrid_random_prior_rej_survival_simu

Hybrid: Simulations, Survival analysis, Using random informative prior from previous trial

---

Description

Hybrid: Simulations, Survival analysis, Using random informative prior from previous trial

Usage

```
hybrid_random_prior_rej_survival_simu(
  HR_0,
  evt_num_0,
  HR,
  lambda,
  s,
  alpha_2,
```

```
  surv_rate,
  evt_num,
  evt_max,
  HR_cut,
  cp_min,
  gamma,
  samp_multip,
  sim_num,
  beta
)
```

Arguments

HR_0	Hazards ratio from previous trial
evt_num_0	Number of events from previous trial
HR	Hazard ratio (test vs control)
lambda	'lambda' as used by this function; see Examples.
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha_2	Type I error for the two-sided test
surv_rate	Survival rate used to translate the number of events into a sample size
evt_num	Total number of events at the final analysis
evt_max	Maximum number of events
HR_cut	Hazard-ratio cut-off for early stopping at the interim analysis
cp_min	Promising zone cp_min
gamma	Parameter chosen for the credible interval modified predictive power (CI_MPP)
samp_multip	Multiplication factor applied to the sample size when it is increased
sim_num	Number of simulation replicates
beta	Type II error rate, i.e. 1 - power

Value

The simulations are conducted with both non-informative prior and informative prior

References

Gao, P. Improving the effectiveness of sample size re-estimation: an operating characteristic focused, hybrid frequentist-Bayesian approach, Statistics in Medicine, 2025; 44:e10310. To link to this article: https://onlinelibrary.wiley.com/doi/10.1002/sim.10310.

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796.

C. R. Mehta, S. J. Pocock. Adaptive increase in sample size when interim results are promising: A practical guide with examples. Statistics in Medicine. Volume30, Issue28, 10 December 2011, Pages 3267-3284

Examples

```
hybrid_random_prior_rej_survival_simu(HR_0 = 0.63, evt_num_0 = 40, HR = 1, lambda = 1,
s = c(0.5,1), alpha_2 = 0.05, surv_rate = 0.5, evt_num = 88, evt_max = 331, HR_cut = 0.95,
cp_min = 0.27, gamma = 0.5, samp_multip = 5, beta = 0.1, sim_num = 20)
```

---

hybrid_sz *Two-stage design: the hybrid design*

Description

Two-stage design: the hybrid design

Usage

```
hybrid_sz(alpha, beta, p_0, p_low, p_1, d_12_cut)
```

Arguments

alpha	One-sided type I error.
beta	Type II error.
p_0	Response rate indicating low activity with insufficient clinical benefit.
p_low	Minimally clinically beneficial response rate.
p_1	Assumed response rate.
d_12_cut	Min(n2-n1) sets the minimal difference between n2 and n1 for the design.

Value

n1: Number of patients at first look.

n_2: Number of patients at second look. n_2 is also the total sample size.

r1: If no more than r1 responses are observed at the first look, then the trial would be stopped for futility.

r_2: The null hypothesis will be rejected if at least r_2 responses are observed at the end of the trial.

EN(p0) is the expected sample size under the null hypothesis.

PET(p0) is the probability of early termination under the null hypothesis.

PET_p is the probability of early termination under p=p_1.

PET_p_low is the probability of early termination under p=p_low.

power_p is the power under p=p_1.

power_p_low is the power under p=p_low.

Type I error is the probability of rejecting the null hypothesis under p<=p_0.

The minimax design has the smallest n2 among all possible choices of (n1,r1,n_2,r_2).

The optimal design has the smallest EN(p0)) among all possible choices of (n1,r1,n_2,r_2).

The n1 for the average design is the average of n1's from the minimax and the optimal designs.

References

R. Simon. Optimal Two-Stage Designs for Phase II Clinical Trials. Controlled Clinical Trials 10:1-10 (1989).

P. Gao & W. Zhang (15 Apr 2024): Adaptive sequential design for phase II single-arm oncology trials: an expansion of Simon's design, Journal of Biopharmaceutical Statistics, DOI: 10.1080/10543406.2024.2341673. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2341673.

Examples

```
hybrid_sz(alpha=c(0.001,0.024),beta=0.1,p_0=0.2,p_low=0.4,p_1=0.55,d_12_cut=0)
```

`interim_analysis` *The interim analysis can be conducted for both two-stage and three-stage designs*

Description

The interim analysis can be conducted for both two-stage and three-stage designs

Usage

```
interim_analysis(p_0, r_final, n_inter, n_final, x_inter, beta, N_max)
```

Arguments

`p_0`	Response rate indicating low activity with insufficient clinical benefit.
`r_final`	For two-stage designs, r_final=r2. For the three-stage design, r_final=r3.
`n_inter`	Number of patients at the interim look. For two-stage designs, n_inter=n1. For the three-stage design, n_inter=n2.
`n_final`	For two-stage designs, n_inter=n2. For the three-stage design, n_inter=n3.
`x_inter`	Number of responses observed at the interim look.
`beta`	The conditional type II error. 1-beta is the desired conditional power.
`N_max`	Pre-selected maximum sample size.

Value

n_new: is the new sample size.

r_new (without continuity correction) and r_new (with continuity correction) are thresholds such that the null hypothesis will be rejected at n_new if at least r_new responses are observed. Simulations on type I error will help to determine if continuity correction is needed.

References

R. Simon. Optimal Two-Stage Designs for Phase II Clinical Trials. Controlled Clinical Trials 10:1-10 (1989).

P. Gao & W. Zhang (15 Apr 2024): Adaptive sequential design for phase II single-arm oncology trials: an expansion of Simon's design, Journal of Biopharmaceutical Statistics, DOI: 10.1080/10543406.2024.2341673. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2341673.

P. Gao, J.H. Ware, C. Mehta, (2008), Sample size re-estimation for adaptive sequential designs. Journal of Biopharmaceutical Statistics, 18: 1184–1196, 2008.

Examples

```
interim_analysis(p_0=0.2,r_final=17,n_inter=22,n_final=56,x_inter=7,beta=0.1,N_max=120)
```

---

masd_est_back_no_drop *Multiple comparisons Group sequential design: Final analysis, With one sample size change, orgin_comp==comp2*

Description

Multiple comparisons Group sequential design: Final analysis, With one sample size change, orgin_comp==comp2

Usage

```
masd_est_back_no_drop(
  s,
  c_bry,
  snew,
  c_bry_new,
  theta_hat_inter_m1,
  theta_hat_inter_m1_sd,
  inter_vt,
  theta_hat_last_ad_m1,
  theta_hat_last_ad_m1_sd,
  last_vt_ad,
  alpha_2,
  dist
)
```

Arguments

s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
c_bry	Vector of critical boundaries for each analysis
snew	Vector of new information fractions after the sample size is changed
c_bry_new	Critical boundaries after the sample size is changed
theta_hat_inter_m1	'theta_hat_inter_m1' as used by this function; see Examples.
theta_hat_inter_m1_sd	'theta_hat_inter_m1_sd' as used by this function; see Examples.
inter_vt	Index of the interim analysis at which the sample size is re-estimated (1-based)
theta_hat_last_ad_m1	'theta_hat_last_ad_m1' as used by this function; see Examples.
theta_hat_last_ad_m1_sd	'theta_hat_last_ad_m1_sd' as used by this function; see Examples.
last_vt_ad	Index of the last analysis after the sample size change
alpha_2	Type I error for the two-sided test
dist	Indicator of the endpoint / distribution type

Value

A named list containing the following elements: 'p-value', 'confidence interval'.

References

P. Gao & Y. Li (2024) Adaptive Multiple Comparison Sequential Design (AMCSD) for clinical trials, Journal of Biopharmaceutical Statistics, 34:3, 424-440, DOI:10.1080/10543406.2023.2233590. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2023.2233590

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
masd_est_back_no_drop(s = c(0.3,0.7,1), c_bry = c(4.347011, 2.845787, 2.380956), snew = c(0.5,1),
c_bry_new = c(3.310743,2.781890), theta_hat_inter_m1 = c(1.2,1.3,1.5), theta_hat_inter_m1_sd = 1,
inter_vt = 1, theta_hat_last_ad_m1 = c(2.2,1.4,1.8), theta_hat_last_ad_m1_sd = 1,
```

```
last_vt_ad = 2, alpha_2 = 0.05, dist = 1)
```

`masd_est_back_with_drop` *Multiple comparisons Group sequential design: Final analysis, With one sample size change, orgin_comp>comp2*

Description

Multiple comparisons Group sequential design: Final analysis, With one sample size change, orgin_comp>comp2

Usage

```
masd_est_back_with_drop(
  s,
  c_bry,
  snew,
  c_bry_new,
  theta_hat_inter_m1,
  theta_hat_inter_m1_sd,
  theta_hat_inter_m2,
  theta_hat_inter_m2_sd,
  inter_vt,
  theta_hat_last_ad_m2,
  theta_hat_last_ad_m2_sd,
  last_vt_ad,
  alpha_2,
  dist
)
```

Arguments

`s`	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
`c_bry`	Vector of critical boundaries for each analysis
`snew`	Vector of new information fractions after the sample size is changed
`c_bry_new`	Critical boundaries after the sample size is changed
`theta_hat_inter_m1`	'theta_hat_inter_m1' as used by this function; see Examples.
`theta_hat_inter_m1_sd`	'theta_hat_inter_m1_sd' as used by this function; see Examples.
`theta_hat_inter_m2`	'theta_hat_inter_m2' as used by this function; see Examples.

`theta_hat_inter_m2_sd`
: 'theta_hat_inter_m2_sd' as used by this function; see Examples.

`inter_vt`
: Index of the interim analysis at which the sample size is re-estimated (1-based)

`theta_hat_last_ad_m2`
: 'theta_hat_last_ad_m2' as used by this function; see Examples.

`theta_hat_last_ad_m2_sd`
: 'theta_hat_last_ad_m2_sd' as used by this function; see Examples.

`last_vt_ad`
: Index of the last analysis after the sample size change

`alpha_2`
: Type I error for the two-sided test

`dist`
: Indicator of the endpoint / distribution type

Value

A named list containing the following elements: 'p-value', 'confidence interval'.

References

P. Gao & Y. Li (2024) Adaptive Multiple Comparison Sequential Design (AMCSD) for clinical trials, Journal of Biopharmaceutical Statistics, 34:3, 424-440, DOI:10.1080/10543406.2023.2233590. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2023.2233590

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
masd_est_back_with_drop(s = c(0.3,0.7,1), c_bry = c(4.347011,2.845787,2.380956), snew = c(0.5,1),
c_bry_new = c(3.310743,2.781890), theta_hat_inter_m1 = c(1.2,1.3,1.5), theta_hat_inter_m1_sd = 1,
theta_hat_inter_m2 = c(1.3,1.5), theta_hat_inter_m2_sd = 1, inter_vt = 1,
theta_hat_last_ad_m2 = c(2.2,1.4), theta_hat_last_ad_m2_sd = 1, last_vt_ad = 2,
alpha_2 = 0.05, dist = 1)
```

`masd_est_ci` *Multiple comparisons Group sequential design: Final analysis, Without sample size change*

Description

Multiple comparisons Group sequential design: Final analysis, Without sample size change

Usage

```
masd_est_ci(
  s,
  c_bry,
  theta_hat_last_m1,
  theta_hat_last_m1_sd,
  last_vt,
  alpha_2,
  dist
)
```

Arguments

`s`	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
`c_bry`	Vector of critical boundaries for each analysis
`theta_hat_last_m1`	'theta_hat_last_m1' as used by this function; see Examples.
`theta_hat_last_m1_sd`	'theta_hat_last_m1_sd' as used by this function; see Examples.
`last_vt`	Index of the analysis at which the trial stopped
`alpha_2`	Type I error for the two-sided test
`dist`	Indicator of the endpoint / distribution type

Value

A named list containing the following elements: 'p-value', 'confidence interval'.

References

P. Gao & Y. Li (2024) Adaptive Multiple Comparison Sequential Design (AMCSD) for clinical trials, Journal of Biopharmaceutical Statistics, 34:3, 424-440, DOI:10.1080/10543406.2023.2233590. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2023.2233590

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024

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P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
masd_est_ci(s = c(1/3, 2/3, 1), c_bry = c(3.984298, 3.961146, 2.349682),
theta_hat_last_m1 = 0.35, theta_hat_last_m1_sd = 0.6,
last_vt = 1, alpha_2 = 0.05, dist = 1)
```

`masd_new_samsz` *Multiple comparisons Group sequential design: Interim analysis, Non-survival analysis, Use theta_interim*

Description

Multiple comparisons Group sequential design: Interim analysis, Non-survival analysis, Use theta_interim

Usage

```
masd_new_samsz(
  s,
  c_bry,
  snew,
  inter_vt,
  theta_hat_inter_m1,
  theta_hat_inter_m1_sd,
  theta_hat_inter_m2,
  theta_hat_inter_m2_sd,
  beta,
  n_control_inter,
  dist
)
```

Arguments

`s`	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
`c_bry`	Vector of critical boundaries for each analysis
`snew`	Vector of new information fractions after the sample size is changed
`inter_vt`	Index of the interim analysis at which the sample size is re-estimated (1-based)

`theta_hat_inter_m1`
: 'theta_hat_inter_m1' as used by this function; see Examples.

`theta_hat_inter_m1_sd`
: 'theta_hat_inter_m1_sd' as used by this function; see Examples.

`theta_hat_inter_m2`
: 'theta_hat_inter_m2' as used by this function; see Examples.

`theta_hat_inter_m2_sd`
: 'theta_hat_inter_m2_sd' as used by this function; see Examples.

`beta`
: Type II error rate, i.e. 1 - power

`n_control_inter`
: Sample size of the control arm at the interim analysis

`dist`
: Indicator of the endpoint / distribution type

Value

A named list containing the following elements: 'Interim analysis hypothesis test', 'Wald statistics', 'Critical boundary', 'Estimated effect size: theta', 'remaining effect size', 'c_alpha', 'c_power_m1', 'c_power_m2', 'N_control_new', 'new information fraction', 'New critical boundary'.

References

P. Gao & Y. Li (2024) Adaptive Multiple Comparison Sequential Design (AMCSD) for clinical trials, Journal of Biopharmaceutical Statistics, 34:3, 424-440, DOI:10.1080/10543406.2023.2233590. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2023.2233590

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P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
masd_new_samsz(s=c(1/3,2/3,1), c_bry=c(3.984298, 3.961146, 2.349682), snew=1, inter_vt=2,
theta_hat_inter_m1=c(1.2,1.5,1.1), theta_hat_inter_m1_sd=0.2, theta_hat_inter_m2=c(1.2,1.5),
theta_hat_inter_m2_sd=0.2, beta=0.1, n_control_inter=65, dist=1)
```

`masd_new_samsz_survival` *Multiple comparisons Group sequential design: Interim analysis, Survival analysis, Use theta_interim*

Description

Multiple comparisons Group sequential design: Interim analysis, Survival analysis, Use theta_interim

Usage

```
masd_new_samsz_survival(
  s,
  c_bry,
  snew,
  inter_vt,
  theta_hat_inter_m1,
  theta_hat_inter_m1_sd,
  theta_hat_inter_m2,
  theta_hat_inter_m2_sd,
  beta,
  tot_events_inter_m1,
  dist
)
```

Arguments

`s`	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
`c_bry`	Vector of critical boundaries for each analysis
`snew`	Vector of new information fractions after the sample size is changed
`inter_vt`	Index of the interim analysis at which the sample size is re-estimated (1-based)
`theta_hat_inter_m1`	'theta_hat_inter_m1' as used by this function; see Examples.
`theta_hat_inter_m1_sd`	'theta_hat_inter_m1_sd' as used by this function; see Examples.
`theta_hat_inter_m2`	'theta_hat_inter_m2' as used by this function; see Examples.
`theta_hat_inter_m2_sd`	'theta_hat_inter_m2_sd' as used by this function; see Examples.
`beta`	Type II error rate, i.e. 1 - power
`tot_events_inter_m1`	'tot_events_inter_m1' as used by this function; see Examples.
`dist`	Indicator of the endpoint / distribution type

Value

A named list containing the following elements: 'Interim analysis hypothesis test', 'Wald statistics', 'Critical boundary', 'Assumed effect size: theta', 'remaining effect size', 'c_alpha', 'c_power_m1', 'c_power_m2', 'new events between a test arm and control', 'new total events', 'new information fraction', 'New critical boundary'.

References

P. Gao & Y. Li (2024) Adaptive Multiple Comparison Sequential Design (AMCSD) for clinical trials, Journal of Biopharmaceutical Statistics, 34:3, 424-440, DOI:10.1080/10543406.2023.2233590. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2023.2233590

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

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P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
masd_new_samsz_survival(s = c(1/3,2/3,1), c_bry = c(3.984298, 3.961146, 2.349682), snew = 1,
inter_vt = 2, theta_hat_inter_m1 = c(1.2,1.5,1.1),
theta_hat_inter_m1_sd = 1.2, theta_hat_inter_m2 = c(1.2,1.5),
theta_hat_inter_m2_sd = 1.2, beta = 0.1, tot_events_inter_m1 = 65, dist = 1)
```

---

masd_new_samsz_theta *Multiple comparisons Group sequential design: Interim analysis, Non-survival analysis, Input theta*

Description

Multiple comparisons Group sequential design: Interim analysis, Non-survival analysis, Input theta

Usage

```
masd_new_samsz_theta(
  theta,
  s,
  c_bry,
  snew,
```

```
  inter_vt,
  theta_hat_inter_m1,
  theta_hat_inter_m1_sd,
  theta_hat_inter_m2,
  theta_hat_inter_m2_sd,
  beta,
  n_control_inter,
  dist
)
```

Arguments

theta	Assumed effect size
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
c_bry	Vector of critical boundaries for each analysis
snew	Vector of new information fractions after the sample size is changed
inter_vt	Index of the interim analysis at which the sample size is re-estimated (1-based)
theta_hat_inter_m1	'theta_hat_inter_m1' as used by this function; see Examples.
theta_hat_inter_m1_sd	'theta_hat_inter_m1_sd' as used by this function; see Examples.
theta_hat_inter_m2	'theta_hat_inter_m2' as used by this function; see Examples.
theta_hat_inter_m2_sd	'theta_hat_inter_m2_sd' as used by this function; see Examples.
beta	Type II error rate, i.e. 1 - power
n_control_inter	Sample size of the control arm at the interim analysis
dist	Indicator of the endpoint / distribution type

Value

A named list containing the following elements: 'Interim analysis hypothesis test', 'Wald statistics', 'Critical boundary', 'Assumed effect size: theta', 'remaining effect size', 'c_alpha', 'c_power_m1', 'c_power_m2', 'N_control_new', 'new information fraction', 'New critical boundary'.

References

P. Gao & Y. Li (2024) Adaptive Multiple Comparison Sequential Design (AMCSD) for clinical trials, Journal of Biopharmaceutical Statistics, 34:3, 424-440, DOI:10.1080/10543406.2023.2233590. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2023.2233590

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024

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P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
masd_new_samsz_theta(theta = c(0,0.2,0), s = c(1/3,2/3,1),
c_bry = c(3.984298, 3.961146, 2.349682), snew = 1, inter_vt = 2,
theta_hat_inter_m1 = c(1.2,1.5,1.1), theta_hat_inter_m1_sd = 0.2,
theta_hat_inter_m2 = c(1.2,1.5), theta_hat_inter_m2_sd = 0.2,
beta = 0.1, n_control_inter = 65, dist = 1)
```

---

masd_new_samsz_theta_survival

Multiple comparisons Group sequential design: Interim analysis, Survival analysis, Input theta

---

Description

Multiple comparisons Group sequential design: Interim analysis, Survival analysis, Input theta

Usage

```
masd_new_samsz_theta_survival(
  theta,
  s,
  c_bry,
  snew,
  inter_vt,
  theta_hat_inter_m1,
  theta_hat_inter_m1_sd,
  theta_hat_inter_m2,
  theta_hat_inter_m2_sd,
  beta,
  tot_events_inter_m1,
  dist
)
```

Arguments

theta	Assumed effect size
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
c_bry	Vector of critical boundaries for each analysis
snew	Vector of new information fractions after the sample size is changed
inter_vt	Index of the interim analysis at which the sample size is re-estimated (1-based)
theta_hat_inter_m1	'theta_hat_inter_m1' as used by this function; see Examples.
theta_hat_inter_m1_sd	'theta_hat_inter_m1_sd' as used by this function; see Examples.
theta_hat_inter_m2	'theta_hat_inter_m2' as used by this function; see Examples.
theta_hat_inter_m2_sd	'theta_hat_inter_m2_sd' as used by this function; see Examples.
beta	Type II error rate, i.e. 1 - power
tot_events_inter_m1	'tot_events_inter_m1' as used by this function; see Examples.
dist	Indicator of the endpoint / distribution type

Value

A named list containing the following elements: 'Interim analysis hypothesis test', 'Wald statistics', 'Critical boundary', 'Assumed effect size: theta', 'remaining effect size', 'c_alpha', 'c_power_m1', 'c_power_m2', 'new events between a test arm and control', 'new total events', 'new information fraction', 'New critical boundary'.

References

P. Gao & Y. Li (2024) Adaptive Multiple Comparison Sequential Design (AMCSD) for clinical trials, Journal of Biopharmaceutical Statistics, 34:3, 424-440, DOI:10.1080/10543406.2023.2233590. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2023.2233590

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

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P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
masd_new_samsz_theta_survival(theta=c(0,0.2,0), s=c(1/3,2/3,1),
c_bry=c(3.984298, 3.961146, 2.349682), snew=1, inter_vt=2,
theta_hat_inter_m1=c(1.2,1.5,1.1), theta_hat_inter_m1_sd=0.2, theta_hat_inter_m2=c(1.2,1.5),
theta_hat_inter_m2_sd=0.2, beta=0.1, tot_events_inter_m1=65, dist=1)
```

---

masd_power_simu_adapt_binary

Multiple comparisons Group sequential design: Simulations, Binary distribution, Operating characteristics

---

Description

Multiple comparisons Group sequential design: Simulations, Binary distribution, Operating characteristics

Usage

```
masd_power_simu_adapt_binary(
  p_t,
  p_c,
  direction,
  s,
  bry_type,
  alpha_2,
  theta_cut,
  beta,
  samsz,
  N_max,
  sim_num
)
```

Arguments

p_t	Event (response) proportion in the test arm
p_c	Event (response) proportion in the control arm
direction	Test direction: 1 = larger p is better, 0 = smaller p is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
bry_type	Critical boundary type: 1 = O'Brien-Fleming, 2 = Pocock, 3 = alpha-spending
alpha_2	Type I error for the two-sided test
theta_cut	Efficacy cut-off on the effect-size scale applied at the interim analysis
beta	Type II error rate, i.e. 1 - power
samsz	Planned sample size of the control arm used in the simulation
N_max	Maximum allowed sample size (control arm)
sim_num	Number of simulation replicates

Value

A matrix in which each row corresponds to one simulation replicate and the columns hold the simulated operating characteristics (e.g. rejection indicators, sample sizes and stopping stages).

References

P. Gao & Y. Li (2024) Adaptive Multiple Comparison Sequential Design (AMCSD) for clinical trials, Journal of Biopharmaceutical Statistics, 34:3, 424-440, DOI:10.1080/10543406.2023.2233590. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2023.2233590

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

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P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
masd_power_simu_adapt_binary(p_t = c(0.4,0.4,0.4), p_c = 0.4, direction = 1, s = c(1/3,2/3,1),
bry_type = 1, alpha_2 = 0.05, theta_cut = 0.01, beta = 0.1, samsz = 100,
N_max = 200, sim_num = 20)
```

---

masd_power_simu_adapt_neg_binomial

Multiple comparisons Group sequential design: Simulations, Negative binomial distribution, Operating characteristics

---

Description

Multiple comparisons Group sequential design: Simulations, Negative binomial distribution, Operating characteristics

Usage

```
masd_power_simu_adapt_neg_binomial(
  r_t,
  r_c,
  kappa,
  direction,
```

```
  s,
  bry_type,
  alpha_2,
  beta,
  theta_cut,
  samsz,
  N_max,
  sim_num
)
```

Arguments

r_t	Rate parameter of the test arm (negative binomial endpoint)
r_c	Rate parameter of the control arm (negative binomial endpoint)
kappa	Dispersion (size) parameter of the negative binomial distribution
direction	Test direction: 1 = larger r is better, 0 = smaller r is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
bry_type	Critical boundary type: 1 = O'Brien-Fleming, 2 = Pocock, 3 = alpha-spending
alpha_2	Type I error for the two-sided test
beta	Type II error rate, i.e. 1 - power
theta_cut	Efficacy cut-off on the effect-size scale applied at the interim analysis
samsz	Planned sample size of the control arm used in the simulation
N_max	Maximum allowed sample size (control arm)
sim_num	Number of simulation replicates

Value

A matrix in which each row corresponds to one simulation replicate and the columns hold the simulated operating characteristics (e.g. rejection indicators, sample sizes and stopping stages).

References

P. Gao & Y. Li (2024) Adaptive Multiple Comparison Sequential Design (AMCSD) for clinical trials, Journal of Biopharmaceutical Statistics, 34:3, 424-440, DOI:10.1080/10543406.2023.2233590. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2023.2233590

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
masd_power_simu_adapt_neg_binomial(r_t = c(1.1,1.1,1.1), r_c = 1.1, kappa = 1, direction = 1,
s = c(1/3,2/3,1), bry_type = 1, alpha_2 = 0.05, beta = 0.1, theta_cut = 0.01, samsz = 100,
N_max = 500, sim_num = 20)
```

`masd_power_simu_adapt_normal`

Multiple comparisons Group sequential design: Simulations, Normal distribution, Operating characteristics

---

Description

Multiple comparisons Group sequential design: Simulations, Normal distribution, Operating characteristics

Usage

```
masd_power_simu_adapt_normal(
  mu_t,
  mu_c,
  sigma_t,
  sigma_c,
  direction,
  s,
  bry_type,
  alpha_2,
  beta,
  theta_cut,
  samsz,
  N_max,
  sim_num
)
```

Arguments

`mu_t`	Means of the test arm
`mu_c`	Means of the control arm
`sigma_t`	Standard deviation of the test arm
`sigma_c`	Standard deviation of the control arm
`direction`	Test direction: 1 = larger mu is better, 0 = smaller mu is better
`s`	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
`bry_type`	Critical boundary type: 1 = O'Brien-Fleming, 2 = Pocock, 3 = alpha-spending

alpha_2	Type I error for the two-sided test
beta	Type II error rate, i.e. 1 - power
theta_cut	Efficacy cut-off on the effect-size scale applied at the interim analysis
samsz	Planned sample size of the control arm used in the simulation
N_max	Maximum allowed sample size (control arm)
sim_num	Number of simulation replicates

Value

A named list containing the following elements: 'simulation summary', 'planned control', 'planned total'.

References

P. Gao & Y. Li (2024) Adaptive Multiple Comparison Sequential Design (AMCSD) for clinical trials, Journal of Biopharmaceutical Statistics, 34:3, 424-440, DOI:10.1080/10543406.2023.2233590. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2023.2233590

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

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P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
masd_power_simu_adapt_normal(mu_t = c(0,0,0), mu_c = 0, sigma_t = 1, sigma_c = 1, direction = 1,
s = c(1/3,2/3,1), bry_type = 1, alpha_2 = 0.05, beta = 0.1, theta_cut = 0.01, samsz = 100,
N_max = 500, sim_num = 20)
```

---

masd_power_simu_adapt_poisson

Multiple comparisons Group sequential design: Simulations, Poisson distribution, Operating characteristics

---

Description

Multiple comparisons Group sequential design: Simulations, Poisson distribution, Operating characteristics

Usage

```
masd_power_simu_adapt_poisson(
  lambda_t,
  lambda_c,
  direction,
  s,
  bry_type,
  alpha_2,
  beta,
  theta_cut,
  samsz,
  N_max,
  sim_num
)
```

Arguments

lambda_t	Event rate in the test arm (Poisson / negative binomial endpoint)
lambda_c	Event rate in the control arm (Poisson / negative binomial endpoint)
direction	Test direction: 1 = larger lambda is better, 0 = smaller lambda is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
bry_type	Critical boundary type: 1 = O'Brien-Fleming, 2 = Pocock, 3 = alpha-spending
alpha_2	Type I error for the two-sided test
beta	Type II error rate, i.e. 1 - power
theta_cut	Efficacy cut-off on the effect-size scale applied at the interim analysis
samsz	Planned sample size of the control arm used in the simulation
N_max	Maximum allowed sample size (control arm)
sim_num	Number of simulation replicates

Value

A named list containing the following elements: 'simulation summary', 'planned control', 'planned total'.

References

P. Gao & Y. Li (2024) Adaptive Multiple Comparison Sequential Design (AMCSD) for clinical trials, Journal of Biopharmaceutical Statistics, 34:3, 424-440, DOI:10.1080/10543406.2023.2233590. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2023.2233590

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024

May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
masd_power_simu_adapt_poisson(lambda_t = c(1.1,1.1,1.1), lambda_c = 1.1, direction = 1,
s = c(1/3,2/3,1), bry_type = 1, alpha_2 = 0.05, beta = 0.1, theta_cut = 0.01, samsz = 100,
N_max = 500, sim_num = 20)
```

`masd_power_simu_adapt_survival`

Multiple comparisons Group sequential design: Simulations, Survival analysis, Operating characteristics

---

Description

Multiple comparisons Group sequential design: Simulations, Survival analysis, Operating characteristics

Usage

```
masd_power_simu_adapt_survival(
  HR,
  s,
  bry_type,
  alpha_2,
  surv_rate,
  HR_cut,
  evt_num,
  evt_max,
  beta,
  sim_num
)
```

Arguments

`HR`	Hazard ratio (test vs control)
`s`	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
`bry_type`	Critical boundary type: 1 = O'Brien-Fleming, 2 = Pocock, 3 = alpha-spending

alpha_2	Type I error for the two-sided test
surv_rate	Survival rate used to translate the number of events into a sample size
HR_cut	Hazard-ratio cut-off for early stopping at the interim analysis
evt_num	Total number of events at the final analysis
evt_max	Maximum number of events
beta	Type II error rate, i.e. 1 - power
sim_num	Number of simulation replicates

Value

A matrix in which each row corresponds to one simulation replicate and the columns hold the simulated operating characteristics (e.g. rejection indicators, sample sizes and stopping stages).

References

P. Gao & Y. Li (2024) Adaptive Multiple Comparison Sequential Design (AMCSD) for clinical trials, Journal of Biopharmaceutical Statistics, 34:3, 424-440, DOI:10.1080/10543406.2023.2233590. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2023.2233590

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
masd_power_simu_adapt_survival(HR = c(0.8,0.8), s = c(1/3,2/3,1), bry_type = 1, alpha_2 = 0.05,
surv_rate = 0.5, HR_cut = 0.95, evt_num = 800, evt_max = 1200, beta = 0.1, sim_num = 2)
```

---

masd_simu_OC_binary *Multiple comparisons Group sequential design: Simulations, Binary distribution, Optimizing adaptive sequential design*

Description

Multiple comparisons Group sequential design: Simulations, Binary distribution, Optimizing adaptive sequential design

Usage

```
masd_simu_OC_binary(
  groups,
  p_c,
  direction,
  s1,
  s2,
  alpha_2,
  alpha_2_alps_s1,
  alpha_2_alps_s2,
  theta_cut,
  samsz_1,
  samsz_2,
  N_max_1,
  N_max_2,
  beta,
  sim_num
)
```

Arguments

groups	Vector of group labels used in the simulation
p_c	Event (response) proportion in the control arm
direction	Test direction: 1 = larger p is better, 0 = smaller p is better
s1	Information fractions for the first stage / first group
s2	Information fractions for the second stage / second group
alpha_2	Type I error for the two-sided test
alpha_2_alps_s1	Type I error spent up to the interim analysis (stage 1 / group 1)
alpha_2_alps_s2	Cumulative type I error spent at the final analysis (stage 2 / group 2)
theta_cut	Efficacy cut-off on the effect-size scale applied at the interim analysis
samsz_1	Planned sample size (control arm) of the first stage / group
samsz_2	Planned sample size (control arm) of the second stage / group
N_max_1	Maximum allowed sample size (control arm) of the first stage / group
N_max_2	Maximum allowed sample size (control arm) of the second stage / group
beta	Type II error rate, i.e. 1 - power
sim_num	Number of simulation replicates

Value

A named list containing the following elements: 'Looks', 'Information fractions', 'O'Brien-Fleming boundaries'.

References

P. Gao & Y. Li (2024) Adaptive Multiple Comparison Sequential Design (AMCSD) for clinical trials, Journal of Biopharmaceutical Statistics, 34:3, 424-440, DOI:10.1080/10543406.2023.2233590. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2023.2233590

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
masd_simu_OC_binary(
groups = rbind(c(0.2,0.3,0.4),c(0.3,0.4,0.5),c(0.4,0.5,0.6),c(0.5,0.6,0.7)),
p_c = 0.2, direction = 1, s1 = c(1/3,2/3,1), s2 = c(0.5,1), alpha_2 = 0.05,
alpha_2_alps_s1 = c(0.001,0.001,0.048), alpha_2_alps_s2 = c(0.001,0.049), theta_cut = 0.01,
samsz_1 = 100, samsz_2 = 150, N_max_1 = 200, N_max_2 = 300, beta = 0.1, sim_num = 2)
```

---

masd_simu_OC_neg_binomial

Multiple comparisons Group sequential design: Simulations, Negative binomial distribution, Optimizing adaptive sequential design

---

Description

Multiple comparisons Group sequential design: Simulations, Negative binomial distribution, Optimizing adaptive sequential design

Usage

```
masd_simu_OC_neg_binomial(
  groups,
  r_c,
  kappa,
  direction,
  s1,
  s2,
  alpha_2,
```

```
  alpha_2_alps_s1,
  alpha_2_alps_s2,
  theta_cut,
  samsz_1,
  samsz_2,
  N_max_1,
  N_max_2,
  beta,
  sim_num
)
```

Arguments

groups	Vector of group labels used in the simulation
r_c	Rate parameter of the control arm (negative binomial endpoint)
kappa	Dispersion (size) parameter of the negative binomial distribution
direction	Test direction: 1 = larger r is better, 0 = smaller r is better
s1	Information fractions for the first stage / first group
s2	Information fractions for the second stage / second group
alpha_2	Type I error for the two-sided test
alpha_2_alps_s1	Type I error spent up to the interim analysis (stage 1 / group 1)
alpha_2_alps_s2	Cumulative type I error spent at the final analysis (stage 2 / group 2)
theta_cut	Efficacy cut-off on the effect-size scale applied at the interim analysis
samsz_1	Planned sample size (control arm) of the first stage / group
samsz_2	Planned sample size (control arm) of the second stage / group
N_max_1	Maximum allowed sample size (control arm) of the first stage / group
N_max_2	Maximum allowed sample size (control arm) of the second stage / group
beta	Type II error rate, i.e. 1 - power
sim_num	Number of simulation replicates

Value

A named list containing the following elements: 'Looks', 'Information fractions', 'O'Brien-Fleming boundaries'.

References

P. Gao & Y. Li (2024) Adaptive Multiple Comparison Sequential Design (AMCSD) for clinical trials, Journal of Biopharmaceutical Statistics, 34:3, 424-440, DOI:10.1080/10543406.2023.2233590. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2023.2233590

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
masd_simu_OC_neg_binomial(
groups = rbind(c(0.2,0.3,0.4),c(0.3,0.4,0.5),c(0.4,0.5,0.6),c(0.5,0.6,0.7)), r_c = 0.1,
kappa = 1, direction = 1, s1 = c(1/3,2/3,1), s2 = c(0.5,1), alpha_2 = 0.05,
alpha_2_alps_s1 = c(0.001,0.001,0.048), alpha_2_alps_s2 = c(0.001,0.049), theta_cut = 0.01,
samsz_1 = 100, samsz_2 = 150, N_max_1 = 200, N_max_2 = 300, beta = 0.1, sim_num = 2)
```

---

masd_simu_OC_normal *Multiple comparisons Group sequential design: Simulations, Normal distribution, Optimizing adaptive sequential design*

Description

Multiple comparisons Group sequential design: Simulations, Normal distribution, Optimizing adaptive sequential design

Usage

```
masd_simu_OC_normal(
  groups,
  mu_c,
  sigma_t,
  sigma_c,
  direction,
  s1,
  s2,
  alpha_2,
  alpha_2_alps_s1,
  alpha_2_alps_s2,
  theta_cut,
  samsz_1,
  samsz_2,
  N_max_1,
```

```
  N_max_2,
  beta,
  sim_num
)
```

Arguments

groups	Vector of group labels used in the simulation
mu_c	Mean of the control arm
sigma_t	Standard deviation of the test arm
sigma_c	Standard deviation of the control arm
direction	Test direction: 1 = larger mu is better, 0 = smaller mu is better
s1	Information fractions for the first stage / first group
s2	Information fractions for the second stage / second group
alpha_2	Type I error for the two-sided test
alpha_2_alps_s1	Type I error spent up to the interim analysis (stage 1 / group 1)
alpha_2_alps_s2	Cumulative type I error spent at the final analysis (stage 2 / group 2)
theta_cut	Efficacy cut-off on the effect-size scale applied at the interim analysis
samsz_1	Planned sample size (control arm) of the first stage / group
samsz_2	Planned sample size (control arm) of the second stage / group
N_max_1	Maximum allowed sample size (control arm) of the first stage / group
N_max_2	Maximum allowed sample size (control arm) of the second stage / group
beta	Type II error rate, i.e. 1 - power
sim_num	Number of simulation replicates

Value

A named list containing the following elements: 'Looks', 'Information fractions', 'O'Brien-Fleming boundaries'.

References

P. Gao & Y. Li (2024) Adaptive Multiple Comparison Sequential Design (AMCSD) for clinical trials, Journal of Biopharmaceutical Statistics, 34:3, 424-440, DOI:10.1080/10543406.2023.2233590. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2023.2233590

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
masd_simu_OC_normal(
groups = rbind(c(0.3,0.4,0.5),c(0.1,0.2,0.3),c(0.3,0.4,0.5),c(0.1,0.2,0.3)),
mu_c = 0, sigma_t = 1, sigma_c = 1, direction = 1, s1 = c(1/3,2/3,1), s2 = c(0.5,1),
alpha_2 = 0.05, alpha_2_alps_s1 = c(0.001,0.001,0.048), alpha_2_alps_s2 = c(0.001,0.049),
theta_cut = 0.01, samsz_1 = 100, samsz_2 = 150, N_max_1 = 200, N_max_2 = 300,
beta = 0.1, sim_num = 2)
```

---

masd_simu_OC_poisson *Multiple comparisons Group sequential design: Simulations, Poisson distribution, Optimizing adaptive sequential design*

Description

Multiple comparisons Group sequential design: Simulations, Poisson distribution, Optimizing adaptive sequential design

Usage

```
masd_simu_OC_poisson(
  groups,
  lambda_c,
  direction,
  s1,
  s2,
  alpha_2,
  alpha_2_alps_s1,
  alpha_2_alps_s2,
  theta_cut,
  samsz_1,
  samsz_2,
  N_max_1,
  N_max_2,
  beta,
  sim_num
)
```

Arguments

groups	Vector of group labels used in the simulation
lambda_c	Event rate in the control arm (Poisson / negative binomial endpoint)
direction	Test direction: 1 = larger lambda is better, 0 = smaller lambda is better
s1	Information fractions for the first stage / first group
s2	Information fractions for the second stage / second group
alpha_2	Type I error for the two-sided test
alpha_2_alps_s1	Type I error spent up to the interim analysis (stage 1 / group 1)
alpha_2_alps_s2	Cumulative type I error spent at the final analysis (stage 2 / group 2)
theta_cut	Efficacy cut-off on the effect-size scale applied at the interim analysis
samsz_1	Planned sample size (control arm) of the first stage / group
samsz_2	Planned sample size (control arm) of the second stage / group
N_max_1	Maximum allowed sample size (control arm) of the first stage / group
N_max_2	Maximum allowed sample size (control arm) of the second stage / group
beta	Type II error rate, i.e. 1 - power
sim_num	Number of simulation replicates

Value

A named list containing the following elements: 'Looks', 'Information fractions', 'O'Brien-Fleming boundaries'.

References

P. Gao & Y. Li (2024) Adaptive Multiple Comparison Sequential Design (AMCSD) for clinical trials, Journal of Biopharmaceutical Statistics, 34:3, 424-440, DOI:10.1080/10543406.2023.2233590. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2023.2233590

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
masd_simu_OC_poisson(
groups = rbind(c(0.2,0.3,0.4),c(0.3,0.4,0.5),c(0.4,0.5,0.6),c(0.5,0.6,0.7)),
lambda_c = 0, direction = 1, s1 = c(1/3,2/3,1), s2 = c(0.5,1), alpha_2 = 0.05,
alpha_2_alps_s1 = c(0.001,0.001,0.048), alpha_2_alps_s2 = c(0.001,0.049),
theta_cut = 0.01, samsz_1 = 100, samsz_2 = 150, N_max_1 = 200, N_max_2 = 300,
beta = 0.1, sim_num = 2)
```

---

masd_simu_OC_survival *Multiple comparisons Group sequential design: Simulations, Survival analysis, Optimizing adaptive sequential design*

Description

Multiple comparisons Group sequential design: Simulations, Survival analysis, Optimizing adaptive sequential design

Usage

```
masd_simu_OC_survival(
  groups,
  s1,
  s2,
  alpha_2,
  alpha_2_alps_s1,
  alpha_2_alps_s2,
  surv_rate,
  evt_num_1,
  evt_num_2,
  evt_max_1,
  evt_max_2,
  HR_cut,
  beta,
  sim_num
)
```

Arguments

groups	Vector of group labels used in the simulation
s1	Information fractions for the first stage / first group
s2	Information fractions for the second stage / second group
alpha_2	Type I error for the two-sided test
alpha_2_alps_s1	Type I error spent up to the interim analysis (stage 1 / group 1)

alpha_2_alps_s2	Cumulative type I error spent at the final analysis (stage 2 / group 2)
surv_rate	Survival rate used to translate the number of events into a sample size
evt_num_1	Number of events for the first stage / group
evt_num_2	Number of events for the second stage / group
evt_max_1	Maximum number of events for the first stage / group
evt_max_2	Maximum number of events for the second stage / group
HR_cut	Hazard-ratio cut-off for early stopping at the interim analysis
beta	Type II error rate, i.e. 1 - power
sim_num	Number of simulation replicates

Value

A named list containing the following elements: 'Looks', 'Information fractions', 'O'Brien-Fleming boundaries'.

References

P. Gao & Y. Li (2024) Adaptive Multiple Comparison Sequential Design (AMCSD) for clinical trials, Journal of Biopharmaceutical Statistics, 34:3, 424-440, DOI:10.1080/10543406.2023.2233590. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2023.2233590

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
masd_simu_OC_survival(
groups = rbind(c(1,1,1),c(0.9,0.85,0.8),c(0.8,0.84,0.85),c(0.5,0.6,0.7)),
s1 = c(1/3,2/3,1), s2 = c(0.5,1), alpha_2 = 0.05, alpha_2_alps_s1 = c(0.001,0.001,0.048),
alpha_2_alps_s2 = c(0.001,0.049), surv_rate = 0.5, evt_num_1 = 200, evt_num_2 = 300,
evt_max_1 = 800, evt_max_2 = 1000, HR_cut = 0.95, beta = 0.1, sim_num = 2)
```

`midpnt_sz` *Two-stage design: the midpoint design*

Description

Two-stage design: the midpoint design

Usage

```
midpnt_sz(alpha, beta, p_0, p_low, p_1, q, d_12_cut)
```

Arguments

`alpha`	One-sided type I error.
`beta`	Type II error.
`p_0`	Response rate indicating low activity with insufficient clinical benefit.
`p_low`	Minimally clinically beneficial response rate.
`p_1`	Assumed response rate.
`q`	0<q<1.
`d_12_cut`	Min(n2-n1) sets the minimal difference between n2 and n1 for the design.

Value

n1: Number of patients at first look.

n_2: Number of patients at second look. n_2 is also the total sample size.

r1: If no more than r1 responses are observed at the first look, then the trial would be stopped for futility.

r_2: The null hypothesis will be rejected if at least r_2 responses are observed at the end of the trial.

EN(p0) is the expected sample size under the null hypothesis.

PET(p0) is the probability of early termination under the null hypothesis.

PET_p is the probability of early termination under p=p_1.

PET_p_low is the probability of early termination under p=p_low.

power_p is the power under p=p_1.

power_p_low is the power under p=p_low.

Type I error is the probability of rejecting the null hypothesis under p<=p_0.

The minimax design has the smallest n_2 among all possible choices of (n1,r1,n2,r2).

The optimal design has the smallest EN(p_0)) among all possible choices of (n1,r1,n_2,r_2).

The n1 for the average design is the average of n1's from the minimax and the optimal designs.

References

R. Simon. Optimal Two-Stage Designs for Phase II Clinical Trials. Controlled Clinical Trials 10:1-10 (1989).

P. Gao & W. Zhang (15 Apr 2024): Adaptive sequential design for phase II single-arm oncology trials: an expansion of Simon's design, Journal of Biopharmaceutical Statistics, DOI: 10.1080/10543406.2024.2341673. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2341673.

Examples

```
midpnt_sz(alpha=c(0.001,0.024),beta=0.1,p_0=0.2,p_low=0.33,p_1=0.4,q=0.5,d_12_cut=5)
```

`MSD_power_alsp_boundary_binary_diff`

Multiple comparisons Group sequential design: Binary distribution, Power calculation, Alpha-spending boundary

---

Description

Multiple comparisons Group sequential design: Binary distribution, Power calculation, Alpha-spending boundary

Usage

```
MSD_power_alsp_boundary_binary_diff(
  p_t,
  p_c,
  margin,
  direction,
  s,
  alpha,
  sampsz_control,
  rand_ratio,
  dist1,
  dist2
)
```

Arguments

`p_t`	Event (response) proportion in the test arm
`p_c`	Event (response) proportion in the control arm
`margin`	Non-inferiority / superiority margin
`direction`	Test direction: 1 = larger p is better, 0 = smaller p is better
`s`	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1

alpha	One-sided significance level (type I error rate)
sampsz_control	Control arm sample size
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
dist1	Endpoint / distribution indicator for the first stage
dist2	Endpoint / distribution indicator for the second stage

Value

A named list containing the following elements: 'power', 'Type I error control'.

References

P. Gao & Y. Li (2024) Adaptive Multiple Comparison Sequential Design (AMCSD) for clinical trials, Journal of Biopharmaceutical Statistics, 34:3, 424-440, DOI:10.1080/10543406.2023.2233590. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2023.2233590

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
MSD_power_alsp_boundary_binary_diff(p_t = c(0.2,0.3,0.4), p_c = 0.5, margin = 0.1,
direction = 1, s = c(1/3,2/3,1), alpha = c(0.001,0.001,0.048), sampsz_control = 68,
rand_ratio = 1, dist1 = 1, dist2 = 1)
```

MSD_power_alsp_boundary_neg_binomial

Multiple comparisons Group sequential design: Negative binomial distribution, Power calculation, Alpha-spending boundary

---

Description

Multiple comparisons Group sequential design: Negative binomial distribution, Power calculation, Alpha-spending boundary

Usage

```
MSD_power_alsp_boundary_neg_binomial(
  r_t,
  r_c,
  margin,
  direction,
  s,
  alpha,
  sampsz_control,
  rand_ratio,
  nu_t,
  kappa,
  dist
)
```

Arguments

r_t	Rate parameter of the test arm (negative binomial endpoint)
r_c	Rate parameter of the control arm (negative binomial endpoint)
margin	Non-inferiority / superiority margin
direction	Test direction: 1 = larger r is better, 0 = smaller r is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha	One-sided significance level (type I error rate)
sampsz_control	Control arm sample size
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
nu_t	exposure time
kappa	dispersion parameter
dist	Indicator of the endpoint / distribution type

Value

A named list containing the following elements: 'power', 'Type I error control', 'Reference'.

References

P. Gao & Y. Li (2024) Adaptive Multiple Comparison Sequential Design (AMCSD) for clinical trials, Journal of Biopharmaceutical Statistics, 34:3, 424-440, DOI:10.1080/10543406.2023.2233590. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2023.2233590

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024

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P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
MSD_power_alsp_boundary_neg_binomial(r_t=c(0.2,0.3,0.4), r_c=0.6, margin=0.1, direction=1,
s=c(1/3,2/3,1), alpha = c(0.001,0.001,0.023), sampsz_control = 90, rand_ratio = 1,
nu_t = 1, kappa = 1, dist = 1)
```

MSD_power_alsp_boundary_normal

Multiple comparisons Group sequential design: Normal distribution, Power calculation, Alpha-spending boundary

---

Description

Multiple comparisons Group sequential design: Normal distribution, Power calculation, Alpha-spending boundary

Usage

```
MSD_power_alsp_boundary_normal(
  mu_t,
  mu_c,
  std_t,
  std_c,
  margin,
  direction,
  s,
  alpha,
  sampsz_control,
  rand_ratio,
  dist1,
  dist2
)
```

Arguments

mu_t	Means of the test arm
mu_c	Means of the control arm

std_t	Standard deviation of the test arm
std_c	Standard deviation of the control arm
margin	Non-inferiority / superiority margin
direction	Test direction: 1 = larger mu is better, 0 = smaller mu is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha	One-sided significance level (type I error rate)
sampsz_control	Control arm sample size
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
dist1	Endpoint / distribution indicator for the first stage
dist2	Endpoint / distribution indicator for the second stage

Value

A named list containing the following elements: 'power', 'Type I error control'.

References

P. Gao & Y. Li (2024) Adaptive Multiple Comparison Sequential Design (AMCSD) for clinical trials, Journal of Biopharmaceutical Statistics, 34:3, 424-440, DOI:10.1080/10543406.2023.2233590. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2023.2233590

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
MSD_power_alsp_boundary_normal(mu_t = c(0.2,0.3,0.4), mu_c = 0, std_t = 1, std_c = 1,
margin = 0, direction = 1, s = c(1/3,2/3,1),
alpha = c(0.001,0.001,0.023), sampsz_control = 148, rand_ratio = 1, dist1 = 1, dist2 = 1)
```

`MSD_power_alsp_boundary_poisson` *Multiple comparisons Group sequential design: Poisson distribution, Power calculation, Alpha-spending boundary*

Description

Multiple comparisons Group sequential design: Poisson distribution, Power calculation, Alpha-spending boundary

Usage

```
MSD_power_alsp_boundary_poisson(
  lambda_t,
  lambda_c,
  margin,
  direction,
  s,
  alpha,
  sampsz_control,
  rand_ratio,
  dist1,
  dist2
)
```

Arguments

`lambda_t`	Event rate in the test arm (Poisson / negative binomial endpoint)
`lambda_c`	Event rate in the control arm (Poisson / negative binomial endpoint)
`margin`	Non-inferiority / superiority margin
`direction`	Test direction: 1 = larger lambda is better, 0 = smaller lambda is better
`s`	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
`alpha`	One-sided significance level (type I error rate)
`sampsz_control`	Control arm sample size
`rand_ratio`	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
`dist1`	Endpoint / distribution indicator for the first stage
`dist2`	Endpoint / distribution indicator for the second stage

Value

A named list containing the following elements: 'power', 'Type I error control'.

References

P. Gao & Y. Li (2024) Adaptive Multiple Comparison Sequential Design (AMCSD) for clinical trials, Journal of Biopharmaceutical Statistics, 34:3, 424-440, DOI:10.1080/10543406.2023.2233590. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2023.2233590

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
MSD_power_alsp_boundary_poisson(lambda_t = c(0.2,0.3,0.4), lambda_c = 0.5, margin = 0.1,
direction = 2, s = c(1/3,2/3,1),
alpha = c(0.001,0.001,0.023), sampsz_control = 67, rand_ratio = 1, dist1 = 1, dist2 = 1)
```

`MSD_power_alsp_boundary_survival_Schoenfeld`

Multiple comparisons Group sequential design: Survival analysis, Power calculation, Alpha-spending boundary

---

Description

Multiple comparisons Group sequential design: Survival analysis, Power calculation, Alpha-spending boundary

Usage

```
MSD_power_alsp_boundary_survival_Schoenfeld(
  HR,
  margin,
  direction,
  s,
  alpha,
  events_tot,
  rand_ratio,
  dist1,
  dist2
)
```

Arguments

HR	Hazard ratio (test vs control)
margin	Non-inferiority / superiority margin
direction	Test direction: 1 = larger HR is better, 0 = smaller HR is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha	One-sided significance level (type I error rate)
events_tot	'events_tot' as used by this function; see Examples.
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
dist1	Endpoint / distribution indicator for the first stage
dist2	Endpoint / distribution indicator for the second stage

Value

A named list containing the following elements: 'power', 'Type I error control', 'reference'.

References

P. Gao & Y. Li (2024) Adaptive Multiple Comparison Sequential Design (AMCSD) for clinical trials, Journal of Biopharmaceutical Statistics, 34:3, 424-440, DOI:10.1080/10543406.2023.2233590. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2023.2233590

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
MSD_power_alsp_boundary_survival_Schoenfeld(HR = c(0.2,0.3,0.4), margin = 1.1, direction = 2,
s = c(1/3,2/3,1), alpha = c(0.001,0.001,0.023),
events_tot = 17, rand_ratio = 1, dist1 = 1, dist2 = 1)
```

MSD_power_OF_boundary_binary_diff *Multiple comparisons Group sequential design: Binary distribution, Power calculation, O'Brien-Fleming boundary*

Description

Multiple comparisons Group sequential design: Binary distribution, Power calculation, O'Brien-Fleming boundary

Usage

```
MSD_power_OF_boundary_binary_diff(
  p_t,
  p_c,
  margin,
  direction,
  s,
  alpha,
  sampsz_control,
  rand_ratio,
  dist1,
  dist2
)
```

Arguments

p_t	Event (response) proportion in the test arm
p_c	Event (response) proportion in the control arm
margin	Non-inferiority / superiority margin
direction	Test direction: 1 = larger p is better, 0 = smaller p is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha	One-sided significance level (type I error rate)
sampsz_control	Control arm sample size
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
dist1	Endpoint / distribution indicator for the first stage
dist2	Endpoint / distribution indicator for the second stage

Value

A named list containing the following elements: 'power', 'Type I error control'.

References

P. Gao & Y. Li (2024) Adaptive Multiple Comparison Sequential Design (AMCSD) for clinical trials, Journal of Biopharmaceutical Statistics, 34:3, 424-440, DOI:10.1080/10543406.2023.2233590. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2023.2233590

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
MSD_power_OF_boundary_binary_diff(p_t = 0.4, p_c = 0.3, margin = 0.1, direction = 0,
s = c(1/3, 2/3, 1), alpha = 0.025, sampsz_control = 100,
rand_ratio = 1, dist1 = 1, dist2 = 1)
```

MSD_power_OF_boundary_neg_binomial

Multiple comparisons Group sequential design: Negative binomial distribution, Power calculation, O'Brien-Fleming boundary

---

Description

Multiple comparisons Group sequential design: Negative binomial distribution, Power calculation, O'Brien-Fleming boundary

Usage

```
MSD_power_OF_boundary_neg_binomial(
  r_t,
  r_c,
  margin,
  direction,
  s,
  alpha,
  sampsz_control,
  rand_ratio,
  nu_t,
  kappa,
```

```
  dist1,
  dist2
)
```

Arguments

r_t	Rate parameter of the test arm (negative binomial endpoint)
r_c	Rate parameter of the control arm (negative binomial endpoint)
margin	Non-inferiority / superiority margin
direction	Test direction: 1 = larger r is better, 0 = smaller r is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha	One-sided significance level (type I error rate)
sampsz_control	Control arm sample size
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
nu_t	exposure time
kappa	dispersion parameter
dist1	Endpoint / distribution indicator for the first stage
dist2	Endpoint / distribution indicator for the second stage

Value

A named list containing the following elements: 'power', 'Type I error control', 'Reference'.

References

P. Gao & Y. Li (2024) Adaptive Multiple Comparison Sequential Design (AMCSD) for clinical trials, Journal of Biopharmaceutical Statistics, 34:3, 424-440, DOI:10.1080/10543406.2023.2233590. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2023.2233590

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
MSD_power_OF_boundary_neg_binomial(r_t = c(1.1, 1.1, 1.1), r_c = 1.1, margin = 0.1,
direction = 0, s = c(1/3, 2/3, 1), alpha = 0.025, sampsz_control = 100, rand_ratio = 1,
nu_t = 6, kappa = 1, dist1 = 1, dist2 = 1)
```

MSD_power_OF_boundary_normal

Multiple comparisons Group sequential design: Normal distribution, Power calculation, O'Brien-Fleming boundary

---

Description

Multiple comparisons Group sequential design: Normal distribution, Power calculation, O'Brien-Fleming boundary

Usage

```
MSD_power_OF_boundary_normal(
  mu_t,
  mu_c,
  std_t,
  std_c,
  margin,
  direction,
  s,
  alpha,
  sampsz_control,
  rand_ratio,
  dist1,
  dist2
)
```

Arguments

mu_t	Means of the test arm
mu_c	Means of the control arm
std_t	Standard deviation of the test arm
std_c	Standard deviation of the control arm
margin	Non-inferiority / superiority margin
direction	Test direction: 1 = larger mu is better, 0 = smaller mu is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha	One-sided significance level (type I error rate)

sampsz_control	Control arm sample size
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
dist1	Endpoint / distribution indicator for the first stage
dist2	Endpoint / distribution indicator for the second stage

Value

A named list containing the following elements: 'power', 'Type I error control'.

References

P. Gao & Y. Li (2024) Adaptive Multiple Comparison Sequential Design (AMCSD) for clinical trials, Journal of Biopharmaceutical Statistics, 34:3, 424-440, DOI:10.1080/10543406.2023.2233590. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2023.2233590

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
MSD_power_OF_boundary_normal(mu_t = 2.6, mu_c = 0.6, std_t = 9.43, std_c = 9.86, margin = 0.1,
direction = 0, s = c(1/3, 2/3, 1),
alpha = 0.025, sampsz_control = 100, rand_ratio = 1, dist1 = 1, dist2 = 1)
```

MSD_power_OF_boundary_poisson

Multiple comparisons Group sequential design: Poisson distribution, Power calculation, O'Brien-Fleming boundary

---

Description

Multiple comparisons Group sequential design: Poisson distribution, Power calculation, O'Brien-Fleming boundary

Usage

```
MSD_power_OF_boundary_poisson(
  lambda_t,
  lambda_c,
  margin,
  direction,
  s,
  alpha,
  sampsz_control,
  rand_ratio,
  dist1,
  dist2
)
```

Arguments

lambda_t	Event rate in the test arm (Poisson / negative binomial endpoint)
lambda_c	Event rate in the control arm (Poisson / negative binomial endpoint)
margin	Non-inferiority / superiority margin
direction	Test direction: 1 = larger lambda is better, 0 = smaller lambda is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha	One-sided significance level (type I error rate)
sampsz_control	Control arm sample size
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
dist1	Endpoint / distribution indicator for the first stage
dist2	Endpoint / distribution indicator for the second stage

Value

A named list containing the following elements: 'power', 'Type I error control'.

References

P. Gao & Y. Li (2024) Adaptive Multiple Comparison Sequential Design (AMCSD) for clinical trials, Journal of Biopharmaceutical Statistics, 34:3, 424-440, DOI:10.1080/10543406.2023.2233590. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2023.2233590

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
MSD_power_OF_boundary_poisson(lambda_t = 1.1, lambda_c = 1.0, margin = 0.1, direction = 0,
s = c(1/3, 2/3, 1), alpha = 0.025, sampsz_control = 100, rand_ratio = 1, dist1 = 1, dist2 = 1)
```

MSD_power_OF_boundary_survival_Schoenfeld

Multiple comparisons Group sequential design: Survival analysis, Power calculation, O'Brien-Fleming boundary

---

Description

Multiple comparisons Group sequential design: Survival analysis, Power calculation, O'Brien-Fleming boundary

Usage

```
MSD_power_OF_boundary_survival_Schoenfeld(
  HR,
  margin,
  direction,
  s,
  alpha,
  events_tot,
  rand_ratio,
  dist1,
  dist2
)
```

Arguments

HR	Hazard ratio (test vs control)
margin	Non-inferiority / superiority margin
direction	Test direction: 1 = larger HR is better, 0 = smaller HR is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha	One-sided significance level (type I error rate)
events_tot	'events_tot' as used by this function; see Examples.

rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
dist1	Endpoint / distribution indicator for the first stage
dist2	Endpoint / distribution indicator for the second stage

Value

A named list containing the following elements: 'power', 'Type I error control', 'reference'.

References

P. Gao & Y. Li (2024) Adaptive Multiple Comparison Sequential Design (AMCSD) for clinical trials, Journal of Biopharmaceutical Statistics, 34:3, 424-440, DOI:10.1080/10543406.2023.2233590. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2023.2233590

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
MSD_power_OF_boundary_survival_Schoenfeld(HR = 0.7, margin = 0.1, direction = 0,
s = c(1/3, 2/3, 1), alpha = 0.025, events_tot = 100,
rand_ratio = 1, dist1 = 1, dist2 = 1)
```

---

msd_power_simu_binary *Multiple comparisons Group sequential design: Simulations, Binary distribution, Type I error and power*

Description

Multiple comparisons Group sequential design: Simulations, Binary distribution, Type I error and power

Usage

```
msd_power_simu_binary(
  p_t,
  p_c,
  direction,
  s,
  bry_type,
  alpha_2,
  samsz,
  sim_num
)
```

Arguments

p_t	Event (response) proportion in the test arm
p_c	Event (response) proportion in the control arm
direction	Test direction: 1 = larger p is better, 0 = smaller p is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
bry_type	Critical boundary type: 1 = O'Brien-Fleming, 2 = Pocock, 3 = alpha-spending
alpha_2	Type I error for the two-sided test
samsz	Planned sample size of the control arm used in the simulation
sim_num	Number of simulation replicates

Value

A named list containing the following elements: 'simulation summary', 'planned control sample size', 'planned total sample size'.

References

P. Gao & Y. Li (2024) Adaptive Multiple Comparison Sequential Design (AMCSD) for clinical trials, Journal of Biopharmaceutical Statistics, 34:3, 424-440, DOI:10.1080/10543406.2023.2233590. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2023.2233590

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
msd_power_simu_binary(p_t = c(0.4,0.4), p_c = 0.4, direction = 1, s = c(1/3,2/3,1),
bry_type = 1, alpha_2 = 0.05, samsz = 100, sim_num = 20)
```

`msd_power_simu_neg_binomial` *Multiple comparisons Group sequential design: Simulations, Negative binomial distribution, Type I error and power*

Description

Multiple comparisons Group sequential design: Simulations, Negative binomial distribution, Type I error and power

Usage

```
msd_power_simu_neg_binomial(
  r_t,
  r_c,
  kappa,
  direction,
  s,
  bry_type,
  alpha_2,
  samsz,
  sim_num
)
```

Arguments

`r_t`	Rate parameter of the test arm (negative binomial endpoint)
`r_c`	Rate parameter of the control arm (negative binomial endpoint)
`kappa`	Dispersion (size) parameter of the negative binomial distribution
`direction`	Test direction: 1 = larger r is better, 0 = smaller r is better
`s`	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
`bry_type`	Critical boundary type: 1 = O'Brien-Fleming, 2 = Pocock, 3 = alpha-spending
`alpha_2`	Type I error for the two-sided test
`samsz`	Planned sample size of the control arm used in the simulation
`sim_num`	Number of simulation replicates

Value

A named list containing the following elements: 'simulation summary', 'planned control', 'planned total'.

References

P. Gao & Y. Li (2024) Adaptive Multiple Comparison Sequential Design (AMCSD) for clinical trials, Journal of Biopharmaceutical Statistics, 34:3, 424-440, DOI:10.1080/10543406.2023.2233590. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2023.2233590

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

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P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
msd_power_simu_neg_binomial(r_t = c(1.1,1.1,1.1), r_c = 1.1, kappa = 1, direction = 1,
s = c(1/3,2/3,1), bry_type = 1, alpha_2 = 0.05, samsz = 100, sim_num = 20)
```

---

msd_power_simu_normal *Multiple comparisons Group sequential design: Simulations, Normal distribution, Type I error and power*

Description

Multiple comparisons Group sequential design: Simulations, Normal distribution, Type I error and power

Usage

```
msd_power_simu_normal(
  mu_t,
  mu_c,
  sigma_t,
  sigma_c,
  direction,
  s,
```

```
  bry_type,
  alpha_2,
  samsz,
  sim_num
)
```

Arguments

mu_t	Means of the test arm
mu_c	Means of the control arm
sigma_t	Standard deviation of the test arm
sigma_c	Standard deviation of the control arm
direction	Test direction: 1 = larger mu is better, 0 = smaller mu is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
bry_type	Critical boundary type: 1 = O'Brien-Fleming, 2 = Pocock, 3 = alpha-spending
alpha_2	Type I error for the two-sided test
samsz	Planned sample size of the control arm used in the simulation
sim_num	Number of simulation replicates

Value

A matrix in which each row corresponds to one simulation replicate and the columns hold the simulated operating characteristics (e.g. rejection indicators, sample sizes and stopping stages).

References

P. Gao & Y. Li (2024) Adaptive Multiple Comparison Sequential Design (AMCSD) for clinical trials, Journal of Biopharmaceutical Statistics, 34:3, 424-440, DOI:10.1080/10543406.2023.2233590. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2023.2233590

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
msd_power_simu_normal(mu_t = c(0,0,0), mu_c = 0, sigma_t = 1, sigma_c = 1, direction = 1,
s = c(1/3,2/3,1), bry_type = 1, alpha_2 = 0.05, samsz = 100, sim_num = 20)
```

---

msd_power_simu_poisson

Multiple comparisons Group sequential design: Simulations, Poisson distribution, Type I error and power

---

Description

Multiple comparisons Group sequential design: Simulations, Poisson distribution, Type I error and power

Usage

```
msd_power_simu_poisson(
  lambda_c,
  lambda_t,
  direction,
  s,
  bry_type,
  alpha_2,
  samsz,
  sim_num
)
```

Arguments

lambda_c	Event rate in the control arm (Poisson / negative binomial endpoint)
lambda_t	Event rate in the test arm (Poisson / negative binomial endpoint)
direction	Test direction: 1 = larger lambda is better, 0 = smaller lambda is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
bry_type	Critical boundary type: 1 = O'Brien-Fleming, 2 = Pocock, 3 = alpha-spending
alpha_2	Type I error for the two-sided test
samsz	Planned sample size of the control arm used in the simulation
sim_num	Number of simulation replicates

Value

A named list containing the following elements: 'simulation summary', 'planned control', 'planned total'.

References

P. Gao & Y. Li (2024) Adaptive Multiple Comparison Sequential Design (AMCSD) for clinical trials, Journal of Biopharmaceutical Statistics, 34:3, 424-440, DOI:10.1080/10543406.2023.2233590. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2023.2233590

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
msd_power_simu_poisson(lambda_c = 0.8, lambda_t = c(0.8,0.8,0.8), direction = 1,
s = c(1/3,2/3,1), bry_type = 1, alpha_2 = 0.05, samsz = 100, sim_num = 20)
```

`msd_power_simu_survival`

Multiple comparisons Group sequential design: Simulations, Survival analysis, Type I error and power

---

Description

Multiple comparisons Group sequential design: Simulations, Survival analysis, Type I error and power

Usage

```
msd_power_simu_survival(HR, s, bry_type, alpha_2, surv_rate, evt_num, sim_num)
```

Arguments

`HR`	Hazard ratio (test vs control)
`s`	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
`bry_type`	Critical boundary type: 1 = O'Brien-Fleming, 2 = Pocock, 3 = alpha-spending
`alpha_2`	Type I error for the two-sided test
`surv_rate`	Survival rate used to translate the number of events into a sample size
`evt_num`	Total number of events at the final analysis
`sim_num`	Number of simulation replicates

Value

A named list containing the following elements: 'simulation summary', 'planned control', 'planned total'.

References

P. Gao & Y. Li (2024) Adaptive Multiple Comparison Sequential Design (AMCSD) for clinical trials, Journal of Biopharmaceutical Statistics, 34:3, 424-440, DOI:10.1080/10543406.2023.2233590. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2023.2233590

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
msd_power_simu_survival(HR = c(0.8,0.8), s = c(1/3,2/3,1), bry_type = 1, alpha_2 = 0.05,
surv_rate = 0.5, evt_num = 800, sim_num = 20)
```

MSD_Sample_size_alsp_boundary_binary_diff

Multiple comparisons Group sequential design: Binary distribution, Sample size calculation, Alpha-spending boundary

---

Description

Multiple comparisons Group sequential design: Binary distribution, Sample size calculation, Alpha-spending boundary

Usage

```
MSD_Sample_size_alsp_boundary_binary_diff(
  p_t,
  p_c,
  margin,
  direction,
  s,
```

```
  alpha,
  beta,
  rand_ratio,
  dist1,
  dist2
)
```

Arguments

p_t	Event (response) proportion in the test arm
p_c	Event (response) proportion in the control arm
margin	Non-inferiority / superiority margin
direction	Test direction: 1 = larger p is better, 0 = smaller p is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha	One-sided significance level (type I error rate)
beta	Type II error rate, i.e. 1 - power
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
dist1	Endpoint / distribution indicator for the first stage
dist2	Endpoint / distribution indicator for the second stage

Value

A named list containing the following elements: 'test arm sample size', 'control arm sample size', 'sample size for each dose in a two arm study with same critical boudary', 'sample size for control arm corresponding to each dose in a two arm study with same critical boudary', 'Type I error control'.

References

P. Gao & Y. Li (2024) Adaptive Multiple Comparison Sequential Design (AMCSD) for clinical trials, Journal of Biopharmaceutical Statistics, 34:3, 424-440, DOI:10.1080/10543406.2023.2233590. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2023.2233590

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
MSD_Sample_size_alsp_boundary_binary_diff(p_t = 0.4, p_c = 0.3, margin = 0.1, direction = 0,
s = c(1/3, 2/3, 1), alpha = 0.025, beta = 0.1, rand_ratio = 1, dist1 = 1, dist2 = 1)
```

MSD_Sample_size_alsp_boundary_neg_binomial

Multiple comparisons Group sequential design: Negative binomial distribution, Sample size calculation, Alpha-spending boundary

---

Description

Multiple comparisons Group sequential design: Negative binomial distribution, Sample size calculation, Alpha-spending boundary

Usage

```
MSD_Sample_size_alsp_boundary_neg_binomial(
  r_t,
  r_c,
  margin,
  direction,
  s,
  alpha,
  beta,
  rand_ratio,
  nu_t,
  kappa,
  dist1,
  dist2
)
```

Arguments

r_t	Rate parameter of the test arm (negative binomial endpoint)
r_c	Rate parameter of the control arm (negative binomial endpoint)
margin	Non-inferiority / superiority margin
direction	Test direction: 1 = larger r is better, 0 = smaller r is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha	One-sided significance level (type I error rate)
beta	Type II error rate, i.e. 1 - power
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm

nu_t	exposure time
kappa	dispersion parameter
dist1	Endpoint / distribution indicator for the first stage
dist2	Endpoint / distribution indicator for the second stage

Value

A named list containing the following elements: 'test arm sample size', 'control arm sample size', 'sample size for each dose in a two arm study with same critical boudary', 'sample size for control arm corresponding to each dose in a two arm study with same critical boudary', 'Type I error control', 'Reference'.

References

P. Gao & Y. Li (2024) Adaptive Multiple Comparison Sequential Design (AMCSD) for clinical trials, Journal of Biopharmaceutical Statistics, 34:3, 424-440, DOI:10.1080/10543406.2023.2233590. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2023.2233590

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
MSD_Sample_size_alsp_boundary_neg_binomial(r_t = c(0.2,0.3,0.4), r_c = 0.6, margin = 0.1,
direction = 1, s = c(1/3,2/3,1), alpha = c(0.001,0.001,0.023), beta = 0.1, rand_ratio = 1,
nu_t = 1, kappa = 1, dist1 = 1, dist2 = 1)
```

MSD_Sample_size_alsp_boundary_normal

Multiple comparisons Group sequential design: Normal distribution, Sample size calculation, Alpha-spending boundary

---

Description

Multiple comparisons Group sequential design: Normal distribution, Sample size calculation, Alpha-spending boundary

Usage

```
MSD_Sample_size_alsp_boundary_normal(
  mu_t,
  mu_c,
  std_t,
  std_c,
  margin,
  direction,
  s,
  alpha,
  beta,
  rand_ratio,
  dist1,
  dist2
)
```

Arguments

mu_t	Means of the test arm
mu_c	Means of the control arm
std_t	Standard deviation of the test arm
std_c	Standard deviation of the control arm
margin	Non-inferiority / superiority margin
direction	Test direction: 1 = larger mu is better, 0 = smaller mu is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha	One-sided significance level (type I error rate)
beta	Type II error rate, i.e. 1 - power
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
dist1	Endpoint / distribution indicator for the first stage
dist2	Endpoint / distribution indicator for the second stage

Value

A named list containing the following elements: 'test arm sample size', 'control arm sample size', 'sample size for each dose in a two arm study with same critical boudary', 'sample size for control arm corresponding to each dose in a two arm study with same critical boudary', 'Type I error control'.

References

P. Gao & Y. Li (2024) Adaptive Multiple Comparison Sequential Design (AMCSD) for clinical trials, Journal of Biopharmaceutical Statistics, 34:3, 424-440, DOI:10.1080/10543406.2023.2233590. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2023.2233590

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
MSD_Sample_size_alsp_boundary_normal(mu_t = 2.6, mu_c = 0.6, std_t = 9.43, std_c = 9.86,
margin = 0.1, direction = 0, s = c(1/3, 2/3, 1),
alpha = 0.025, beta = 0.1, rand_ratio = 1, dist1 = 1, dist2 = 1)
```

`MSD_Sample_size_alsp_boundary_poisson`

Multiple comparisons Group sequential design: Poisson distribution, Sample size calculation, Alpha-spending boundary

---

Description

Multiple comparisons Group sequential design: Poisson distribution, Sample size calculation, Alpha-spending boundary

Usage

```
MSD_Sample_size_alsp_boundary_poisson(
  lambda_t,
  lambda_c,
  margin,
  direction,
  s,
  alpha,
  beta,
  rand_ratio,
  dist1,
  dist2
)
```

Arguments

lambda_t	Event rate in the test arm (Poisson / negative binomial endpoint)
lambda_c	Event rate in the control arm (Poisson / negative binomial endpoint)
margin	Non-inferiority / superiority margin
direction	Test direction: 1 = larger lambda is better, 0 = smaller lambda is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha	One-sided significance level (type I error rate)
beta	Type II error rate, i.e. 1 - power
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
dist1	Endpoint / distribution indicator for the first stage
dist2	Endpoint / distribution indicator for the second stage

Value

A named list containing the following elements: 'test arm sample size', 'control arm sample size', 'sample size for each dose in a two arm study with same critical boudary', 'sample size for control arm corresponding to each dose in a two arm study with same critical boudary', 'Type I error control'.

References

P. Gao & Y. Li (2024) Adaptive Multiple Comparison Sequential Design (AMCSD) for clinical trials, Journal of Biopharmaceutical Statistics, 34:3, 424-440, DOI:10.1080/10543406.2023.2233590. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2023.2233590

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
MSD_Sample_size_alsp_boundary_poisson(lambda_t = 1.1, lambda_c = 1.0, margin = 0.1,
direction = 0, s = c(1/3, 2/3, 1), alpha = 0.025,
beta = 0.1, rand_ratio = 1, dist1 = 1, dist2 = 1)
```

`MSD_Sample_size_alsp_boundary_survival_Schoenfeld` *Multiple comparisons Group sequential design: Survival analysis, Sample size calculation, Alpha-spending boundary*

Description

Multiple comparisons Group sequential design: Survival analysis, Sample size calculation, Alpha-spending boundary

Usage

```
MSD_Sample_size_alsp_boundary_survival_Schoenfeld(
  HR,
  margin,
  direction,
  s,
  alpha,
  beta,
  rand_ratio,
  dist1,
  dist2
)
```

Arguments

`HR`	Hazard ratio (test vs control)
`margin`	Non-inferiority / superiority margin
`direction`	Test direction: 1 = larger HR is better, 0 = smaller HR is better
`s`	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
`alpha`	One-sided significance level (type I error rate)
`beta`	Type II error rate, i.e. 1 - power
`rand_ratio`	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
`dist1`	Endpoint / distribution indicator for the first stage
`dist2`	Endpoint / distribution indicator for the second stage

Value

A named list containing the following elements: 'Combined number of events between a dose and control', 'total number of events from all doses and control', 'combined number of events in each dose and control in a two arm study with same critical boudary', 'Type I error control', 'reference'.

References

P. Gao & Y. Li (2024) Adaptive Multiple Comparison Sequential Design (AMCSD) for clinical trials, Journal of Biopharmaceutical Statistics, 34:3, 424-440, DOI:10.1080/10543406.2023.2233590. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2023.2233590

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

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P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
MSD_Sample_size_alsp_boundary_survival_Schoenfeld(HR = 0.7, margin = 0.1, direction = 0,
s = c(1/3, 2/3, 1), alpha = 0.025, beta = 0.1,
rand_ratio = 1, dist1 = 1, dist2 = 1)
```

MSD_Sample_size_OF_boundary_binary_diff

Multiple comparisons Group sequential design: Binary distribution, Sample size calculation, O'Brien-Fleming boundary

---

Description

Multiple comparisons Group sequential design: Binary distribution, Sample size calculation, O'Brien-Fleming boundary

Usage

```
MSD_Sample_size_OF_boundary_binary_diff(
  p_t,
  p_c,
  margin,
  direction,
  s,
  alpha,
  beta,
  rand_ratio,
  dist1,
  dist2
)
```

Arguments

p_t	Event (response) proportion in the test arm
p_c	Event (response) proportion in the control arm
margin	Non-inferiority / superiority margin
direction	Test direction: 1 = larger p is better, 0 = smaller p is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha	One-sided significance level (type I error rate)
beta	Type II error rate, i.e. 1 - power
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
dist1	Endpoint / distribution indicator for the first stage
dist2	Endpoint / distribution indicator for the second stage

Value

A named list containing the following elements: 'test arm sample size', 'control arm sample size', 'sample size for each dose in a two arm study with same critical boudary', 'sample size for control arm corresponding to each dose in a two arm study with same critical boudary', 'Type I error control'.

References

P. Gao & Y. Li (2024) Adaptive Multiple Comparison Sequential Design (AMCSD) for clinical trials, Journal of Biopharmaceutical Statistics, 34:3, 424-440, DOI:10.1080/10543406.2023.2233590. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2023.2233590

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
MSD_Sample_size_OF_boundary_binary_diff(p_t = 0.4, p_c = 0.3, margin = 0.1, direction = 0,
s = c(1/3, 2/3, 1), alpha = 0.025, beta = 0.1,
rand_ratio = 1, dist1 = 1, dist2 = 1)
```

`MSD_Sample_size_OF_boundary_neg_binomial`
Multiple comparisons Group sequential design: Negative binomial distribution, Sample size calculation, O'Brien-Fleming boundary

Description

Multiple comparisons Group sequential design: Negative binomial distribution, Sample size calculation, O'Brien-Fleming boundary

Usage

```
MSD_Sample_size_OF_boundary_neg_binomial(
  r_t,
  r_c,
  margin,
  direction,
  s,
  alpha,
  beta,
  rand_ratio,
  nu_t,
  kappa,
  dist1,
  dist2
)
```

Arguments

`r_t`	Rate parameter of the test arm (negative binomial endpoint)
`r_c`	Rate parameter of the control arm (negative binomial endpoint)
`margin`	Non-inferiority / superiority margin
`direction`	Test direction: 1 = larger r is better, 0 = smaller r is better
`s`	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
`alpha`	One-sided significance level (type I error rate)
`beta`	Type II error rate, i.e. 1 - power
`rand_ratio`	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
`nu_t`	exposure time
`kappa`	dispersion parameter
`dist1`	Endpoint / distribution indicator for the first stage
`dist2`	Endpoint / distribution indicator for the second stage

Value

A named list containing the following elements: 'test arm sample size', 'control arm sample size', 'sample size for each dose in a two arm study with same critical boudary', 'sample size for control arm corresponding to each dose in a two arm study with same critical boudary', 'Type I error control', 'Reference'.

References

P. Gao & Y. Li (2024) Adaptive Multiple Comparison Sequential Design (AMCSD) for clinical trials, Journal of Biopharmaceutical Statistics, 34:3, 424-440, DOI:10.1080/10543406.2023.2233590. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2023.2233590

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
MSD_Sample_size_OF_boundary_neg_binomial(r_t = c(1.1, 1.1, 1.1), r_c = 1.1, margin = 0.1,
direction = 0, s = c(1/3, 2/3, 1),
alpha = 0.025, beta = 0.1, rand_ratio = 1, nu_t = 6, kappa = 1, dist1 = 1, dist2 = 1)
```

MSD_Sample_size_OF_boundary_normal

Multiple comparisons Group sequential design: Normal distribution, Sample size calculation, O'Brien-Fleming boundary

---

Description

Multiple comparisons Group sequential design: Normal distribution, Sample size calculation, O'Brien-Fleming boundary

Usage

```
MSD_Sample_size_OF_boundary_normal(
  mu_t,
  mu_c,
  std_t,
```

```
  std_c,
  margin,
  direction,
  s,
  alpha,
  beta,
  rand_ratio,
  dist1,
  dist2
)
```

Arguments

mu_t	Means of the test arm
mu_c	Means of the control arm
std_t	Standard deviation of the test arm
std_c	Standard deviation of the control arm
margin	Non-inferiority / superiority margin
direction	Test direction: 1 = larger mu is better, 0 = smaller mu is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha	One-sided significance level (type I error rate)
beta	Type II error rate, i.e. 1 - power
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
dist1	Endpoint / distribution indicator for the first stage
dist2	Endpoint / distribution indicator for the second stage

Value

A named list containing the following elements: 'test arm sample size', 'control arm sample size', 'sample size for each dose in a two arm study with same critical boudary', 'sample size for control arm corresponding to each dose in a two arm study with same critical boudary', 'Type I error control'.

References

P. Gao & Y. Li (2024) Adaptive Multiple Comparison Sequential Design (AMCSD) for clinical trials, Journal of Biopharmaceutical Statistics, 34:3, 424-440, DOI:10.1080/10543406.2023.2233590. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2023.2233590

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
MSD_Sample_size_OF_boundary_normal(mu_t = 2.6, mu_c = 0.6, std_t = 9.43, std_c = 9.86,
margin = 0.1, direction = 0, s = c(1/3, 2/3, 1),
alpha = 0.025, beta = 0.1, rand_ratio = 1, dist1 = 1, dist2 = 1)
```

MSD_Sample_size_OF_boundary_poisson

Multiple comparisons Group sequential design: Poisson distribution, Sample size calculation, O'Brien-Fleming boundary

---

Description

Multiple comparisons Group sequential design: Poisson distribution, Sample size calculation, O'Brien-Fleming boundary

Usage

```
MSD_Sample_size_OF_boundary_poisson(
  lambda_t,
  lambda_c,
  margin,
  direction,
  s,
  alpha,
  beta,
  rand_ratio,
  dist1,
  dist2
)
```

Arguments

lambda_t	Event rate in the test arm (Poisson / negative binomial endpoint)
lambda_c	Event rate in the control arm (Poisson / negative binomial endpoint)
margin	Non-inferiority / superiority margin
direction	Test direction: 1 = larger lambda is better, 0 = smaller lambda is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1

alpha	One-sided significance level (type I error rate)
beta	Type II error rate, i.e. 1 - power
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
dist1	Endpoint / distribution indicator for the first stage
dist2	Endpoint / distribution indicator for the second stage

Value

A named list containing the following elements: 'test arm sample size', 'control arm sample size', 'sample size for each dose in a two arm study with same critical boudary', 'sample size for control arm corresponding to each dose in a two arm study with same critical boudary', 'Type I error control'.

References

P. Gao & Y. Li (2024) Adaptive Multiple Comparison Sequential Design (AMCSD) for clinical trials, Journal of Biopharmaceutical Statistics, 34:3, 424-440, DOI:10.1080/10543406.2023.2233590. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2023.2233590

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
MSD_Sample_size_OF_boundary_poisson(lambda_t = 1.1, lambda_c = 1.0, margin = 0.1, direction = 0,
s = c(1/3, 2/3, 1), alpha = 0.025,
beta = 0.1, rand_ratio = 1, dist1 = 1, dist2 = 1)
```

MSD_Sample_size_OF_boundary_survival_Schoenfeld

Multiple comparisons Group sequential design: Survival analysis, Sample size calculation, O'Brien-Fleming boundary

---

Description

Multiple comparisons Group sequential design: Survival analysis, Sample size calculation, O'Brien-Fleming boundary

Usage

```
MSD_Sample_size_OF_boundary_survival_Schoenfeld(
  HR,
  margin,
  direction,
  s,
  alpha,
  beta,
  rand_ratio,
  dist1,
  dist2
)
```

Arguments

HR	Hazard ratio (test vs control)
margin	Non-inferiority / superiority margin
direction	Test direction: 1 = larger HR is better, 0 = smaller HR is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha	One-sided significance level (type I error rate)
beta	Type II error rate, i.e. 1 - power
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
dist1	Endpoint / distribution indicator for the first stage
dist2	Endpoint / distribution indicator for the second stage

Value

A named list containing the following elements: 'Combined number of events between a dose and control', 'total number of events from all doses and control', 'combined number of events in each dose and control in a two arm study with same critical boudary', 'Type I error control', 'reference'.

References

P. Gao & Y. Li (2024) Adaptive Multiple Comparison Sequential Design (AMCSD) for clinical trials, Journal of Biopharmaceutical Statistics, 34:3, 424-440, DOI:10.1080/10543406.2023.2233590. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2023.2233590

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
MSD_Sample_size_OF_boundary_survival_Schoenfeld(HR = 0.7, margin = 0.1, direction = 0,
s = c(1/3, 2/3, 1), alpha = 0.025, beta = 0.1, rand_ratio = 1, dist1 = 1, dist2 = 1)
```

---

new_sample_size_hybrid

Hybrid: New sample size estimation

Description

Hybrid: New sample size estimation

Usage

```
new_sample_size_hybrid(
  N_planned,
  c_bry,
  t_prior,
  theta_prior,
  N_inter,
  t_inter,
  theta_hat_inter,
  gamma,
  beta
)
```

Arguments

N_planned	Planned sample size at the final analysis
c_bry	Vector of critical boundaries for each analysis
t_prior	The prior is assumed to have a normal distribution. This is the mean of the prior distribution
theta_prior	The prior distribution of theta is assumed to have a normal distribution. The Fisher's information time is the reciprocal of the variance from the prior distribution
N_inter	Sample size at interim analysis
t_inter	Information time at interim analysis

theta_hat_inter
: Treatment effect estimate observed at the interim analysis

gamma
: Parameter chosen for the credible interval modified predictive power (CI_MPP)

beta
: Type II error rate, i.e. 1 - power

Value

The new sample sizes are calculated with both non-informative prior and informative prior

References

Gao, P. Improving the effectiveness of sample size re-estimation: an operating characteristic focused, hybrid frequentist-Bayesian approach, Statistics in Medicine, 2025; 44:e10310. To link to this article: https://onlinelibrary.wiley.com/doi/10.1002/sim.10310.

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796.

C. R. Mehta, S. J. Pocock. Adaptive increase in sample size when interim results are promising: A practical guide with examples. Statistics in Medicine. Volume30, Issue28, 10 December 2011, Pages 3267-3284

Examples

```
new_sample_size_hybrid(N_planned = 100, c_bry = 1.96, t_prior = 45, theta_prior = 0.5,
N_inter = 60, t_inter = 50, theta_hat_inter = 0.3, gamma = 0.5, beta = 0.1)
```

---

one_arm_ad_3_stg_binary

Simulations: adaptive three stage design

Description

Simulations: adaptive three stage design

Usage

```
one_arm_ad_3_stg_binary(
  p_1,
  p_0,
  n_1,
  r_1,
  n_2,
  r_2,
  r_2_e = NA,
```

```
  n_3,
  r_3,
  N_max,
  beta,
  sim_num
)
```

Arguments

p_1	The assumed response rate.
p_0	Response rate indicating low activity with insufficient clinical benefit.
n_1	Number of patients at first look.
r_1	If no more than r_1 responses are observed at the first look, then the trial would be stopped for futility.
n_2	Number of patients at second look.
r_2	If no more than r_2 responses are observed at the second look, then the trial would be stopped for futility.
r_2_e	The trial would be stopped for superiority if at least r_2_e responses are observed at the second look. If r_2_e is not used in the design, enter NA.
n_3	Number of patients at third look.
r_3	If no more than r_3 responses are observed at the third look, then the null hypothesis will not be rejected.
N_max	Maximum sample size for the trial.
beta	Type II error. The target power is 1-beta.
sim_num	Purpose of simulation: To verify type I error control by setting p_1=p_0, To evaluate the operating characteristics of the adaptive design and to determine if continuity correction is necessary.

Value

Average sample size is EN(p_1).

Rate of termination is PET(p_1)

If rejection rate without continuity correction does not exceed alpha, the continuity correction is not needed for this group of parameters p_0,n_1,r_1,n_2,r_2,r_2_e,n_3,r_3. Otherwise, continuity correction should be applied.

References

R. Simon. Optimal Two-Stage Designs for Phase II Clinical Trials. Controlled Clinical Trials 10:1-10 (1989).

P. Gao & W. Zhang (15 Apr 2024): Adaptive sequential design for phase II single-arm oncology trials: an expansion of Simon's design, Journal of Biopharmaceutical Statistics, DOI: 10.1080/10543406.2024.2341673. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2341673.

P. Gao, J.H. Ware, C. Mehta, (2008), Sample size re-estimation for adaptive sequential designs. Journal of Biopharmaceutical Statistics, 18: 1184–1196, 2008.

Examples

```
one_arm_ad_3_stg_binary(p_1=0.2,p_0=0.2,n_1=37,r_1=8,n_2=100,r_2=22,r_2_e=33,
n_3=105,r_3=29,N_max=150,beta=0.1,sim_num=20)
```

`one_arm_ad_two_stg_binary` *Simulations: adaptive two stage design*

Description

Simulations: adaptive two stage design

Usage

```
one_arm_ad_two_stg_binary(
  p_1,
  p_0,
  n_1,
  r_1,
  r_1_e = NA,
  n_2,
  r_2,
  N_max,
  beta,
  sim_num
)
```

Arguments

`p_1`	The assumed response rate.
`p_0`	Response rate indicating low activity with insufficient clinical benefit.
`n_1`	Number of patients at first look.
`r_1`	If no more than r_1 responses are observed at the first look, then the trial would be stopped for futility.
`r_1_e`	The trial would be stopped for superiority if at least r_1_e responses are observed at the first look. If r_1_e is not used in the design, enter NA.
`n_2`	Number of patients at second look.
`r_2`	If no more than r_2 responses are observed at the second look, then the null hypothesis will be rejected.
`N_max`	Maximum sample size for the trial.
`beta`	Type II error. The target power is 1-beta.
`sim_num`	Purpose of simulation: To verify type I error control by setting p_1=p_0, To evaluate the operating characteristics of the adaptive design and to determine if continuity correction is necessary.

Value

Average sample size is EN(p_1).

Rate of termination is PET(p_1)

If rejection rate without continuity correction does not exceed alpha, the continuity correction is not needed for this group of parameters p_0,n_1,r_1,r_1_e,n_2,r_2. Otherwise, continuity correction should be applied.

References

R. Simon. Optimal Two-Stage Designs for Phase II Clinical Trials. Controlled Clinical Trials 10:1-10 (1989).

P. Gao & W. Zhang (15 Apr 2024): Adaptive sequential design for phase II single-arm oncology trials: an expansion of Simon's design, Journal of Biopharmaceutical Statistics, DOI: 10.1080/10543406.2024.2341673. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2341673.

P. Gao, J.H. Ware, C. Mehta, (2008), Sample size re-estimation for adaptive sequential designs. Journal of Biopharmaceutical Statistics, 18: 1184–1196, 2008.

Examples

```
one_arm_ad_two_stg_binary(p_1=0.2,p_0=0.2,n_1=37,r_1=9,r_1_e=NA,n_2=53,r_2=16,
N_max=140,beta=0.1,sim_num=20)
```

---

one_arm_rej_2_stg_binary

Simulations: Two stage fixed expanded Simon's design: either hybrid or mid-point design

---

Description

Simulations: Two stage fixed expanded Simon's design: either hybrid or mid-point design

Usage

```
one_arm_rej_2_stg_binary(p_1, p_0, n_1, r_1_f, r_1_e = NA, n_2, r_2, sim_num)
```

Arguments

p_1	The assumed response rate.
p_0	Response rate indicating low activity with insufficient clinical benefit.
n_1	Number of patients at first look.
r_1_f	If no more than r_1 responses are observed at the first look, then the trial would be stopped for futility.

r_1_e	The trial would be stopped for superiority if at least r_1_e responses are observed at the first look. If r_1_e is not used in the design, enter NA.
n_2	Number of patients at second look.
r_2	If no more than r_2 responses are observed at the second look, then the null hypothesis will be rejected.
sim_num	Purpose of simulation: To verify type I error control by setting p_1=p_0, To verify the parameters n_1,r_1_f,r_1_e,n_2,r_2 are correctly chosen, such that the rejection rate matches that from the design table from either the hybrid design or the mid-point design.

Value

Average sample size is EN(p_1).

Rate of termination is PET(p_1)

References

R. Simon. Optimal Two-Stage Designs for Phase II Clinical Trials. Controlled Clinical Trials 10:1-10 (1989).

P. Gao & W. Zhang (15 Apr 2024): Adaptive sequential design for phase II single-arm oncology trials: an expansion of Simon's design, Journal of Biopharmaceutical Statistics, DOI: 10.1080/10543406.2024.2341673. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2341673.

P. Gao, J.H. Ware, C. Mehta, (2008), Sample size re-estimation for adaptive sequential designs. Journal of Biopharmaceutical Statistics, 18: 1184–1196, 2008.

Examples

```
one_arm_rej_2_stg_binary(p_1=0.2,p_0=0.2,n_1=100,r_1_f=25,r_1_e=33,
n_2=105,r_2=29,sim_num=20)
```

---

one_arm_rej_3_stg_binary

Simulations: Expanded Simon's design: the three stage design, no sample size change

---

Description

Simulations: Expanded Simon's design: the three stage design, no sample size change

Usage

```
one_arm_rej_3_stg_binary(
  p_1,
  p_0,
  n_1,
  r_1,
  n_2,
  r_2_f,
  r_2_e = NA,
  n_3,
  r_3,
  sim_num
)
```

Arguments

p_1	The assumed response rate.
p_0	Response rate indicating low activity with insufficient clinical benefit.
n_1	Number of patients at first look.
r_1	If no more than r_1 responses are observed at the first look, then the trial would be stopped for futility.
n_2	Number of patients at second look.
r_2_f	If no more than responses are observed at the second look, then the trial would be stopped for futility.
r_2_e	The trial would be stopped for superiority if at least r_2_e responses are observed at the first look. If r_2_e is not used in the design, enter NA.
n_3	Number of patients at third look.
r_3	If at least r_2 responses are observed at the third look, then the null hypothesis will be rejected.
sim_num	Purpose of simulation: To verify type I error control by setting p_1=p_0, To verify the parameters n_1,r_1,n_2,r_2_f,r_2_e,n_3,r_3 are correctly chosen, such that the rejection rate matches that from the design table of the three-stage design.

Value

Average sample size is EN(p_1).

Rate of termination is PET(p_1)

References

R. Simon. Optimal Two-Stage Designs for Phase II Clinical Trials. Controlled Clinical Trials 10:1-10 (1989).

P. Gao & W. Zhang (15 Apr 2024): Adaptive sequential design for phase II single-arm oncology trials: an expansion of Simon's design, Journal of Biopharmaceutical Statistics, DOI: 10.1080/10543406.2024.2341673.

To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2341673.

P. Gao, J.H. Ware, C. Mehta, (2008), Sample size re-estimation for adaptive sequential designs. Journal of Biopharmaceutical Statistics, 18: 1184–1196, 2008.

Examples

```
one_arm_rej_3_stg_binary(p_1=0.2,p_0=0.2,n_1=37,r_1=8,n_2=100,r_2_f=22,r_2_e=33,
n_3=105,r_3=29,sim_num=20)
```

`one_arm_rej_simon_binary`

Simulations: two stage fixed Simon's design

Description

Simulations: two stage fixed Simon's design

Usage

```
one_arm_rej_simon_binary(p_1, p_0, n_1, r_1, n_2, r_2, sim_num)
```

Arguments

`p_1`	The assumed response rate.
`p_0`	Response rate indicating low activity with insufficient clinical benefit.
`n_1`	Number of patients at first look.
`r_1`	If no more than r_1 responses are observed at the first look, then the trial would be stopped for futility.
`n_2`	Number of patients at second look.
`r_2`	If no more than r_2 responses are observed at the second look, then the null hypothesis will be rejected.
`sim_num`	Purpose of simulation: To verify type I error control by setting p_1=p_0, To verify the parameters n_1,r_1,n_2,r_2 are correctly chosen, such that the trial has 1-beta power if the true response rate is p_1.

Value

Average sample size is EN(p_1).

Rate of termination is PET(p_1)

References

R. Simon. Optimal Two-Stage Designs for Phase II Clinical Trials. Controlled Clinical Trials 10:1-10 (1989).

P. Gao & W. Zhang (15 Apr 2024): Adaptive sequential design for phase II single-arm oncology trials: an expansion of Simon's design, Journal of Biopharmaceutical Statistics, DOI: 10.1080/10543406.2024.2341673. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2341673.

P. Gao, J.H. Ware, C. Mehta, (2008), Sample size re-estimation for adaptive sequential designs. Journal of Biopharmaceutical Statistics, 18: 1184–1196, 2008.

Examples

```
one_arm_rej_simon_binary(p_1=0.4,p_0=0.2,n_1=37,r_1=9,n_2=53,r_2=16,sim_num=20)
```

---

power_alsp_boundary_binary_diff

Group sequential designs / Adaptive sequential designs: Binary distribution, Superiority trial, Power calculation, Alpha-spending boundary

---

Description

Group sequential designs / Adaptive sequential designs: Binary distribution, Superiority trial, Power calculation, Alpha-spending boundary

Usage

```
power_alsp_boundary_binary_diff(
  p_t,
  p_c,
  s,
  alpha_2,
  sampsz_control,
  rand_ratio
)
```

Arguments

p_t	Mean of the test arm
p_c	Mean of the control arm
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha_2	Type I error for the two-sided test
sampsz_control	Control arm sample size
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm

Value

The output will display the power

Examples

```
power_alsp_boundary_binary_diff(p_t = 0.2, p_c = 0.6, s = c(1/3,2/3,1),
alpha_2 = c(0.001,0.001,0.048), sampsz_control = 27, rand_ratio = 1)
```

---

power_alsp_boundary_binary_diff_NI

Group sequential designs / Adaptive sequential designs: Binary distribution, Non-inferiority trial, Power calculation, Alpha-spending boundary

---

Description

Group sequential designs / Adaptive sequential designs: Binary distribution, Non-inferiority trial, Power calculation, Alpha-spending boundary

Usage

```
power_alsp_boundary_binary_diff_NI(
  p_t,
  p_c,
  margin,
  direction,
  s,
  alpha,
  sampsz_control,
  rand_ratio
)
```

Arguments

p_t	Mean of the test arm
p_c	Mean of the control arm
margin	Non-inferiority margin
direction	Test direction: 1 = larger p_t is better, 0 = smaller p_t is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha	One-sided significance level (type I error rate)
sampsz_control	Control arm sample size
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm

Value

The output will display the power

Examples

```
power_alsp_boundary_binary_diff_NI(p_t = 0.2, p_c = 0.6, margin = 0.15, direction = 1,
s = c(1/3,2/3,1), alpha = c(0.001,0.001,0.023), sampsz_control = 14, rand_ratio = 1)
```

---

power_alsp_boundary_neg_binomial

Group sequential designs / Adaptive sequential designs: Negative binomial distribution, Superiority trial, Power calculation, Alpha-spending boundary

---

Description

Group sequential designs / Adaptive sequential designs: Negative binomial distribution, Superiority trial, Power calculation, Alpha-spending boundary

Usage

```
power_alsp_boundary_neg_binomial(
  r_t,
  r_c,
  s,
  alpha_2,
  sampsz_control,
  rand_ratio,
  nu_t,
  kappa
)
```

Arguments

r_t	Mean of the test arm
r_c	Mean of the control arm
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha_2	Type I error for the two-sided test
sampsz_control	Control arm sample size
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
nu_t	exposure time
kappa	dispersion parameter

Value

The output will display the power

Examples

```
power_alsp_boundary_neg_binomial(r_t = 1, r_c = 0.8, s = 1, alpha_2 = 0.05,
sampsz_control = 897, rand_ratio = 1, nu_t = 1, kappa = 1)
```

---

power_alsp_boundary_neg_binomial_NI

Group sequential designs / Adaptive sequential designs: Negative binomial distribution, Non-inferiority trial, Power calculation, Alpha-spending boundary

---

Description

Group sequential designs / Adaptive sequential designs: Negative binomial distribution, Non-inferiority trial, Power calculation, Alpha-spending boundary

Usage

```
power_alsp_boundary_neg_binomial_NI(
  r_t,
  r_c,
  margin,
  direction,
  s,
  alpha,
  sampsz_control,
  rand_ratio,
  nu_t,
  kappa
)
```

Arguments

r_t	Mean of the test arm
r_c	Mean of the control arm
margin	Non-inferiority margin
direction	Test direction: 1 = larger r_t is better, 0 = smaller r_t is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha	One-sided significance level (type I error rate)
sampsz_control	Control arm sample size

rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
nu_t	exposure time
kappa	dispersion parameter

Value

The output will display the power

Examples

```
power_alsp_boundary_neg_binomial_NI(r_t = 1, r_c = 0.8, margin = 0, direction = 1, s = 1,
alpha = 0.025, sampsz_control = 897, rand_ratio = 1, nu_t = 1, kappa = 1)
```

---

power_alsp_boundary_normal

Group sequential designs / Adaptive sequential designs: Normal distribution, Superiority trial, Power calculation, Alpha-spending boundary

---

Description

Group sequential designs / Adaptive sequential designs: Normal distribution, Superiority trial, Power calculation, Alpha-spending boundary

Usage

```
power_alsp_boundary_normal(
  mu_t,
  mu_c,
  std_t,
  std_c,
  s,
  sampsz_control,
  rand_ratio,
  alpha_2
)
```

Arguments

mu_t	Mean of the test arm
mu_c	Mean of the control arm
std_t	Standard deviation of the test arm
std_c	Standard deviation of the control arm

s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
sampsz_control	Control arm sample size
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
alpha_2	Type I error for the two-sided test

Value

The output will display the power

Examples

```
power_alsp_boundary_normal(mu_t = 0.2, mu_c = 0, std_t = 1, std_c = 1, s = c(1/3,2/3,1),
sampsz_control = 527, rand_ratio = 1, alpha_2 = c(0.001,0.001,0.048))
```

---

power_alsp_boundary_normal_NI

Group sequential designs / Adaptive sequential designs: Normal distribution, Non-inferiority trial, Power calculation, Alpha-spending boundary

---

Description

Group sequential designs / Adaptive sequential designs: Normal distribution, Non-inferiority trial, Power calculation, Alpha-spending boundary

Usage

```
power_alsp_boundary_normal_NI(
  mu_t,
  mu_c,
  std_t,
  std_c,
  margin,
  direction,
  s,
  sampsz_control,
  rand_ratio,
  alpha
)
```

Arguments

mu_t	Mean of the test arm
mu_c	Mean of the control arm
std_t	Standard deviation of the test arm
std_c	Standard deviation of the control arm
margin	Non-inferiority margin
direction	Test direction: 1 = larger mu is better, 0 = smaller mu is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
sampsz_control	Control arm sample size
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
alpha	One-sided significance level (type I error rate)

Value

The output will display the power

Examples

```
power_alsp_boundary_normal_NI(mu_t = 0.2, mu_c = 0, std_t = 1, std_c = 1, margin = 0.15,
direction = 1, s = c(1/3,2/3,1), sampsz_control = 534, rand_ratio = 1, alpha = c(0.001,0.001,0.023))
```

---

power_alsp_boundary_poisson

Group sequential designs / Adaptive sequential designs: Poisson distribution, Superiority trial, Power calculation, Alpha-spending boundary

---

Description

Group sequential designs / Adaptive sequential designs: Poisson distribution, Superiority trial, Power calculation, Alpha-spending boundary

Usage

```
power_alsp_boundary_poisson(
  lambda_t,
  lambda_c,
  s,
  alpha_2,
  sampsz_control,
  rand_ratio
)
```

Arguments

lambda_t	Mean of the test arm
lambda_c	Mean of the control arm
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha_2	Type I error for the two-sided test
sampsz_control	Control arm sample size
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm

Value

The output will display the power

Examples

```
power_alsp_boundary_poisson(lambda_t = 0.2, lambda_c = 0.4, s = c(1/3,2/3,1),
alpha_2 = c(0.001,0.001,0.048), sampsz_control = 158, rand_ratio = 1)
```

---

power_alsp_boundary_poisson_NI

Group sequential designs / Adaptive sequential designs: Poisson distribution, Non-inferiority trial, Power calculation, Alpha-spending boundary

---

Description

Group sequential designs / Adaptive sequential designs: Poisson distribution, Non-inferiority trial, Power calculation, Alpha-spending boundary

Usage

```
power_alsp_boundary_poisson_NI(
  lambda_t,
  lambda_c,
  margin,
  direction,
  s,
  alpha,
  sampsz_control,
  rand_ratio
)
```

Arguments

lambda_t	Mean of the test arm
lambda_c	Mean of the control arm
margin	Non-inferiority margin
direction	Test direction: 1 = larger lambda is better, 0 = smaller lambda is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha	One-sided significance level (type I error rate)
sampsz_control	Control arm sample size
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm

Value

The output will display the power

Examples

```
power_alsp_boundary_poisson_NI(lambda_t = 0.2, lambda_c = 0.4, margin = 0.15, direction = 1,
s = c(1/3,2/3,1), alpha = c(0.001,0.001,0.023), sampsz_control = 52, rand_ratio = 1)
```

---

power_alsp_boundary_survival_Schoenfeld

Group sequential designs / Adaptive sequential designs: Survival analysis, Superiority trial, Power calculation, Alpha-spending boundary

---

Description

Group sequential designs / Adaptive sequential designs: Survival analysis, Superiority trial, Power calculation, Alpha-spending boundary

Usage

```
power_alsp_boundary_survival_Schoenfeld(HR, s, events_tot, alpha_2, rand_ratio)
```

Arguments

HR	Hazards ratio of test arm vs. the control arm
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
events_tot	Total number of events
alpha_2	Type I error for the two-sided test
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm

Value

The output will display the power

Examples

```
power_alsp_boundary_survival_Schoenfeld(HR = 0.8, s = c(0.5,1), events_tot = 841,
alpha_2 = c(0.001,0.0499), rand_ratio = 1)
```

---

power_alsp_boundary_survival_Schoenfeld_NI

Group sequential designs / Adaptive sequential designs: Survival analysis, Non-inferiority trial, Power calculation, Alpha-spending boundary

---

Description

Group sequential designs / Adaptive sequential designs: Survival analysis, Non-inferiority trial, Power calculation, Alpha-spending boundary

Usage

```
power_alsp_boundary_survival_Schoenfeld_NI(
  HR,
  margin,
  direction,
  s,
  events_tot,
  alpha,
  rand_ratio
)
```

Arguments

HR	Hazards ratio of test arm vs. the control arm
margin	Non-inferiority margin
direction	Test direction: 1 = larger HR is better, 0 = smaller HR is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
events_tot	Total number of events
alpha	One-sided significance level (type I error rate)
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm

Value

The output will display the power

Examples

```
power_alsp_boundary_survival_Schoenfeld_NI(HR = 0.8, margin = 1.1, direction = 1, s = c(0.5,1),
events_tot = 416, alpha = c(0.001,0.024), rand_ratio = 1)
```

---

power_binary_diff *Fixed sample designs: Binary distribution, Superiority trial, Power calculation*

Description

Fixed sample designs: Binary distribution, Superiority trial, Power calculation

Usage

```
power_binary_diff(p_t, p_c, alpha_2, n_control, rand_ratio)
```

Arguments

p_t	The event rate of the test arm
p_c	The event rate of the control arm
alpha_2	One-sided type I error rate used for boundary calibration
n_control	Sample size of the control arm
rand_ratio	Randomization ratio is the ratio of the number of subjects in the test arm vs. the number of subjects in the control arm

Value

The output will show the power

Examples

```
power_binary_diff(p_t = 0.4, p_c = 0.3, alpha_2 = 0.05, n_control = 53, rand_ratio = 1)
```

power_binary_diff_NI *Fixed sample designs: Binary distribution, Non-inferiority trial, Power calculation*

Description

Fixed sample designs: Binary distribution, Non-inferiority trial, Power calculation

Usage

```
power_binary_diff_NI(p_t, p_c, margin, direction, alpha, n_control, rand_ratio)
```

Arguments

p_t	The event rate of the test arm
p_c	The event rate of the control arm
margin	the non-inferiority margin
direction	Test direction: 1 = larger p_t,p_c are better, 0 = smaller p_t,p_c are better
alpha	The type I error for the one-sided test
n_control	Sample size of the control arm
rand_ratio	Randomization ratio is the ratio of the number of subjects in the test arm vs. the number of subjects in the control arm

Value

The output will show the power

Examples

```
power_binary_diff_NI(p_t = 0.4, p_c = 0.3, margin = 0.1, direction = 0, alpha = 0.025,
n_control = 53, rand_ratio = 1)
```

power_OF_boundary_binary_diff

Group sequential designs / Adaptive sequential designs: Binary distribution, Superiority trial, Power calculation, O'Brien-Fleming boundary

Description

Group sequential designs / Adaptive sequential designs: Binary distribution, Superiority trial, Power calculation, O'Brien-Fleming boundary

Usage

```
power_OF_boundary_binary_diff(p_t, p_c, s, alpha_2, sampsz_control, rand_ratio)
```

Arguments

p_t	Mean of the test arm
p_c	Mean of the control arm
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha_2	Type I error for the two-sided test
sampsz_control	Control arm sample size
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm

Value

The output will display the power

Examples

```
power_OF_boundary_binary_diff(p_t = 0.4, p_c = 0.3, s = c(1/3, 2/3, 1), alpha_2 = 0.05,
sampsz_control = 100, rand_ratio = 1)
```

---

power_OF_boundary_binary_diff_NI

Group sequential designs / Adaptive sequential designs: Binary distribution, Non-inferiority trial, Power calculation, O'Brien-Fleming boundary

---

Description

Group sequential designs / Adaptive sequential designs: Binary distribution, Non-inferiority trial, Power calculation, O'Brien-Fleming boundary

Usage

```
power_OF_boundary_binary_diff_NI(
  p_t,
  p_c,
  margin,
  direction,
  s,
  alpha,
  sampsz_control,
  rand_ratio
)
```

Arguments

p_t	Mean of the test arm
p_c	Mean of the control arm
margin	Non-inferiority margin
direction	Test direction: 1 = larger p_t is better, 0 = smaller p_t is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha	One-sided significance level (type I error rate)
sampsz_control	Control arm sample size
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm

Value

The output will display the power

Examples

```
power_OF_boundary_binary_diff_NI(p_t = 0.4, p_c = 0.3, margin = 0.1, direction = 0,
s = c(1/3, 2/3, 1), alpha = 0.025, sampsz_control = 100, rand_ratio = 1)
```

---

power_OF_boundary_neg_binomial

Group sequential designs / Adaptive sequential designs: Negative binomial distribution, Superiority trial, Power calculation, O'Brien-Fleming boundary

---

Description

Group sequential designs / Adaptive sequential designs: Negative binomial distribution, Superiority trial, Power calculation, O'Brien-Fleming boundary

Usage

```
power_OF_boundary_neg_binomial(
  r_t,
  r_c,
  s,
  alpha_2,
  sampsz_control,
  rand_ratio,
  nu_t,
  kappa
)
```

Arguments

r_t	Mean of the test arm
r_c	Mean of the control arm
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha_2	Type I error for the two-sided test
sampsz_control	Control arm sample size
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
nu_t	exposure time
kappa	dispersion parameter

Value

The output will display the power

Examples

```
power_OF_boundary_neg_binomial(r_t = c(1.1, 1.1, 1.1), r_c = 1.1, s = c(1/3, 2/3, 1),
alpha_2 = 0.05, sampsz_control = 100, rand_ratio = 1, nu_t = 6, kappa = 1)
```

---

power_OF_boundary_neg_binomial_NI

Group sequential designs / Adaptive sequential designs: Negative binomial distribution, Non-inferiority trial, Power calculation, O'Brien-Fleming boundary

---

Description

Group sequential designs / Adaptive sequential designs: Negative binomial distribution, Non-inferiority trial, Power calculation, O'Brien-Fleming boundary

Usage

```
power_OF_boundary_neg_binomial_NI(
  r_t,
  r_c,
  margin,
  direction,
  s,
  alpha,
  sampsz_control,
  rand_ratio,
  nu_t,
  kappa
)
```

Arguments

r_t	Mean of the test arm
r_c	Mean of the control arm
margin	Non-inferiority margin
direction	Test direction: 1 = larger r_t is better, 0 = smaller r_t is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha	One-sided significance level (type I error rate)
sampsz_control	Control arm sample size
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
nu_t	exposure time
kappa	dispersion parameter

Value

The output will display the power

Examples

```
power_OF_boundary_neg_binomial_NI(r_t = c(1.1, 1.1, 1.1), r_c = 1.1, margin = 0.1,
direction = 0, s = c(1/3, 2/3, 1), alpha = 0.025, sampsz_control = 100, rand_ratio = 1,
nu_t = 6, kappa = 1)
```

---

power_OF_boundary_normal

Group sequential designs / Adaptive sequential designs: Normal distribution, Superiority trial, Power calculation, O'Brien-Fleming boundary

---

Description

Group sequential designs / Adaptive sequential designs: Normal distribution, Superiority trial, Power calculation, O'Brien-Fleming boundary

Usage

```
power_OF_boundary_normal(
  mu_t,
  mu_c,
  std_t,
  std_c,
  s,
```

```
  sampsz_control,
  rand_ratio,
  alpha_2
)
```

Arguments

mu_t	Mean of the test arm
mu_c	Mean of the control arm
std_t	Standard deviation of the test arm
std_c	Standard deviation of the control arm
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
sampsz_control	Control arm sample size
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
alpha_2	Type I error for the two-sided test

Value

The output will display the power

Examples

```
power_OF_boundary_normal(mu_t = 2.6, mu_c = 0.6, std_t = 9.43, std_c = 9.86, s = c(1/3, 2/3, 1),
sampsz_control = 100, rand_ratio = 1, alpha_2 = 0.05)
```

---

power_OF_boundary_normal_NI

Group sequential designs / Adaptive sequential designs: Normal distribution, Non-inferiority trial, Power calculation, O'Brien-Fleming boundary

---

Description

Group sequential designs / Adaptive sequential designs: Normal distribution, Non-inferiority trial, Power calculation, O'Brien-Fleming boundary

Usage

```
power_OF_boundary_normal_NI(
  mu_t,
  mu_c,
  std_t,
  std_c,
  margin,
  direction,
  s,
  sampsz_control,
  rand_ratio,
  alpha
)
```

Arguments

mu_t	Mean of the test arm
mu_c	Mean of the control arm
std_t	Standard deviation of the test arm
std_c	Standard deviation of the control arm
margin	Non-inferiority margin
direction	Test direction: 1 = larger mu is better, 0 = smaller mu is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
sampsz_control	Control arm sample size
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
alpha	One-sided significance level (type I error rate)

Value

The output will display the power

Examples

```
power_OF_boundary_normal_NI(mu_t = 2.6, mu_c = 0.6, std_t = 9.43, std_c = 9.86, margin = 0.1,
direction = 0, s = c(1/3, 2/3, 1), sampsz_control = 100, rand_ratio = 1, alpha = 0.025)
```

power_OF_boundary_poisson

Group sequential designs / Adaptive sequential designs: Poisson distribution, Superiority trial, Power calculation, O'Brien-Fleming boundary

Description

Group sequential designs / Adaptive sequential designs: Poisson distribution, Superiority trial, Power calculation, O'Brien-Fleming boundary

Usage

```
power_OF_boundary_poisson(
  lambda_t,
  lambda_c,
  s,
  alpha_2,
  sampsz_control,
  rand_ratio
)
```

Arguments

lambda_t	Mean of the test arm
lambda_c	Mean of the control arm
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha_2	Type I error for the two-sided test
sampsz_control	Control arm sample size
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm

Value

The output will display the power

Examples

```
power_OF_boundary_poisson(lambda_t = 1.1, lambda_c = 1.0, s = c(1/3, 2/3, 1),
alpha_2 = 0.05, sampsz_control = 100, rand_ratio = 1)
```

power_OF_boundary_poisson_NI

Group sequential designs / Adaptive sequential designs: Poisson distribution, Non-inferiority trial, Power calculation, O'Brien-Fleming boundary

Description

Group sequential designs / Adaptive sequential designs: Poisson distribution, Non-inferiority trial, Power calculation, O'Brien-Fleming boundary

Usage

```
power_OF_boundary_poisson_NI(
  lambda_t,
  lambda_c,
  margin,
  direction,
  s,
  alpha,
  sampsz_control,
  rand_ratio
)
```

Arguments

lambda_t	Mean of the test arm
lambda_c	Mean of the control arm
margin	Non-inferiority margin
direction	Test direction: 1 = larger lambda is better, 0 = smaller lambda is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha	One-sided significance level (type I error rate)
sampsz_control	Control arm sample size
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm

Value

The output will display the power

Examples

```
power_OF_boundary_poisson_NI(lambda_t = 1.1, lambda_c = 1.0, margin = 0.1, direction = 0,
s = c(1/3, 2/3, 1), alpha = 0.025, sampsz_control = 100, rand_ratio = 1)
```

power_OF_boundary_survival_Schoenfeld

Group sequential designs / Adaptive sequential designs: Survival analysis, Superiority trial, Power calculation, O'Brien-Fleming boundary

Description

Group sequential designs / Adaptive sequential designs: Survival analysis, Superiority trial, Power calculation, O'Brien-Fleming boundary

Usage

```
power_OF_boundary_survival_Schoenfeld(HR, s, events_tot, alpha_2, rand_ratio)
```

Arguments

HR	Hazards ratio of test arm vs. the control arm
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
events_tot	Total number of events
alpha_2	Type I error for the two-sided test
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm

Value

The output will display the power

Examples

```
power_OF_boundary_survival_Schoenfeld(HR = 0.7, s = c(1/3, 2/3, 1), events_tot = 100,
alpha_2 = 0.05, rand_ratio = 1)
```

power_OF_boundary_survival_Schoenfeld_NI

Group sequential designs / Adaptive sequential designs: Survival analysis, Non-inferiority trial, Power calculation, O'Brien-Fleming boundary

Description

Group sequential designs / Adaptive sequential designs: Survival analysis, Non-inferiority trial, Power calculation, O'Brien-Fleming boundary

Usage

```
power_OF_boundary_survival_Schoenfeld_NI(
  HR,
  margin,
  direction,
  s,
  events_tot,
  alpha,
  rand_ratio
)
```

Arguments

HR	Hazards ratio of test arm vs. the control arm
margin	Non-inferiority margin
direction	Test direction: 1 = larger HR is better, 0 = smaller HR is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
events_tot	Total number of events
alpha	One-sided significance level (type I error rate)
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm

Value

The output will display the power

Examples

```
power_OF_boundary_survival_Schoenfeld_NI(HR = 0.7, margin = 0.1, direction = 0,
s = c(1/3, 2/3, 1), events_tot = 100, alpha = 0.025, rand_ratio = 1)
```

---

power_pocock_boundary_binary_diff

Group sequential designs / Adaptive sequential designs: Binary distribution, Superiority trial, Power calculation, Pocock boundary

---

Description

Group sequential designs / Adaptive sequential designs: Binary distribution, Superiority trial, Power calculation, Pocock boundary

Usage

```
power_pocock_boundary_binary_diff(
  p_t,
  p_c,
  s,
  alpha_2,
  sampsz_control,
  rand_ratio
)
```

Arguments

p_t	Mean of the test arm
p_c	Mean of the control arm
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha_2	Type I error for the two-sided test
sampsz_control	Control arm sample size
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm

Value

The output will display the power

Examples

```
power_pocock_boundary_binary_diff(p_t = 0.4, p_c = 0.3, s = c(1/3, 2/3, 1),
alpha_2 = 0.05, sampsz_control = 100, rand_ratio = 1)
```

---

power_pocock_boundary_binary_diff_NI

Group sequential designs / Adaptive sequential designs: Binary distribution, Non-inferiority trial, Power calculation, Pocock boundary

---

Description

Group sequential designs / Adaptive sequential designs: Binary distribution, Non-inferiority trial, Power calculation, Pocock boundary

Usage

```
power_pocock_boundary_binary_diff_NI(
  p_t,
  p_c,
  margin,
  direction,
  s,
  alpha,
  sampsz_control,
  rand_ratio
)
```

Arguments

p_t	Mean of the test arm
p_c	Mean of the control arm
margin	Non-inferiority margin
direction	Test direction: 1 = larger p_t is better, 0 = smaller p_t is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha	One-sided significance level (type I error rate)
sampsz_control	Control arm sample size
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm

Value

The output will display the power

Examples

```
power_pocock_boundary_binary_diff_NI(p_t = 0.4, p_c = 0.3, margin = 0.1, direction = 0,
s = c(1/3, 2/3, 1), alpha = 0.025, sampsz_control = 100, rand_ratio = 1)
```

---

power_pocock_boundary_neg_binomial

Group sequential designs / Adaptive sequential designs: Negative binomial distribution, Superiority trial, Power calculation, Pocock boundary

---

Description

Group sequential designs / Adaptive sequential designs: Negative binomial distribution, Superiority trial, Power calculation, Pocock boundary

Usage

```
power_pocock_boundary_neg_binomial(
  r_t,
  r_c,
  s,
  alpha_2,
  sampsz_control,
  rand_ratio,
  nu_t,
  kappa
)
```

Arguments

r_t	Mean of the test arm
r_c	Mean of the control arm
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha_2	Type I error for the two-sided test
sampsz_control	Control arm sample size
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
nu_t	exposure time
kappa	dispersion parameter

Value

The output will display the power

Examples

```
power_pocock_boundary_neg_binomial(r_t = c(1.1, 1.1, 1.1), r_c = 1.1, s = c(1/3, 2/3, 1),
alpha_2 = 0.05, sampsz_control = 100, rand_ratio = 1, nu_t = 6, kappa = 1)
```

---

power_pocock_boundary_neg_binomial_NI

Group sequential designs / Adaptive sequential designs: Negative binomial distribution, Non-inferiority trial, Power calculation, Pocock boundary

---

Description

Group sequential designs / Adaptive sequential designs: Negative binomial distribution, Non-inferiority trial, Power calculation, Pocock boundary

Usage

```
power_pocock_boundary_neg_binomial_NI(
  r_t,
  r_c,
  margin,
  direction,
  s,
  alpha,
  sampsz_control,
  rand_ratio,
  nu_t,
  kappa
)
```

Arguments

r_t	Mean of the test arm
r_c	Mean of the control arm
margin	Non-inferiority margin
direction	Test direction: 1 = larger r_t is better, 0 = smaller r_t is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha	One-sided significance level (type I error rate)
sampsz_control	Control arm sample size
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
nu_t	exposure time
kappa	dispersion parameter

Value

The output will display the power

Examples

```
power_pocock_boundary_neg_binomial_NI(r_t = c(1.1, 1.1, 1.1), r_c = 1.1, margin = 0.1,
direction = 0, s = c(1/3, 2/3, 1), alpha = 0.025, sampsz_control = 100, rand_ratio = 1,
nu_t = 6, kappa = 1)
```

power_pocock_boundary_normal *Group sequential designs / Adaptive sequential designs: Normal distribution, Superiority trial, Power calculation, Pocock boundary*

Description

Group sequential designs / Adaptive sequential designs: Normal distribution, Superiority trial, Power calculation, Pocock boundary

Usage

```
power_pocock_boundary_normal(
  mu_t,
  mu_c,
  std_t,
  std_c,
  s,
  sampsz_control,
  rand_ratio,
  alpha_2
)
```

Arguments

mu_t	Mean of the test arm
mu_c	Mean of the control arm
std_t	Standard deviation of the test arm
std_c	Standard deviation of the control arm
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
sampsz_control	Control arm sample size
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
alpha_2	Type I error for the two-sided test

Value

The output will display the power

Examples

```
power_pocock_boundary_normal(mu_t = 2.6, mu_c = 0.6, std_t = 9.43, std_c = 9.86,
s = c(1/3, 2/3, 1), sampsz_control = 100, rand_ratio = 1, alpha_2 = 0.05)
```

power_pocock_boundary_normal_NI

Group sequential designs / Adaptive sequential designs: Normal distribution, Non-inferiority trial, Power calculation, Pocock boundary

Description

Group sequential designs / Adaptive sequential designs: Normal distribution, Non-inferiority trial, Power calculation, Pocock boundary

Usage

```
power_pocock_boundary_normal_NI(
  mu_t,
  mu_c,
  std_t,
  std_c,
  margin,
  direction,
  s,
  sampsz_control,
  rand_ratio,
  alpha
)
```

Arguments

mu_t	Mean of the test arm
mu_c	Mean of the control arm
std_t	Standard deviation of the test arm
std_c	Standard deviation of the control arm
margin	Non-inferiority margin
direction	Test direction: 1 = larger mu is better, 0 = smaller mu is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
sampsz_control	Control arm sample size
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
alpha	One-sided significance level (type I error rate)

Value

The output will display the power

Examples

```
power_pocock_boundary_normal_NI(mu_t = 2.6, mu_c = 0.6, std_t = 9.43, std_c = 9.86,
margin = 0.1, direction = 0, s = c(1/3, 2/3, 1), sampsz_control = 100,
rand_ratio = 1, alpha = 0.025)
```

---

power_pocock_boundary_poisson

Group sequential designs / Adaptive sequential designs: Poisson distribution, Superiority trial, Power calculation, Pocock boundary

---

Description

Group sequential designs / Adaptive sequential designs: Poisson distribution, Superiority trial, Power calculation, Pocock boundary

Usage

```
power_pocock_boundary_poisson(
  lambda_t,
  lambda_c,
  s,
  alpha_2,
  sampsz_control,
  rand_ratio
)
```

Arguments

lambda_t	Mean of the test arm
lambda_c	Mean of the control arm
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha_2	Type I error for the two-sided test
sampsz_control	Control arm sample size
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm

Value

The output will display the power

Examples

```
power_pocock_boundary_poisson(lambda_t = 1.1, lambda_c = 1.0, s = c(1/3, 2/3, 1),
alpha_2 = 0.05, sampsz_control = 100, rand_ratio = 1)
```

power_pocock_boundary_poisson_NI *Group sequential designs / Adaptive sequential designs: Poisson distribution, Non-inferiority trial, Power calculation, Pocock boundary*

Description

Group sequential designs / Adaptive sequential designs: Poisson distribution, Non-inferiority trial, Power calculation, Pocock boundary

Usage

```
power_pocock_boundary_poisson_NI(
  lambda_t,
  lambda_c,
  margin,
  direction,
  s,
  alpha,
  sampsz_control,
  rand_ratio
)
```

Arguments

lambda_t	Mean of the test arm
lambda_c	Mean of the control arm
margin	Non-inferiority margin
direction	Test direction: 1 = larger lambda is better, 0 = smaller lambda is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha	One-sided significance level (type I error rate)
sampsz_control	Control arm sample size
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm

Value

The output will display the power

Examples

```
power_pocock_boundary_poisson_NI(lambda_t = 1.1, lambda_c = 1.0, margin = 0.1, direction = 0,
s = c(1/3, 2/3, 1), alpha = 0.025, sampsz_control = 100, rand_ratio = 1)
```

power_pocock_boundary_survival_Schoenfeld
Group sequential designs / Adaptive sequential designs: Survival analysis, Superiority trial, Power calculation, Pocock boundary

Description

Group sequential designs / Adaptive sequential designs: Survival analysis, Superiority trial, Power calculation, Pocock boundary

Usage

```
power_pocock_boundary_survival_Schoenfeld(
  HR,
  s,
  events_tot,
  alpha_2,
  rand_ratio
)
```

Arguments

HR	Hazards ratio of test arm vs. the control arm
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
events_tot	Total number of events
alpha_2	Type I error for the two-sided test
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm

Value

The output will display the power

Examples

```
power_pocock_boundary_survival_Schoenfeld(HR = 0.7, s = c(1/3, 2/3, 1), events_tot = 100,
alpha_2 = 0.05, rand_ratio = 1)
```

power_pocock_boundary_survival_Schoenfeld_NI *Group sequential designs / Adaptive sequential designs: Survival analysis, Non-inferiority trial, Power calculation, Pocock boundary*

Description

Group sequential designs / Adaptive sequential designs: Survival analysis, Non-inferiority trial, Power calculation, Pocock boundary

Usage

```
power_pocock_boundary_survival_Schoenfeld_NI(
  HR,
  margin,
  direction,
  s,
  events_tot,
  alpha,
  rand_ratio
)
```

Arguments

HR	Hazards ratio of test arm vs. the control arm
margin	Non-inferiority margin
direction	Test direction: 1 = larger HR is better, 0 = smaller HR is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
events_tot	Total number of events
alpha	One-sided significance level (type I error rate)
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm

Value

The output will display the power

Examples

```
power_pocock_boundary_survival_Schoenfeld_NI(HR = 0.7, margin = 0.1, direction = 0,
s = c(1/3, 2/3, 1), events_tot = 100, alpha = 0.025, rand_ratio = 1)
```

power_two_sample_neg_binomial *Fixed sample designs: Negative binomial distribution, Superiority trial, Power calculation*

Description

Fixed sample designs: Negative binomial distribution, Superiority trial, Power calculation

Usage

```
power_two_sample_neg_binomial(
  r_t,
  r_c,
  alpha_2,
  n_control,
  rand_ratio,
  nu_t,
  kappa
)
```

Arguments

r_t	The event rate of the test arm
r_c	The event rate of the control arm
alpha_2	The type I error for the two-sided test
n_control	Sample size of the control arm
rand_ratio	The ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
nu_t	The exposure time
kappa	The dispersion parameter

Value

The output will show the power

Examples

```
power_two_sample_neg_binomial(r_t = c(1.1, 1.1, 1.1), r_c = 1.1, alpha_2 = 0.05,
n_control = 53, rand_ratio = 1, nu_t = 6, kappa = 1)
```

power_two_sample_neg_binomial_NI *Fixed sample designs: Negative binomial distribution, Non-inferiority trial, Power calculation*

Description

Fixed sample designs: Negative binomial distribution, Non-inferiority trial, Power calculation

Usage

```
power_two_sample_neg_binomial_NI(
  r_t,
  r_c,
  margin,
  direction,
  alpha,
  n_control,
  rand_ratio,
  nu_t,
  kappa
)
```

Arguments

r_t	The event rate of the test arm
r_c	The event rate of the control arm
margin	The non-inferiority margin
direction	Test direction: 1 = larger r_t,r_c are better, 0 = smaller r_t,r_c are better
alpha	The type I error for the one-sided test
n_control	Sample size of the control arm
rand_ratio	The ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
nu_t	The exposure time
kappa	The dispersion parameter

Value

The output will show the power

Examples

```
power_two_sample_neg_binomial_NI(r_t = c(1.1, 1.1, 1.1), r_c = 1.1, margin = 0.1, direction = 0,
alpha = 0.025, n_control = 53, rand_ratio = 1, nu_t = 6, kappa = 1)
```

power_two_sample_normal *Fixed sample designs: Normal distribution, Superiority trial, Power calculation*

Description

Fixed sample designs: Normal distribution, Superiority trial, Power calculation

Usage

```
power_two_sample_normal(
  mu_t,
  mu_c,
  sigma_t,
  sigma_c,
  alpha_2,
  n_control,
  rand_ratio
)
```

Arguments

mu_t	The mean of the test arm.
mu_c	The mean of the control arm.
sigma_t	The standard deviation for the test arm.
sigma_c	The standard deviation for the control arm.
alpha_2	The type I error for the two-sided test.
n_control	The sample size for the control arm.
rand_ratio	The randomization ratio of test arm:control arm.

Value

The output will show the power.

Examples

```
power_two_sample_normal(mu_t = 2.6, mu_c = 0.6, sigma_t = 9.43, sigma_c = 9.86,
alpha_2 = 0.05, n_control = 53, rand_ratio = 1)
```

power_two_sample_normal_NI *Fixed sample designs: Normal distribution, Non-inferiority trial, Power calculation*

Description

Fixed sample designs: Normal distribution, Non-inferiority trial, Power calculation

Usage

```
power_two_sample_normal_NI(
  mu_t,
  mu_c,
  sigma_t,
  sigma_c,
  margin,
  direction,
  alpha,
  n_control,
  rand_ratio
)
```

Arguments

mu_t	The mean of the test arm.
mu_c	The mean of the control arm.
sigma_t	The standard deviation for the test arm.
sigma_c	The standard deviation for the control arm.
margin	The non-inferiority margin
direction	If larger mu is better
alpha	The type I error for the two-sided test.
n_control	The sample size for the control arm.
rand_ratio	The randomization ratio of test arm:control arm.

Value

The output will show the power.

Examples

```
power_two_sample_normal_NI(mu_t = 0.3, mu_c = 2, sigma_t = 1, sigma_c = 1, margin = 0.4,
direction = 1, alpha = 0.025, n_control = 100, rand_ratio = 1)
```

power_two_sample_Poisson *Fixed sample designs: Poisson distribution, Superiority trial, Power calculation*

Description

Fixed sample designs: Poisson distribution, Superiority trial, Power calculation

Usage

```
power_two_sample_Poisson(lambda_t, lambda_c, alpha_2, n_control, rand_ratio)
```

Arguments

lambda_t	The event rate of the test arm
lambda_c	The event rate of the control arm
alpha_2	The type I error for the two-sided test
n_control	Sample size of the control arm
rand_ratio	The ratio of the number of subjects in the test arm vs. the number of subjects in the control arm

Value

The output will show the power

Examples

```
power_two_sample_Poisson(lambda_t = 1.1, lambda_c = 1.0, alpha_2 = 0.05,
n_control = 53, rand_ratio = 1)
```

power_two_sample_Poisson_NI *Fixed sample designs: Poisson distribution, Non-inferiority trial, Power calculation*

Description

Fixed sample designs: Poisson distribution, Non-inferiority trial, Power calculation

Usage

```
power_two_sample_Poisson_NI(
  lambda_t,
  lambda_c,
  margin,
  direction,
  alpha,
  n_control,
  rand_ratio
)
```

Arguments

lambda_t	The event rate of the test arm
lambda_c	The event rate of the control arm
margin	The non-inferiority margin
direction	Test direction: 1 = smaller lambda is better, 0 = larger lambda is better
alpha	The type I error for the one-sided test
n_control	Sample size of the control arm
rand_ratio	The ratio of the number of subjects in the test arm vs. the number of subjects in the control arm

Value

the output will show the power

Examples

```
power_two_sample_Poisson_NI(lambda_t = 1.1, lambda_c = 1.0, margin = 0.1, direction = 0,
alpha = 0.025, n_control = 53, rand_ratio = 1)
```

---

power_two_sample_surv_Schoenfeld

Fixed sample designs: Survival analysis, Superiority trial, Power calculation

---

Description

Fixed sample designs: Survival analysis, Superiority trial, Power calculation

Usage

```
power_two_sample_surv_Schoenfeld(HR, alpha_2, event_tot, rand_ratio)
```

Arguments

HR	The hazards ratio of test arm vs. the control arm
alpha_2	The type I error for the two-sided test
event_tot	Total number of events
rand_ratio	The ratio of the number of subjects in the test arm vs. the number of subjects in the control arm

Value

The output will show the power

Examples

```
power_two_sample_surv_Schoenfeld(HR = 0.7, alpha_2 = 0.05, event_tot = 100, rand_ratio = 1)
```

---

power_two_sample_surv_Schoenfeld_NI

Fixed sample designs: Survival analysis, Non-inferiority trial, Power calculation

---

Description

Fixed sample designs: Survival analysis, Non-inferiority trial, Power calculation

Usage

```
power_two_sample_surv_Schoenfeld_NI(
  HR,
  margin,
  direction,
  alpha,
  event_tot,
  rand_ratio
)
```

Arguments

HR	The hazards ratio of test arm vs. the control arm
margin	The non-inferiority margin
direction	Test direction: 1 = smaller HR is better, 0 = larger HR is better
alpha	The type I error for the one-sided test
event_tot	Total number of events
rand_ratio	The ratio of the number of subjects in the test arm vs. the number of subjects in the control arm

Value

The output will show the power

Examples

```
power_two_sample_surv_Schoenfeld_NI(HR = 0.7, margin = 0.1, direction = 0, alpha = 0.025,
event_tot = 100, rand_ratio = 1)
```

Sample_size_alsp_boundary_binary_diff

Group sequential designs / Adaptive sequential designs: Binary distribution, Superiority trial, Sample size calculation, Alpha-spending boundary

---

Description

Group sequential designs / Adaptive sequential designs: Binary distribution, Superiority trial, Sample size calculation, Alpha-spending boundary

Usage

```
Sample_size_alsp_boundary_binary_diff(p_t, p_c, s, alpha_2, beta, rand_ratio)
```

Arguments

p_t	Mean of the test arm
p_c	Mean of the control arm
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha_2	Type I error for the two-sided test
beta	Type II error rate, i.e. 1 - power
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm

Value

The output will show the sample size for the control arm and the test arm

Examples

```
Sample_size_alsp_boundary_binary_diff(p_t = 0.2, p_c = 0.6, s = c(1/3,2/3,1),
alpha_2 = c(0.001,0.001,0.048), beta = 0.1, rand_ratio = 1)
```

`Sample_size_alsp_boundary_binary_diff_NI`

Group sequential designs / Adaptive sequential designs: Binary distribution, Non-inferiority trial, Sample size calculation, Alpha-spending boundary

Description

Group sequential designs / Adaptive sequential designs: Binary distribution, Non-inferiority trial, Sample size calculation, Alpha-spending boundary

Usage

```
Sample_size_alsp_boundary_binary_diff_NI(
  p_t,
  p_c,
  margin,
  direction,
  s,
  alpha,
  beta,
  rand_ratio
)
```

Arguments

`p_t`	Mean of the test arm
`p_c`	Mean of the control arm
`margin`	Non-inferiority margin
`direction`	Test direction: 1 = larger p_t is better, 0 = smaller p_t is better
`s`	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
`alpha`	One-sided significance level (type I error rate)
`beta`	Type II error rate, i.e. 1 - power
`rand_ratio`	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm

Value

The output will show the sample size for the control arm and the test arm

Examples

```
Sample_size_alsp_boundary_binary_diff_NI(p_t = 0.4, p_c = 0.3, margin = 0.1, direction = 0,
s = c(1/3, 2/3, 1), alpha = 0.025, beta = 0.1, rand_ratio = 1)
```

`Sample_size_alsp_boundary_neg_binomial` *Group sequential designs / Adaptive sequential designs: Negative binomial distribution, Superiority trial, Sample size calculation, Alpha-spending boundary*

Description

Group sequential designs / Adaptive sequential designs: Negative binomial distribution, Superiority trial, Sample size calculation, Alpha-spending boundary

Usage

```
Sample_size_alsp_boundary_neg_binomial(
  r_t,
  r_c,
  s,
  alpha_2,
  beta,
  rand_ratio,
  nu_t,
  kappa
)
```

Arguments

`r_t`	Mean of the test arm
`r_c`	Mean of the control arm
`s`	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
`alpha_2`	Type I error for the two-sided test
`beta`	Type II error rate, i.e. 1 - power
`rand_ratio`	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
`nu_t`	exposure time
`kappa`	dispersion parameter

Value

The output will show the sample size for the control arm and the test arm

Examples

```
Sample_size_alsp_boundary_neg_binomial(r_t = 0.2, r_c = 0.4, s = c(1/3,2/3,1),
alpha_2 = c(0.001,0.001,0.048), beta = 0.1, rand_ratio = 1, nu_t = 1, kappa = 1)
```

`Sample_size_alsp_boundary_neg_binomial_NI` *Group sequential designs / Adaptive sequential designs: Negative binomial distribution, Non-inferiority trial, Sample size calculation, Alpha-spending boundary*

Description

Group sequential designs / Adaptive sequential designs: Negative binomial distribution, Non-inferiority trial, Sample size calculation, Alpha-spending boundary

Usage

```
Sample_size_alsp_boundary_neg_binomial_NI(
  r_t,
  r_c,
  margin,
  direction,
  s,
  alpha,
  beta,
  rand_ratio,
  nu_t,
  kappa
)
```

Arguments

`r_t`	Mean of the test arm
`r_c`	Mean of the control arm
`margin`	Non-inferiority margin
`direction`	Test direction: 1 = larger r_t is better, 0 = smaller r_t is better
`s`	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
`alpha`	One-sided significance level (type I error rate)
`beta`	Type II error rate, i.e. 1 - power
`rand_ratio`	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
`nu_t`	exposure time
`kappa`	dispersion parameter

Value

The output will show the sample size for the control arm and the test arm

Examples

```
Sample_size_alsp_boundary_neg_binomial_NI(r_t = 0.2, r_c = 0.4, margin = 0.1, direction = 1,
s = c(1/3,2/3,1), alpha = c(0.001,0.001,0.023), beta = 0.1, rand_ratio = 1, nu_t = 1, kappa = 1)
```

Sample_size_alsp_boundary_normal

Group sequential designs / Adaptive sequential designs: Normal distribution, Superiority trial, Sample size calculation, Alpha-spending boundary

---

Description

Group sequential designs / Adaptive sequential designs: Normal distribution, Superiority trial, Sample size calculation, Alpha-spending boundary

Usage

```
Sample_size_alsp_boundary_normal(
  mu_t,
  mu_c,
  std_t,
  std_c,
  s,
  alpha_2,
  beta,
  rand_ratio
)
```

Arguments

mu_t	Mean of the test arm
mu_c	Mean of the control arm
std_t	Standard deviation of the test arm
std_c	Standard deviation of the control arm
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha_2	Type I error for the two-sided test
beta	Type II error rate, i.e. 1 - power
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm

Value

The output will show the sample size for the control arm and the test arm

Examples

```
Sample_size_alsp_boundary_normal(mu_t = 0.2, mu_c = 0, std_t = 1, std_c = 1, s = c(1/3,2/3,1),
alpha_2 = c(0.001,0.001,0.048), beta = 0.1, rand_ratio = 1)
```

Sample_size_alsp_boundary_normal_NI

Group sequential designs / Adaptive sequential designs: Normal distribution, Non-inferiority trial, Sample size calculation, Alpha-spending boundary

---

Description

Group sequential designs / Adaptive sequential designs: Normal distribution, Non-inferiority trial, Sample size calculation, Alpha-spending boundary

Usage

```
Sample_size_alsp_boundary_normal_NI(
  mu_t,
  mu_c,
  std_t,
  std_c,
  margin,
  direction,
  s,
  alpha,
  beta,
  rand_ratio
)
```

Arguments

mu_t	Mean of the test arm
mu_c	Mean of the control arm
std_t	Standard deviation of the test arm
std_c	Standard deviation of the control arm
margin	Non-inferiority margin
direction	Test direction: 1 = larger mu is better, 0 = smaller mu is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha	One-sided significance level (type I error rate)
beta	Type II error rate, i.e. 1 - power
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm

Value

The output will show the sample size for the control arm and the test arm

Examples

```
Sample_size_alsp_boundary_normal_NI(mu_t = 2.6, mu_c = 0.6, std_t = 9.43, std_c = 9.86,
margin = 0.1, direction = 0, s = c(1/3, 2/3, 1), alpha = 0.025, beta = 0.1, rand_ratio = 1)
```

Sample_size_alsp_boundary_poisson

Group sequential designs / Adaptive sequential designs: Poisson distribution, Superiority trial, Sample size calculation, Alpha-spending boundary

---

Description

Group sequential designs / Adaptive sequential designs: Poisson distribution, Superiority trial, Sample size calculation, Alpha-spending boundary

Usage

```
Sample_size_alsp_boundary_poisson(
  lambda_t,
  lambda_c,
  s,
  alpha_2,
  beta,
  rand_ratio
)
```

Arguments

lambda_t	Mean of the test arm
lambda_c	Mean of the control arm
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha_2	Type I error for the two-sided test
beta	Type II error rate, i.e. 1 - power
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm

Value

The output will show the sample size for the control arm and the test arm

Examples

```
Sample_size_alsp_boundary_poisson(lambda_t = 0.2, lambda_c = 0.4, s = c(1/3,2/3,1),
alpha_2 = c(0.001,0.001,0.048), beta = 0.1, rand_ratio = 1)
```

Sample_size_alsp_boundary_poisson_NI

Group sequential designs / Adaptive sequential designs: Poisson distribution, Non-inferiority trial, Sample size calculation, Alpha-spending boundary

---

Description

Group sequential designs / Adaptive sequential designs: Poisson distribution, Non-inferiority trial, Sample size calculation, Alpha-spending boundary

Usage

```
Sample_size_alsp_boundary_poisson_NI(
  lambda_t,
  lambda_c,
  margin,
  direction,
  s,
  alpha,
  beta,
  rand_ratio
)
```

Arguments

lambda_t	Mean of the test arm
lambda_c	Mean of the control arm
margin	Non-inferiority margin
direction	Test direction: 1 = larger lambda is better, 0 = smaller lambda is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha	One-sided significance level (type I error rate)
beta	Type II error rate, i.e. 1 - power
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm

Value

The output will show the sample size for the control arm and the test arm

Examples

```
Sample_size_alsp_boundary_poisson_NI(lambda_t = 1.1, lambda_c = 1.0, margin = 0.1,
direction = 0, s = c(1/3, 2/3, 1), alpha = 0.025, beta = 0.1, rand_ratio = 1)
```

Sample_size_alsp_boundary_survival_Schoenfeld

Group sequential designs / Adaptive sequential designs: Survival analysis, Superiority trial, Sample size calculation, Alpha-spending boundary

---

Description

Group sequential designs / Adaptive sequential designs: Survival analysis, Superiority trial, Sample size calculation, Alpha-spending boundary

Usage

```
Sample_size_alsp_boundary_survival_Schoenfeld(HR, s, alpha_2, beta, rand_ratio)
```

Arguments

HR	Hazards ratio of test arm vs. the control arm
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha_2	Type I error for the two-sided test
beta	Type II error rate, i.e. 1 - power
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm

Value

The output will show the sample size for the control arm and the test arm

Examples

```
Sample_size_alsp_boundary_survival_Schoenfeld(HR = 0.59, s = c(0.596,1),
alpha_2 = c(0.001,0.0249), beta = 0.1, rand_ratio = 1)
```

`Sample_size_alsp_boundary_survival_Schoenfeld_NI`
Group sequential designs / Adaptive sequential designs: Survival analysis, Non-inferiority trial, Sample size calculation, Alpha-spending boundary

Description

Group sequential designs / Adaptive sequential designs: Survival analysis, Non-inferiority trial, Sample size calculation, Alpha-spending boundary

Usage

```
Sample_size_alsp_boundary_survival_Schoenfeld_NI(
  HR,
  margin,
  direction,
  s,
  alpha,
  beta,
  rand_ratio
)
```

Arguments

`HR`	Hazards ratio of test arm vs. the control arm
`margin`	Non-inferiority margin
`direction`	Test direction: 1 = larger HR is better, 0 = smaller HR is better
`s`	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
`alpha`	One-sided significance level (type I error rate)
`beta`	Type II error rate, i.e. 1 - power
`rand_ratio`	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm

Value

The output will show the sample size for the control arm and the test arm

Examples

```
Sample_size_alsp_boundary_survival_Schoenfeld_NI(HR = 0.7, margin = 0.1, direction = 0,
s = c(1/3, 2/3, 1), alpha = 0.025, beta = 0.1, rand_ratio = 1)
```

sample_size_binary_diff

Fixed sample designs: Binary distribution, Superiority trial, Sample size calculation

Description

Fixed sample designs: Binary distribution, Superiority trial, Sample size calculation

Usage

```
sample_size_binary_diff(p_t, p_c, alpha_2, beta, rand_ratio)
```

Arguments

p_t	The event rate of the test arm
p_c	The event rate of the control arm
alpha_2	One-sided type I error rate used for boundary calibration
beta	Type II error rate, i.e. 1 - power
rand_ratio	Randomization ratio is the ratio of the number of subjects in the test arm vs. the number of subjects in the control arm

Value

The output will show the sample size for the control arm and the test arm

Examples

```
sample_size_binary_diff(p_t = 0.2, p_c = 0.4, alpha_2 = 0.05, beta = 0.1, rand_ratio = 1)
```

sample_size_binary_diff_NI

Fixed sample designs: Binary distribution, Non-inferiority trial, Sample size calculation

Description

Fixed sample designs: Binary distribution, Non-inferiority trial, Sample size calculation

Usage

```
sample_size_binary_diff_NI(
  p_t,
  p_c,
  margin,
  direction,
  alpha,
  beta,
  rand_ratio
)
```

Arguments

p_t	The event rate of the test arm
p_c	The event rate of the control arm
margin	the non-inferiority margin
direction	Test direction: 1 = larger p_t,p_c are better, 0 = smaller p_t,p_c are better
alpha	The type I error for the one-sided test
beta	Type II error rate, i.e. 1 - power
rand_ratio	Randomization ratio is the ratio of the number of subjects in the test arm vs. the number of subjects in the control arm

Value

The output will show the sample size for the control arm and the test arm

Examples

```
sample_size_binary_diff_NI(p_t = 0.4, p_c = 0.3, margin = 0.1, direction = 0, alpha = 0.025,
beta = 0.1, rand_ratio = 1)
```

---

sample_size_neg_binomial

Fixed sample designs: Negative binomial distribution, Superiority trial, Sample size calculation

---

Description

Fixed sample designs: Negative binomial distribution, Superiority trial, Sample size calculation

Usage

```
sample_size_neg_binomial(r_t, r_c, alpha_2, beta, rand_ratio, nu_t, kappa)
```

Arguments

r_t	The event rate of the test arm
r_c	The event rate of the control arm
alpha_2	The type I error for the two-sided test
beta	Type II error rate, i.e. 1 - power
rand_ratio	The ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
nu_t	The exposure time
kappa	The dispersion parameter

Value

The output will show the sample size for the control arm and the test arm

Examples

```
sample_size_neg_binomial(r_t = 0.85, r_c = 1.25, alpha_2 = 0.05, beta = 0.2, rand_ratio = 1,
nu_t = 1, kappa = 1)
```

---

sample_size_neg_binomial_NI

Fixed sample designs: Negative binomial distribution, Non-inferiority trial, Sample size calculation

---

Description

Fixed sample designs: Negative binomial distribution, Non-inferiority trial, Sample size calculation

Usage

```
sample_size_neg_binomial_NI(
  r_t,
  r_c,
  margin,
  direction,
  alpha,
  beta,
  rand_ratio,
  nu_t,
  kappa
)
```

Arguments

r_t	The event rate of the test arm
r_c	The event rate of the control arm
margin	The non-inferiority margin
direction	Test direction: 1 = larger r_t,r_c are better, 0 = smaller r_t,r_c are better
alpha	The type I error for the one-sided test
beta	Type II error rate, i.e. 1 - power
rand_ratio	The ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
nu_t	The exposure time
kappa	The dispersion parameter

Value

The output will show the sample size for the control arm and the test arm

Examples

```
sample_size_neg_binomial_NI(r_t = 0.9, r_c = 1, margin = 0.3, direction = 1, alpha = 0.025,
beta = 0.1, rand_ratio = 1, nu_t = 1, kappa = 1)
```

Sample_size_OF_boundary_binary_diff

Group sequential designs / Adaptive sequential designs: Binary distribution, Superiority trial, Sample size calculation, O'Brien-Fleming boundary

---

Description

Group sequential designs / Adaptive sequential designs: Binary distribution, Superiority trial, Sample size calculation, O'Brien-Fleming boundary

Usage

```
Sample_size_OF_boundary_binary_diff(p_t, p_c, s, alpha_2, beta, rand_ratio)
```

Arguments

p_t	Mean of the test arm
p_c	Mean of the control arm
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha_2	Type I error for the two-sided test

beta	Type II error rate, i.e. 1 - power
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm

Value

The output will show the sample size for the control arm and the test arm

Examples

```
Sample_size_OF_boundary_binary_diff(p_t = 0.4, p_c = 0.3, s = c(1/3, 2/3, 1),
alpha_2 = 0.05, beta = 0.1, rand_ratio = 1)
```

Sample_size_OF_boundary_binary_diff_NI

Group sequential designs / Adaptive sequential designs: Binary distribution, Non-inferiority trial, Sample size calculation, O'Brien-Fleming boundary

---

Description

Group sequential designs / Adaptive sequential designs: Binary distribution, Non-inferiority trial, Sample size calculation, O'Brien-Fleming boundary

Usage

```
Sample_size_OF_boundary_binary_diff_NI(
  p_t,
  p_c,
  margin,
  direction,
  s,
  alpha,
  beta,
  rand_ratio
)
```

Arguments

p_t	Mean of the test arm
p_c	Mean of the control arm
margin	Non-inferiority margin
direction	Test direction: 1 = larger p_t is better, 0 = smaller p_t is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1

alpha	One-sided significance level (type I error rate)
beta	Type II error rate, i.e. 1 - power
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm

Value

The output will show the sample size for the control arm and the test arm

Examples

```
Sample_size_OF_boundary_binary_diff_NI(p_t = 0.4, p_c = 0.3, margin = 0.1, direction = 0,
s = c(1/3, 2/3, 1), alpha = 0.025, beta = 0.1, rand_ratio = 1)
```

Sample_size_OF_boundary_neg_binomial

Group sequential designs / Adaptive sequential designs: Negative binomial distribution, Superiority trial, Sample size calculation, O'Brien-Fleming boundary

---

Description

Group sequential designs / Adaptive sequential designs: Negative binomial distribution, Superiority trial, Sample size calculation, O'Brien-Fleming boundary

Usage

```
Sample_size_OF_boundary_neg_binomial(
  r_t,
  r_c,
  s,
  alpha_2,
  beta,
  rand_ratio,
  nu_t,
  kappa
)
```

Arguments

r_t	Mean of the test arm
r_c	Mean of the control arm
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha_2	Type I error for the two-sided test

beta	Type II error rate, i.e. 1 - power
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
nu_t	exposure time
kappa	dispersion parameter

Value

The output will show the sample size for the control arm and the test arm

Examples

```
Sample_size_OF_boundary_neg_binomial(r_t = 0.2, r_c = 0.4, s = c(1/3,2/3,1), alpha_2 = 0.05,
beta = 0.1, rand_ratio = 1, nu_t = 1, kappa = 1)
```

Sample_size_OF_boundary_neg_binomial_NI

Group sequential designs / Adaptive sequential designs: Negative binomial distribution, Non-inferiority trial, Sample size calculation, O'Brien-Fleming boundary

---

Description

Group sequential designs / Adaptive sequential designs: Negative binomial distribution, Non-inferiority trial, Sample size calculation, O'Brien-Fleming boundary

Usage

```
Sample_size_OF_boundary_neg_binomial_NI(
  r_t,
  r_c,
  margin,
  direction,
  s,
  alpha,
  beta,
  rand_ratio,
  nu_t,
  kappa
)
```

Arguments

r_t	Mean of the test arm
r_c	Mean of the control arm
margin	Non-inferiority margin
direction	Test direction: 1 = larger r_t is better, 0 = smaller r_t is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha	One-sided significance level (type I error rate)
beta	Type II error rate, i.e. 1 - power
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
nu_t	exposure time
kappa	dispersion parameter

Value

The output will show the sample size for the control arm and the test arm

Examples

```
Sample_size_OF_boundary_neg_binomial_NI(r_t = 0.2, r_c = 0.4, margin = 0.1, direction = 1,
s = c(1/3,2/3,1), alpha = 0.025, beta = 0.1, rand_ratio = 1, nu_t = 1, kappa = 1)
```

Sample_size_OF_boundary_normal

Group sequential designs / Adaptive sequential designs: Normal distribution, Superiority trial, Sample size calculation, O'Brien-Fleming boundary

---

Description

Group sequential designs / Adaptive sequential designs: Normal distribution, Superiority trial, Sample size calculation, O'Brien-Fleming boundary

Usage

```
Sample_size_OF_boundary_normal(
  mu_t,
  mu_c,
  std_t,
  std_c,
  s,
  alpha_2,
  beta,
  rand_ratio
)
```

Arguments

mu_t	Mean of the test arm
mu_c	Mean of the control arm
std_t	Standard deviation of the test arm
std_c	Standard deviation of the control arm
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha_2	Type I error for the two-sided test
beta	Type II error rate, i.e. 1 - power
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm

Value

The output will show the sample size for the control arm and the test arm

Examples

```
Sample_size_OF_boundary_normal(mu_t = 2.6, mu_c = 0.6, std_t = 9.43, std_c = 9.86,
s = c(1/3, 2/3, 1), alpha_2 = 0.05, beta = 0.1, rand_ratio = 1)
```

Sample_size_OF_boundary_normal_NI

Group sequential designs / Adaptive sequential designs: Normal distribution, Non-inferiority trial, Sample size calculation, O'Brien-Fleming boundary

---

Description

Group sequential designs / Adaptive sequential designs: Normal distribution, Non-inferiority trial, Sample size calculation, O'Brien-Fleming boundary

Usage

```
Sample_size_OF_boundary_normal_NI(
  mu_t,
  mu_c,
  std_t,
  std_c,
  margin,
  direction,
  s,
  alpha,
  beta,
  rand_ratio
)
```

Arguments

mu_t	Mean of the test arm
mu_c	Mean of the control arm
std_t	Standard deviation of the test arm
std_c	Standard deviation of the control arm
margin	Non-inferiority margin
direction	Test direction: 1 = larger mu is better, 0 = smaller mu is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha	One-sided significance level (type I error rate)
beta	Type II error rate, i.e. 1 - power
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm

Value

The output will show the sample size for the control arm and the test arm

Examples

```
Sample_size_OF_boundary_normal_NI(mu_t = 2.6, mu_c = 0.6, std_t = 9.43, std_c = 9.86,
margin = 0.1, direction = 0, s = c(1/3, 2/3, 1), alpha = 0.025, beta = 0.1, rand_ratio = 1)
```

Sample_size_OF_boundary_poisson

Group sequential designs / Adaptive sequential designs: Poisson distribution, Superiority trial, Sample size calculation, O'Brien-Fleming boundary

---

Description

Group sequential designs / Adaptive sequential designs: Poisson distribution, Superiority trial, Sample size calculation, O'Brien-Fleming boundary

Usage

```
Sample_size_OF_boundary_poisson(
  lambda_t,
  lambda_c,
  s,
  alpha_2,
  beta,
  rand_ratio
)
```

Arguments

lambda_t	Mean of the test arm
lambda_c	Mean of the control arm
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha_2	Type I error for the two-sided test
beta	Type II error rate, i.e. 1 - power
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm

Value

The output will show the sample size for the control arm and the test arm

Examples

```
Sample_size_OF_boundary_poisson(lambda_t = 1.1, lambda_c = 1.0, s = c(1/3, 2/3, 1),
alpha_2 = 0.05, beta = 0.1, rand_ratio = 1)
```

Sample_size_OF_boundary_poisson_NI

Group sequential designs / Adaptive sequential designs: Poisson distribution, Non-inferiority trial, Sample size calculation, O'Brien-Fleming boundary

---

Description

Group sequential designs / Adaptive sequential designs: Poisson distribution, Non-inferiority trial, Sample size calculation, O'Brien-Fleming boundary

Usage

```
Sample_size_OF_boundary_poisson_NI(
  lambda_t,
  lambda_c,
  margin,
  direction,
  s,
  alpha,
  beta,
  rand_ratio
)
```

Arguments

lambda_t	Mean of the test arm
lambda_c	Mean of the control arm
margin	Non-inferiority margin
direction	Test direction: 1 = larger lambda is better, 0 = smaller lambda is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha	One-sided significance level (type I error rate)
beta	Type II error rate, i.e. 1 - power
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm

Value

The output will show the sample size for the control arm and the test arm

Examples

```
Sample_size_OF_boundary_poisson_NI(lambda_t = 1.1, lambda_c = 1.0, margin = 0.1, direction = 0,
s = c(1/3, 2/3, 1), alpha = 0.025, beta = 0.1, rand_ratio = 1)
```

Sample_size_OF_boundary_survival_Schoenfeld

Group sequential designs / Adaptive sequential designs: Survival analysis, Superiority trial, Sample size calculation, O'Brien-Fleming boundary

---

Description

Group sequential designs / Adaptive sequential designs: Survival analysis, Superiority trial, Sample size calculation, O'Brien-Fleming boundary

Usage

```
Sample_size_OF_boundary_survival_Schoenfeld(HR, s, alpha_2, beta, rand_ratio)
```

Arguments

HR	Hazards ratio of test arm vs. the control arm
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha_2	Type I error for the two-sided test
beta	Type II error rate, i.e. 1 - power
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm

Value

The output will show the sample size for the control arm and the test arm

Examples

```
Sample_size_OF_boundary_survival_Schoenfeld(HR = 0.7, s = c(1/3, 2/3, 1),
alpha_2 = 0.05, beta = 0.1, rand_ratio = 1)
```

Sample_size_OF_boundary_survival_Schoenfeld_NI

Group sequential designs / Adaptive sequential designs: Survival analysis, Non-inferiority trial, Sample size calculation, O'Brien-Fleming boundary

---

Description

Group sequential designs / Adaptive sequential designs: Survival analysis, Non-inferiority trial, Sample size calculation, O'Brien-Fleming boundary

Usage

```
Sample_size_OF_boundary_survival_Schoenfeld_NI(
  HR,
  margin,
  direction,
  s,
  alpha,
  beta,
  rand_ratio
)
```

Arguments

HR	Hazards ratio of test arm vs. the control arm
margin	Non-inferiority margin
direction	Test direction: 1 = larger HR is better, 0 = smaller HR is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha	One-sided significance level (type I error rate)
beta	Type II error rate, i.e. 1 - power
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm

Value

The output will show the sample size for the control arm and the test arm

Examples

```
Sample_size_OF_boundary_survival_Schoenfeld_NI(HR = 0.7, margin = 0.1, direction = 0,
s = c(1/3, 2/3, 1), alpha = 0.025, beta = 0.1, rand_ratio = 1)
```

Sample_size_pocock_boundary_binary_diff

Group sequential designs / Adaptive sequential designs: Binary distribution, Superiority trial, Sample size calculation, Pocock boundary

---

Description

Group sequential designs / Adaptive sequential designs: Binary distribution, Superiority trial, Sample size calculation, Pocock boundary

Usage

```
Sample_size_pocock_boundary_binary_diff(p_t, p_c, s, alpha_2, beta, rand_ratio)
```

Arguments

p_t	Mean of the test arm
p_c	Mean of the control arm
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha_2	Type I error for the two-sided test
beta	Type II error rate, i.e. 1 - power
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm

Value

The output will show the sample size for the control arm and the test arm

Examples

```
Sample_size_pocock_boundary_binary_diff(p_t = 0.4, p_c = 0.3, s = c(1/3, 2/3, 1),
alpha_2 = 0.05, beta = 0.1, rand_ratio = 1)
```

`Sample_size_pocock_boundary_binary_diff_NI`

Group sequential designs / Adaptive sequential designs: Binary distribution, Non-inferiority trial, Sample size calculation, Pocock boundary

Description

Group sequential designs / Adaptive sequential designs: Binary distribution, Non-inferiority trial, Sample size calculation, Pocock boundary

Usage

```
Sample_size_pocock_boundary_binary_diff_NI(
  p_t,
  p_c,
  margin,
  direction,
  s,
  alpha,
  beta,
  rand_ratio
)
```

Arguments

`p_t`	Mean of the test arm
`p_c`	Mean of the control arm
`margin`	Non-inferiority margin
`direction`	Test direction: 1 = larger p_t is better, 0 = smaller p_t is better
`s`	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
`alpha`	One-sided significance level (type I error rate)
`beta`	Type II error rate, i.e. 1 - power
`rand_ratio`	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm

Value

The output will show the sample size for the control arm and the test arm

Examples

```
Sample_size_pocock_boundary_binary_diff_NI(p_t = 0.4, p_c = 0.3, margin = 0.1, direction = 0,
s = c(1/3, 2/3, 1), alpha = 0.025, beta = 0.1, rand_ratio = 1)
```

`Sample_size_pocock_boundary_neg_binomial` *Group sequential designs / Adaptive sequential designs: Negative binomial distribution, Superiority trial, Sample size calculation, Pocock boundary*

Description

Group sequential designs / Adaptive sequential designs: Negative binomial distribution, Superiority trial, Sample size calculation, Pocock boundary

Usage

```
Sample_size_pocock_boundary_neg_binomial(
  r_t,
  r_c,
  s,
  alpha_2,
  beta,
  rand_ratio,
  nu_t,
  kappa
)
```

Arguments

`r_t`	Mean of the test arm
`r_c`	Mean of the control arm
`s`	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
`alpha_2`	Type I error for the two-sided test
`beta`	Type II error rate, i.e. 1 - power
`rand_ratio`	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
`nu_t`	exposure time
`kappa`	dispersion parameter

Value

The output will show the sample size for the control arm and the test arm

Examples

```
Sample_size_pocock_boundary_neg_binomial(r_t = 0.2, r_c = 0.4, s = c(1/3,2/3,1),
alpha_2 = 0.05, beta = 0.1, rand_ratio = 1, nu_t = 1, kappa = 1)
```

`Sample_size_pocock_boundary_neg_binomial_NI` *Group sequential designs / Adaptive sequential designs: Negative binomial distribution, Non-inferiority trial, Sample size calculation, Pocock boundary*

Description

Group sequential designs / Adaptive sequential designs: Negative binomial distribution, Non-inferiority trial, Sample size calculation, Pocock boundary

Usage

```
Sample_size_pocock_boundary_neg_binomial_NI(
  r_t,
  r_c,
  margin,
  direction,
  s,
  alpha,
  beta,
  rand_ratio,
  nu_t,
  kappa
)
```

Arguments

`r_t`	Mean of the test arm
`r_c`	Mean of the control arm
`margin`	Non-inferiority margin
`direction`	Test direction: 1 = larger r_t is better, 0 = smaller r_t is better
`s`	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
`alpha`	One-sided significance level (type I error rate)
`beta`	Type II error rate, i.e. 1 - power
`rand_ratio`	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
`nu_t`	exposure time
`kappa`	dispersion parameter

Value

The output will show the sample size for the control arm and the test arm

Examples

```
Sample_size_pocock_boundary_neg_binomial_NI(r_t = 0.2, r_c = 0.4, margin = 0.1, direction = 1,
s = c(1/3,2/3,1), alpha = 0.025, beta = 0.1, rand_ratio = 1, nu_t = 1, kappa = 1)
```

Sample_size_pocock_boundary_normal

Group sequential designs / Adaptive sequential designs: Normal distribution, Superiority trial, Sample size calculation, Pocock boundary

---

Description

Group sequential designs / Adaptive sequential designs: Normal distribution, Superiority trial, Sample size calculation, Pocock boundary

Usage

```
Sample_size_pocock_boundary_normal(
  mu_t,
  mu_c,
  std_t,
  std_c,
  s,
  alpha_2,
  beta,
  rand_ratio
)
```

Arguments

mu_t	Mean of the test arm
mu_c	Mean of the control arm
std_t	Standard deviation of the test arm
std_c	Standard deviation of the control arm
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha_2	Type I error for the two-sided test
beta	Type II error rate, i.e. 1 - power
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm

Value

The output will show the sample size for the control arm and the test arm

Examples

```
Sample_size_pocock_boundary_normal(mu_t = 2.6, mu_c = 0.6, std_t = 9.43, std_c = 9.86,
s = c(1/3, 2/3, 1), alpha_2 = 0.05, beta = 0.1, rand_ratio = 1)
```

Sample_size_pocock_boundary_normal_NI

Group sequential designs / Adaptive sequential designs: Normal distribution, Non-inferiority trial, Sample size calculation, Pocock boundary

---

Description

Group sequential designs / Adaptive sequential designs: Normal distribution, Non-inferiority trial, Sample size calculation, Pocock boundary

Usage

```
Sample_size_pocock_boundary_normal_NI(
  mu_t,
  mu_c,
  std_t,
  std_c,
  margin,
  direction,
  s,
  alpha,
  beta,
  rand_ratio
)
```

Arguments

mu_t	Mean of the test arm
mu_c	Mean of the control arm
std_t	Standard deviation of the test arm
std_c	Standard deviation of the control arm
margin	Non-inferiority margin
direction	Test direction: 1 = larger mu is better, 0 = smaller mu is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha	One-sided significance level (type I error rate)
beta	Type II error rate, i.e. 1 - power
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm

Value

The output will show the sample size for the control arm and the test arm

Examples

```
Sample_size_pocock_boundary_normal_NI(mu_t = 2.6, mu_c = 0.6, std_t = 9.43, std_c = 9.86,
margin = 0.1, direction = 0, s = c(1/3, 2/3, 1), alpha = 0.025, beta = 0.1, rand_ratio = 1)
```

Sample_size_pocock_boundary_poisson

Group sequential designs / Adaptive sequential designs: Poisson distribution, Superiority trial, Sample size calculation, Pocock boundary

---

Description

Group sequential designs / Adaptive sequential designs: Poisson distribution, Superiority trial, Sample size calculation, Pocock boundary

Usage

```
Sample_size_pocock_boundary_poisson(
  lambda_t,
  lambda_c,
  s,
  alpha_2,
  beta,
  rand_ratio
)
```

Arguments

lambda_t	Mean of the test arm
lambda_c	Mean of the control arm
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha_2	Type I error for the two-sided test
beta	Type II error rate, i.e. 1 - power
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm

Value

The output will show the sample size for the control arm and the test arm

Examples

```
Sample_size_pocock_boundary_poisson(lambda_t = 0.2, lambda_c = 0.4, s = c(1/3,2/3,1),
alpha_2 = 0.05, beta = 0.1, rand_ratio = 1)
```

`Sample_size_pocock_boundary_poisson_NI`

Group sequential designs / Adaptive sequential designs: Poisson distribution, Non-inferiority trial, Sample size calculation, Pocock boundary

---

Description

Group sequential designs / Adaptive sequential designs: Poisson distribution, Non-inferiority trial, Sample size calculation, Pocock boundary

Usage

```
Sample_size_pocock_boundary_poisson_NI(
  lambda_t,
  lambda_c,
  margin,
  direction,
  s,
  alpha,
  beta,
  rand_ratio
)
```

Arguments

`lambda_t`	Mean of the test arm
`lambda_c`	Mean of the control arm
`margin`	Non-inferiority margin
`direction`	Test direction: 1 = larger lambda is better, 0 = smaller lambda is better
`s`	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
`alpha`	One-sided significance level (type I error rate)
`beta`	Type II error rate, i.e. 1 - power
`rand_ratio`	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm

Value

The output will show the sample size for the control arm and the test arm

Examples

```
Sample_size_pocock_boundary_poisson_NI(lambda_t = 1.1, lambda_c = 1.0, margin = 0.1,
direction = 0, s = c(1/3, 2/3, 1), alpha = 0.025, beta = 0.1, rand_ratio = 1)
```

Sample_size_pocock_boundary_survival_Schoenfeld

Group sequential designs / Adaptive sequential designs: Survival analysis, Superiority trial, Sample size calculation, Pocock boundary

---

Description

Group sequential designs / Adaptive sequential designs: Survival analysis, Superiority trial, Sample size calculation, Pocock boundary

Usage

```
Sample_size_pocock_boundary_survival_Schoenfeld(
  HR,
  s,
  alpha_2,
  beta,
  rand_ratio
)
```

Arguments

HR	Hazards ratio of test arm vs. the control arm
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha_2	Type I error for the two-sided test
beta	Type II error rate, i.e. 1 - power
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm

Value

The output will show the sample size for the control arm and the test arm

Examples

```
Sample_size_pocock_boundary_survival_Schoenfeld(HR = 0.7, s = c(1/3, 2/3, 1),
alpha_2 = 0.05, beta = 0.1, rand_ratio = 1)
```

`Sample_size_pocock_boundary_survival_Schoenfeld_NI` *Group sequential designs / Adaptive sequential designs: Survival analysis, Non-inferiority trial, Sample size calculation, Pocock boundary*

Description

Group sequential designs / Adaptive sequential designs: Survival analysis, Non-inferiority trial, Sample size calculation, Pocock boundary

Usage

```
Sample_size_pocock_boundary_survival_Schoenfeld_NI(
  HR,
  margin,
  direction,
  s,
  alpha,
  beta,
  rand_ratio
)
```

Arguments

`HR`	Hazards ratio of test arm vs. the control arm
`margin`	Non-inferiority margin
`direction`	Test direction: 1 = larger HR is better, 0 = smaller HR is better
`s`	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
`alpha`	One-sided significance level (type I error rate)
`beta`	Type II error rate, i.e. 1 - power
`rand_ratio`	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm

Value

The output will show the sample size for the control arm and the test arm

Examples

```
Sample_size_pocock_boundary_survival_Schoenfeld_NI(HR = 0.7, margin = 0.1, direction = 0,
s = c(1/3, 2/3, 1), alpha = 0.025, beta = 0.1, rand_ratio = 1)
```

`sample_size_two_sample_normal` *Fixed sample designs: Normal distribution, Superiority trial, Sample size calculation*

Description

Fixed sample designs: Normal distribution, Superiority trial, Sample size calculation

Usage

```
sample_size_two_sample_normal(
  mu_t,
  mu_c,
  sigma_t,
  sigma_c,
  alpha_2,
  beta,
  rand_ratio
)
```

Arguments

`mu_t`	The mean of the test arm.
`mu_c`	The mean of the control arm.
`sigma_t`	The standard deviation for the test arm.
`sigma_c`	The standard deviation for the control arm.
`alpha_2`	The type I error for the two-sided test.
`beta`	Type II error.
`rand_ratio`	The randomization ratio of test arm:control arm.

Value

The output will show the sample size for the control arm and the test arm.

Examples

```
sample_size_two_sample_normal(mu_t = 2, mu_c = 0, sigma_t = 9.79, sigma_c = 9.79,
alpha_2 = 0.05, beta = 0.2, rand_ratio = 1)
```

`sample_size_two_sample_normal_NI` *Fixed sample designs: Normal distribution, Non-inferiority trial, Sample size calculation*

Description

Fixed sample designs: Normal distribution, Non-inferiority trial, Sample size calculation

Usage

```
sample_size_two_sample_normal_NI(
  mu_t,
  mu_c,
  sigma_t,
  sigma_c,
  margin,
  direction,
  alpha,
  beta,
  rand_ratio
)
```

Arguments

`mu_t`	The mean of the test arm.
`mu_c`	The mean of the control arm.
`sigma_t`	The standard deviation for the test arm.
`sigma_c`	The standard deviation for the control arm.
`margin`	The non-inferiority margin
`direction`	If larger mu is better
`alpha`	The type I error for the two-sided test.
`beta`	Type II error.
`rand_ratio`	The randomization ratio of test arm:control arm.

Value

The output will show the sample size for the control arm and the test arm.

Examples

```
sample_size_two_sample_normal_NI(mu_t = 2, mu_c = 2.5, sigma_t = 9.79, sigma_c = 9.79,
margin = 0.2, direction = 2, alpha = 0.05, beta = 0.2, rand_ratio = 1)
```

sample_size_two_sample_Poisson

Fixed sample designs: Poisson distribution, Superiority trial, Sample size calculation

Description

Fixed sample designs: Poisson distribution, Superiority trial, Sample size calculation

Usage

```
sample_size_two_sample_Poisson(lambda_t, lambda_c, alpha_2, beta, rand_ratio)
```

Arguments

lambda_t	The event rate of the test arm
lambda_c	The event rate of the control arm
alpha_2	The type I error for the two-sided test
beta	Type II error rate, i.e. 1 - power
rand_ratio	The ratio of the number of subjects in the test arm vs. the number of subjects in the control arm

Value

The output will show the sample size for the control arm and the test arm

Examples

```
sample_size_two_sample_Poisson(lambda_t = 1.1, lambda_c = 1.0, alpha_2 = 0.05,
beta = 0.1, rand_ratio = 1)
```

sample_size_two_sample_Poisson_NI

Fixed sample designs: Poisson distribution, Non-inferiority trial, Sample size calculation

Description

Fixed sample designs: Poisson distribution, Non-inferiority trial, Sample size calculation

Usage

```
sample_size_two_sample_Poisson_NI(
  lambda_t,
  lambda_c,
  margin,
  direction,
  alpha,
  beta,
  rand_ratio
)
```

Arguments

lambda_t	The event rate of the test arm
lambda_c	The event rate of the control arm
margin	The non-inferiority margin
direction	Test direction: 1 = smaller lambda is better, 0 = larger lambda is better
alpha	The type I error for the one-sided test
beta	Type II error rate, i.e. 1 - power
rand_ratio	The ratio of the number of subjects in the test arm vs. the number of subjects in the control arm

Value

The output will show the sample size for the control arm and the test arm

Examples

```
sample_size_two_sample_Poisson_NI(lambda_t = 1.1, lambda_c = 1.0, margin = 0.1, direction = 0,
alpha = 0.025, beta = 0.1, rand_ratio = 1)
```

---

sample_size_two_sample_surv_Schoenfeld

Fixed sample designs: Survival analysis, Superiority trial, Sample size calculation

---

Description

Fixed sample designs: Survival analysis, Superiority trial, Sample size calculation

Usage

```
sample_size_two_sample_surv_Schoenfeld(HR, alpha_2, beta, rand_ratio)
```

Arguments

HR	The hazards ratio of test arm vs. the control arm
alpha_2	The type I error for the two-sided test
beta	Type II error rate, i.e. 1 - power
rand_ratio	The ratio of the number of subjects in the test arm vs. the number of subjects in the control arm

Value

The output will show the total number of events for the control arm and the test arm

Examples

```
sample_size_two_sample_surv_Schoenfeld(HR = 0.7, alpha_2 = 0.05, beta = 0.1, rand_ratio = 1)
```

---

sample_size_two_sample_surv_Schoenfeld_NI

Fixed sample designs: Survival analysis, Non-inferiority trial, Sample size calculation

---

Description

Fixed sample designs: Survival analysis, Non-inferiority trial, Sample size calculation

Usage

```
sample_size_two_sample_surv_Schoenfeld_NI(
  HR,
  margin,
  direction,
  alpha_2,
  beta,
  rand_ratio
)
```

Arguments

HR	The hazards ratio of test arm vs. the control arm
margin	The non-inferiority margin
direction	Test direction: 1 = smaller HR is better, 0 = larger HR is better
alpha_2	The type I error for the one-sided test
beta	Type II error rate, i.e. 1 - power
rand_ratio	The ratio of the number of subjects in the test arm vs. the number of subjects in the control arm

Value

The output will show the total number of events for the control arm and the test arm

Examples

```
sample_size_two_sample_surv_Schoenfeld_NI(HR = 0.7, margin = 0.1, direction = 0,
alpha_2 = 0.05, beta = 0.1, rand_ratio = 1)
```

---

simon_ph2_sz *Two-stage design: Simon's design*

Description

Two-stage design: Simon's design

Usage

```
simon_ph2_sz(alpha, beta, p_0, p_1)
```

Arguments

alpha	One-sided type I error.
beta	Type II error.
p_0	Response rate indicating low activity with insufficient clinical benefit.
p_1	Assumed response rate.

Value

r1: If no more than r1 responses are observed at the first look, then the trial would be stopped for futility.

n1: Number of patients at first look.

r_2: The null hypothesis will be rejected if at least r_2 responses are observed at the end of the trial.

n_2: Number of patients at second look. n_2 is also the total sample size.

EN(p_0) is the expected sample size under the null hypothesis.

PET(p_0) is the probability of early termination under the null hypothesis.

PET_p_1 is the probability of early termination under p=p_1.

power_p_1 is the power under p=p_1.

Type I error is the probability of rejecting the null hypothesis under p<=p_0.

The minimax design has the smallest n_2 among all possible choices of (n1,r1,n_2,r_2).

The optimal design has the smallest EN(p_0) among all possible choices of (n1,r1,n_2,r_2).

The average design is an augmentation of the original Simon's design (Gao, Zhang. 2024). The n1 for the average design is the average of n1's from the minimax and the optimal designs.

References

R. Simon. Optimal Two-Stage Designs for Phase II Clinical Trials. Controlled Clinical Trials 10:1-10 (1989).

P. Gao & W. Zhang (15 Apr 2024): Adaptive sequential design for phase II single-arm oncology trials: an expansion of Simon's design, Journal of Biopharmaceutical Statistics, DOI: 10.1080/10543406.2024.2341673. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2341673.

Examples

```
simon_ph2_sz(alpha=0.025,beta=0.1,p_0=0.2,p_1=0.33)
```

Two_stage_asd_simu_OC_binary

Phase 2/3 seamless combination Group sequential design: Simulations, Binary distribution, Optimizing adaptive sequential design

---

Description

Phase 2/3 seamless combination Group sequential design: Simulations, Binary distribution, Optimizing adaptive sequential design

Usage

```
Two_stage_asd_simu_OC_binary(
  groups,
  p_c,
  direction,
  s1,
  s2,
  alpha_2,
  alpha_2_alps_s1,
  alpha_2_alps_s2,
  theta_cut,
  samsz_1,
  samsz_2,
  N_max_1,
  N_max_2,
  beta,
  sim_num
)
```

Arguments

groups	Vector of group labels used in the simulation
p_c	Event (response) proportion in the control arm
direction	Test direction: 1 = larger p is better, 0 = smaller p is better
s1	Information fractions for the first stage / first group
s2	Information fractions for the second stage / second group
alpha_2	Type I error for the two-sided test
alpha_2_alps_s1	Type I error spent up to the interim analysis (stage 1 / group 1)
alpha_2_alps_s2	Cumulative type I error spent at the final analysis (stage 2 / group 2)
theta_cut	Efficacy cut-off on the effect-size scale applied at the interim analysis
samsz_1	Planned sample size (control arm) of the first stage / group
samsz_2	Planned sample size (control arm) of the second stage / group
N_max_1	Maximum allowed sample size (control arm) of the first stage / group
N_max_2	Maximum allowed sample size (control arm) of the second stage / group
beta	Type II error rate, i.e. 1 - power
sim_num	Number of simulation replicates

Value

A named list containing the following elements: 'Looks', 'Information fractions', 'O'Brien-Fleming boundaries'.

References

P. Gao, Y. Li (05 May 2024): Adaptive two-stage seamless sequential design for clinical trials, Journal of Biopharmaceutical Statistics, DOI: 10.1080/10543406.2024.2342518. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2342518

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
Two_stage_asd_simu_OC_binary(
groups = rbind(c(0.3,0.4,0.5),c(0.1,0.2,0.3),c(0.1,0.2,0.3),c(0.1,0.2,0.3)), p_c = 0,
direction = 1, s1 = c(1/3,2/3,1), s2 = c(0.5,1), alpha_2 = 0.05,
alpha_2_alps_s1 = c(0.001,0.001,0.048), alpha_2_alps_s2 = c(0.001,0.049),
theta_cut = 0.01, samsz_1 = 100, samsz_2 = 150, N_max_1 = 200, N_max_2 = 300,
beta = 0.1, sim_num = 2)
```

Two_stage_asd_simu_OC_neg_binomial

Phase 2/3 seamless combination Group sequential design: Simulations, Negative binomial distribution, Optimizing adaptive sequential design

---

Description

Phase 2/3 seamless combination Group sequential design: Simulations, Negative binomial distribution, Optimizing adaptive sequential design

Usage

```
Two_stage_asd_simu_OC_neg_binomial(
  groups,
  r_c,
  kappa,
  direction,
  s1,
  s2,
  alpha_2,
  alpha_2_alps_s1,
  alpha_2_alps_s2,
  theta_cut,
  samsz_1,
  samsz_2,
  N_max_1,
  N_max_2,
  beta,
  sim_num
)
```

Arguments

groups	Vector of group labels used in the simulation
r_c	Rate parameter of the control arm (negative binomial endpoint)
kappa	Dispersion (size) parameter of the negative binomial distribution

direction	Test direction: 1 = larger r is better, 0 = smaller r is better
s1	Information fractions for the first stage / first group
s2	Information fractions for the second stage / second group
alpha_2	Type I error for the two-sided test
alpha_2_alps_s1	Type I error spent up to the interim analysis (stage 1 / group 1)
alpha_2_alps_s2	Cumulative type I error spent at the final analysis (stage 2 / group 2)
theta_cut	Efficacy cut-off on the effect-size scale applied at the interim analysis
samsz_1	Planned sample size (control arm) of the first stage / group
samsz_2	Planned sample size (control arm) of the second stage / group
N_max_1	Maximum allowed sample size (control arm) of the first stage / group
N_max_2	Maximum allowed sample size (control arm) of the second stage / group
beta	Type II error rate, i.e. 1 - power
sim_num	Number of simulation replicates

Value

A named list containing the following elements: 'Looks', 'Information fractions', 'O'Brien-Fleming boundaries'.

References

P. Gao, Y. Li (05 May 2024): Adaptive two-stage seamless sequential design for clinical trials, Journal of Biopharmaceutical Statistics, DOI: 10.1080/10543406.2024.2342518. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2342518

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
Two_stage_asd_simu_OC_neg_binomial(
groups = rbind(c(0.3,0.4,0.5),c(0.2,0.2,0.5),c(0.2,0.2,0.3),c(0.2,0.3,0.4)), r_c = 0.2,
kappa = 1, direction = 1, s1 = c(1/3,2/3,1), s2 = c(0.5,1), alpha_2 = 0.05,
alpha_2_alps_s1 = c(0.001,0.001,0.048), alpha_2_alps_s2 = c(0.001,0.049), theta_cut = 0.01,
samsz_1 = 100, samsz_2 = 150, N_max_1 = 200, N_max_2 = 300, beta = 0.1, sim_num = 2)
```

`Two_stage_asd_simu_OC_normal` *Phase 2/3 seamless combination Group sequential design: Simulations, Normal distribution, Optimizing adaptive sequential design*

Description

Phase 2/3 seamless combination Group sequential design: Simulations, Normal distribution, Optimizing adaptive sequential design

Usage

```
Two_stage_asd_simu_OC_normal(
  groups,
  mu_c,
  sigma_t,
  sigma_c,
  direction,
  s1,
  s2,
  alpha_2,
  alpha_2_alps_s1,
  alpha_2_alps_s2,
  theta_cut,
  samsz_1,
  samsz_2,
  N_max_1,
  N_max_2,
  beta,
  sim_num
)
```

Arguments

`groups`	Vector of group labels used in the simulation
`mu_c`	Mean of the control arm
`sigma_t`	Standard deviation of the test arm
`sigma_c`	Standard deviation of the control arm
`direction`	Test direction: 1 = larger mu is better, 0 = smaller mu is better
`s1`	Information fractions for the first stage / first group
`s2`	Information fractions for the second stage / second group
`alpha_2`	Type I error for the two-sided test
`alpha_2_alps_s1`	Type I error spent up to the interim analysis (stage 1 / group 1)

`alpha_2_alps_s2` Cumulative type I error spent at the final analysis (stage 2 / group 2)

`theta_cut` Efficacy cut-off on the effect-size scale applied at the interim analysis

`samsz_1` Planned sample size (control arm) of the first stage / group

`samsz_2` Planned sample size (control arm) of the second stage / group

`N_max_1` Maximum allowed sample size (control arm) of the first stage / group

`N_max_2` Maximum allowed sample size (control arm) of the second stage / group

`beta` Type II error rate, i.e. 1 - power

`sim_num` Number of simulation replicates

Value

A named list containing the following elements: 'Looks', 'Information fractions', 'O'Brien-Fleming boundaries'.

References

P. Gao, Y. Li (05 May 2024): Adaptive two-stage seamless sequential design for clinical trials, Journal of Biopharmaceutical Statistics, DOI: 10.1080/10543406.2024.2342518. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2342518

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
Two_stage_asd_simu_OC_normal(groups = rbind(c(0.2, 0.3, 0.4), c(0.3, 0.4, 0.5)), mu_c = 0,
sigma_t = 1, sigma_c = 1, direction = 1, s1 = c(1/3,2/3,1), s2 = c(0.5,1), alpha_2 = 0.05,
alpha_2_alps_s1 = c(0.001,0.001,0.048), alpha_2_alps_s2 = c(0.001,0.049), theta_cut = 0.01,
samsz_1 = 100, samsz_2 = 150, N_max_1 = 200, N_max_2 = 300, beta = 0.1, sim_num = 2)
```

`Two_stage_asd_simu_OC_poisson` *Phase 2/3 seamless combination Group sequential design: Simulations, Poisson distribution, Optimizing adaptive sequential design*

Description

Phase 2/3 seamless combination Group sequential design: Simulations, Poisson distribution, Optimizing adaptive sequential design

Usage

```
Two_stage_asd_simu_OC_poisson(
  groups,
  lambda_c,
  direction,
  s1,
  s2,
  alpha_2,
  alpha_2_alps_s1,
  alpha_2_alps_s2,
  theta_cut,
  samsz_1,
  samsz_2,
  N_max_1,
  N_max_2,
  beta,
  sim_num
)
```

Arguments

`groups`	Vector of group labels used in the simulation
`lambda_c`	Event rate in the control arm (Poisson / negative binomial endpoint)
`direction`	Test direction: 1 = larger lambda is better, 0 = smaller lambda is better
`s1`	Information fractions for the first stage / first group
`s2`	Information fractions for the second stage / second group
`alpha_2`	Type I error for the two-sided test
`alpha_2_alps_s1`	Type I error spent up to the interim analysis (stage 1 / group 1)
`alpha_2_alps_s2`	Cumulative type I error spent at the final analysis (stage 2 / group 2)
`theta_cut`	Efficacy cut-off on the effect-size scale applied at the interim analysis
`samsz_1`	Planned sample size (control arm) of the first stage / group

samsz_2	Planned sample size (control arm) of the second stage / group
N_max_1	Maximum allowed sample size (control arm) of the first stage / group
N_max_2	Maximum allowed sample size (control arm) of the second stage / group
beta	Type II error rate, i.e. 1 - power
sim_num	Number of simulation replicates

Value

A named list containing the following elements: 'Looks', 'Information fractions', 'O'Brien-Fleming boundaries'.

References

P. Gao, Y. Li (05 May 2024): Adaptive two-stage seamless sequential design for clinical trials, Journal of Biopharmaceutical Statistics, DOI: 10.1080/10543406.2024.2342518. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2342518

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P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
Two_stage_asd_simu_OC_poisson(
groups = rbind(c(0.3,0.4,0.5),c(0.2,0.2,0.5),c(0.2,0.2,0.3),c(0.2,0.3,0.4)), lambda_c = 0.2,
direction = 1, s1 = c(1/3,2/3,1), s2 = c(0.5,1), alpha_2 = 0.05,
alpha_2_alps_s1 = c(0.001,0.001,0.048), alpha_2_alps_s2 = c(0.001,0.049), theta_cut = 0.01,
samsz_1 = 100, samsz_2 = 150, N_max_1 = 200, N_max_2 = 300, beta = 0.1, sim_num = 2)
```

Two_stage_asd_simu_OC_survival

Phase 2/3 seamless combination Group sequential design: Simulations, Survival analysis, Optimizing adaptive sequential design

---

Description

Phase 2/3 seamless combination Group sequential design: Simulations, Survival analysis, Optimizing adaptive sequential design

Usage

```
Two_stage_asd_simu_OC_survival(
  groups,
  s1,
  s2,
  alpha_2,
  alpha_2_alps_s1,
  alpha_2_alps_s2,
  surv_rate,
  evt_num_1,
  evt_num_2,
  evt_max_1,
  evt_max_2,
  HR_cut,
  beta,
  sim_num
)
```

Arguments

groups	Vector of group labels used in the simulation
s1	Information fractions for the first stage / first group
s2	Information fractions for the second stage / second group
alpha_2	Type I error for the two-sided test
alpha_2_alps_s1	Type I error spent up to the interim analysis (stage 1 / group 1)
alpha_2_alps_s2	Cumulative type I error spent at the final analysis (stage 2 / group 2)
surv_rate	Survival rate used to translate the number of events into a sample size
evt_num_1	Number of events for the first stage / group
evt_num_2	Number of events for the second stage / group
evt_max_1	Maximum number of events for the first stage / group
evt_max_2	Maximum number of events for the second stage / group
HR_cut	Hazard-ratio cut-off for early stopping at the interim analysis
beta	Type II error rate, i.e. 1 - power
sim_num	Number of simulation replicates

Value

A named list containing the following elements: 'Looks', 'Information fractions', 'O'Brien-Fleming boundaries'.

References

P. Gao, Y. Li (05 May 2024): Adaptive two-stage seamless sequential design for clinical trials, Journal of Biopharmaceutical Statistics, DOI: 10.1080/10543406.2024.2342518. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2342518

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
Two_stage_asd_simu_OC_survival(groups = rbind(c(0.75,0.8,0.85),c(0.7,0.75,0.8),c(0.65,0.7,0.75)),
s1 = c(1/3,2/3,1), s2 = c(0.5,1), alpha_2 = 0.05, alpha_2_alps_s1 = c(0.001,0.001,0.048),
alpha_2_alps_s2 = c(0.01,0.04), surv_rate = 0.5, evt_num_1 = 200, evt_num_2 = 300,
evt_max_1 = 500, evt_max_2 = 600, HR_cut = 0.95, beta = 0.1, sim_num = 2)
```

---

two_stage_ci_0 *Phase 2/3 seamless combination Group sequential design: Final analysis, Without sample size change, last_vt == 1*

Description

Phase 2/3 seamless combination Group sequential design: Final analysis, Without sample size change, last_vt == 1

Usage

```
two_stage_ci_0(s, theta_hat_0, theta_hat_0_sd, alpha_2, dist)
```

Arguments

s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
theta_hat_0	'theta_hat_0' as used by this function; see Examples.
theta_hat_0_sd	'theta_hat_0_sd' as used by this function; see Examples.
alpha_2	Type I error for the two-sided test
dist	Indicator of the endpoint / distribution type

Value

A named list containing the following elements: 'p-value', 'confidence interval'.

References

P. Gao, Y. Li (05 May 2024): Adaptive two-stage seamless sequential design for clinical trials, Journal of Biopharmaceutical Statistics, DOI: 10.1080/10543406.2024.2342518. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2342518

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

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P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
two_stage_ci_0(s = c(1/3, 2/3, 1), theta_hat_0 = 0.2, theta_hat_0_sd = 0.5,
alpha_2 = 0.05, dist = 1)
```

---

two_stage_ci_1 *Phase 2/3 seamless combination Group sequential design: Final analysis, Without sample size change, last_vt > 1*

Description

Phase 2/3 seamless combination Group sequential design: Final analysis, Without sample size change, last_vt > 1

Usage

```
two_stage_ci_1(
  s,
  c_bry_two_stg,
  c_bry_p3,
  comp,
  theta_hat_p3,
  theta_hat_p3_sd,
  theta_hat_last,
  theta_hat_last_sd,
  last_vt,
```

```
  alpha_2,
  dist
)
```

Arguments

s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
c_bry_two_stg	Critical boundaries of the two-stage design
c_bry_p3	Critical boundaries of the prior (phase 3) study
comp	Type of comparison between arms
theta_hat_p3	Treatment effect estimate from the prior (phase 3) study
theta_hat_p3_sd	Standard error of 'theta_hat_p3'
theta_hat_last	Treatment effect estimate observed at the final analysis
theta_hat_last_sd	Standard error of 'theta_hat_last'
last_vt	Index of the analysis at which the trial stopped
alpha_2	Type I error for the two-sided test
dist	Indicator of the endpoint / distribution type

Value

A named list containing the following elements: 'p-value', 'confidence interval'.

References

P. Gao, Y. Li (05 May 2024): Adaptive two-stage seamless sequential design for clinical trials, Journal of Biopharmaceutical Statistics, DOI: 10.1080/10543406.2024.2342518. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2342518

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
two_stage_ci_1(s = c(1/3,2/3,1), c_bry_two_stg = c(3.938325, 2.784816,2.273793),
c_bry_p3 = c(3.954862,1.977431), comp = 3, theta_hat_p3 = 0.45, theta_hat_p3_sd = 0.6,
theta_hat_last = 2.784816*0.12, theta_hat_last_sd = 0.12, last_vt = 2, alpha_2 = 0.05, dist = 1)
```

two_stage_est_back *Phase 2/3 seamless combination Group sequential design: Final analysis, With one sample size change*

Description

Phase 2/3 seamless combination Group sequential design: Final analysis, With one sample size change

Usage

```
two_stage_est_back(
  s,
  c_bry_two_stg,
  c_bry_p3,
  comp,
  snew,
  c_bry_new,
  c_bry_new_p3,
  theta_hat_inter,
  theta_hat_inter_sd,
  inter_vt,
  theta_hat_last_ad,
  theta_hat_last_ad_sd,
  last_vt_ad,
  theta_hat_inter_p3,
  theta_hat_inter_p3_sd,
  theta_hat_last_ad_p3,
  theta_hat_last_ad_p3_sd,
  alpha_2,
  dist
)
```

Arguments

s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
c_bry_two_stg	Critical boundaries of the two-stage design
c_bry_p3	Critical boundaries of the prior (phase 3) study
comp	Type of comparison between arms
snew	Vector of new information fractions after the sample size is changed
c_bry_new	Critical boundaries after the sample size is changed
c_bry_new_p3	Critical boundaries after the sample size is changed (prior study scale)
theta_hat_inter	Treatment effect estimate observed at the interim analysis

`theta_hat_inter_sd`
: Standard error of 'theta_hat_inter'

`inter_vt`
: Index of the interim analysis at which the sample size is re-estimated (1-based)

`theta_hat_last_ad`
: Treatment effect estimate observed at the last analysis after the sample size change

`theta_hat_last_ad_sd`
: Standard error of 'theta_hat_last_ad'

`last_vt_ad`
: Index of the last analysis after the sample size change

`theta_hat_inter_p3`
: 'theta_hat_inter_p3' as used by this function; see Examples.

`theta_hat_inter_p3_sd`
: 'theta_hat_inter_p3_sd' as used by this function; see Examples.

`theta_hat_last_ad_p3`
: 'theta_hat_last_ad_p3' as used by this function; see Examples.

`theta_hat_last_ad_p3_sd`
: 'theta_hat_last_ad_p3_sd' as used by this function; see Examples.

`alpha_2`
: Type I error for the two-sided test

`dist`
: Indicator of the endpoint / distribution type

Value

A named list containing the following elements: 'p-value', 'confidence interval'.

References

P. Gao, Y. Li (05 May 2024): Adaptive two-stage seamless sequential design for clinical trials, Journal of Biopharmaceutical Statistics, DOI: 10.1080/10543406.2024.2342518. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2342518

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

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P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
two_stage_est_back(s=c(1/3,2/3,1), c_bry_two_stg=c(3.776606,2.670463,2.180424),
c_bry_p3=c(3.954862,1.977431), comp=2, snew=c(0.5,1), c_bry_new=c(3,2.2),
c_bry_new_p3=c(3.2,2.4), theta_hat_inter=0.4, theta_hat_inter_sd=0.35, inter_vt=1,
theta_hat_last_ad=0.5, theta_hat_last_ad_sd=0.23, last_vt_ad=1, theta_hat_inter_p3=0.2,
```

```
theta_hat_inter_p3_sd=0.4, theta_hat_last_ad_p3=0.32, theta_hat_last_ad_p3_sd=0.4,
alpha_2=0.05, dist=1)
```

`two_stage_power_alsp_boundary_binary_diff` *Phase 2/3 seamless combination Group sequential design: Binary distribution, Power calculation, Alpha-spending boundary*

Description

Phase 2/3 seamless combination Group sequential design: Binary distribution, Power calculation, Alpha-spending boundary

Usage

```
two_stage_power_alsp_boundary_binary_diff(
  p_t,
  p_c,
  margin,
  direction,
  s,
  alpha,
  sampsz_control,
  rand_ratio,
  dist1,
  dist2
)
```

Arguments

`p_t`	Event (response) proportion in the test arm
`p_c`	Event (response) proportion in the control arm
`margin`	Non-inferiority / superiority margin
`direction`	Test direction: 1 = larger p is better, 0 = smaller p is better
`s`	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
`alpha`	One-sided significance level (type I error rate)
`sampsz_control`	Control arm sample size
`rand_ratio`	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
`dist1`	Endpoint / distribution indicator for the first stage
`dist2`	Endpoint / distribution indicator for the second stage

Value

A named list containing the following elements: 'power', 'type I error control'.

References

P. Gao, Y. Li (05 May 2024): Adaptive two-stage seamless sequential design for clinical trials, Journal of Biopharmaceutical Statistics, DOI: 10.1080/10543406.2024.2342518. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2342518

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

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P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
two_stage_power_alsp_boundary_binary_diff(p_t = c(0.2,0.3,0.4), p_c = 0.5, margin = 0.15,
direction = 1, s = c(1/3,2/3,1), alpha = c(0.001,0.001,0.023), sampsz_control = 82,
rand_ratio = 1, dist1 = 1, dist2 = 1)
```

---

two_stage_power_alsp_boundary_neg_binomial

Phase 2/3 seamless combination Group sequential design: Negative binomial distribution, Power calculation, Alpha-spending boundary

---

Description

Phase 2/3 seamless combination Group sequential design: Negative binomial distribution, Power calculation, Alpha-spending boundary

Usage

```
two_stage_power_alsp_boundary_neg_binomial(
  r_t,
  r_c,
  margin,
  direction,
  s,
  alpha,
  sampsz_control,
```

```
  rand_ratio,
  nu_t,
  kappa,
  dist1,
  dist2
)
```

Arguments

r_t	Rate parameter of the test arm (negative binomial endpoint)
r_c	Rate parameter of the control arm (negative binomial endpoint)
margin	Non-inferiority / superiority margin
direction	Test direction: 1 = larger r is better, 0 = smaller r is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha	One-sided significance level (type I error rate)
sampsz_control	Control arm sample size
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
nu_t	Follow-up duration of the test arm (negative binomial endpoint)
kappa	Dispersion (size) parameter of the negative binomial distribution
dist1	Endpoint / distribution indicator for the first stage
dist2	Endpoint / distribution indicator for the second stage

Value

A named list containing the following elements: 'power', 'Critical boundaries', 'Critical boundaries for phase 3 only', '1-sided alpha spending', '1-sided cummulative alpha', '2-sided alpha spending', '2-sided cummulative alpha', 'selecting prob at end of phase 2', 'total selection prob at end of phase 2', 'Rejection rate for ech dose', 'total rejection rate', 'conditional rejection rate for each selected dose', 'critical boundary for phase 3 stage', 'Nomimal p-value for phase 3 stage'.

References

P. Gao, Y. Li (05 May 2024): Adaptive two-stage seamless sequential design for clinical trials, Journal of Biopharmaceutical Statistics, DOI: 10.1080/10543406.2024.2342518. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2342518

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
two_stage_power_alsp_boundary_neg_binomial(r_t = c(0.2,0.3,0.4), r_c = 0.6, margin = 0.1,
direction = 1, s = c(1/3,2/3,1), alpha = c(0.001,0.001,0.048), sampsz_control = 111,
rand_ratio = 1, nu_t = 1, kappa = 1, dist1 = 1, dist2 = 1)
```

---

two_stage_power_alsp_boundary_normal

Phase 2/3 seamless combination Group sequential design: Normal distribution, Power calculation, Alpha-spending boundary

---

Description

Phase 2/3 seamless combination Group sequential design: Normal distribution, Power calculation, Alpha-spending boundary

Usage

```
two_stage_power_alsp_boundary_normal(
  mu_t,
  mu_c,
  std_t,
  std_c,
  margin,
  direction,
  s,
  alpha,
  sampsz_control,
  rand_ratio,
  dist1,
  dist2
)
```

Arguments

mu_t	Mean of the test arm
mu_c	Mean of the control arm
std_t	Standard deviation of the test arm
std_c	Standard deviation of the control arm
margin	Non-inferiority / superiority margin
direction	Test direction: 0 = superiority test, 1 = non-inferiority test
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha	One-sided significance level (type I error rate)

sampsz_control	'sampsz_control' as used by this function; see Examples.
rand_ratio	Randomization ratio, sample size of the test arm over the control arm
dist1	Endpoint / distribution indicator for the first stage
dist2	Endpoint / distribution indicator for the second stage

Value

A named list containing the following elements: 'power', 'type I error control'.

References

P. Gao, Y. Li (05 May 2024): Adaptive two-stage seamless sequential design for clinical trials, Journal of Biopharmaceutical Statistics, DOI: 10.1080/10543406.2024.2342518. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2342518

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
two_stage_power_alsp_boundary_normal(mu_t = c(0.2,0.3,0.4), mu_c = 0, std_t = 1, std_c = 1,
margin = 0.01, direction = 1, s = c(1/3,2/3,1), alpha = c(0.001,0.001,0.023),
sampsz_control = 180, rand_ratio = 1, dist1 = 1, dist2 = 1)
```

---

two_stage_power_alsp_boundary_poisson

Phase 2/3 seamless combination Group sequential design: Poisson distribution, Power calculation, Alpha-spending boundary

---

Description

Phase 2/3 seamless combination Group sequential design: Poisson distribution, Power calculation, Alpha-spending boundary

Usage

```
two_stage_power_alsp_boundary_poisson(
  lambda_t,
  lambda_c,
  margin,
  direction,
  s,
  alpha,
  sampsz_control,
  rand_ratio,
  dist1,
  dist2
)
```

Arguments

lambda_t	Event rate in the test arm (Poisson / negative binomial endpoint)
lambda_c	Event rate in the control arm (Poisson / negative binomial endpoint)
margin	Non-inferiority / superiority margin
direction	Test direction: 1 = larger lambda is better, 0 = smaller lambda is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha	One-sided significance level (type I error rate)
sampsz_control	Control arm sample size
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
dist1	Endpoint / distribution indicator for the first stage
dist2	Endpoint / distribution indicator for the second stage

Value

A named list containing the following elements: 'power', 'type I error control'.

References

P. Gao, Y. Li (05 May 2024): Adaptive two-stage seamless sequential design for clinical trials, Journal of Biopharmaceutical Statistics, DOI: 10.1080/10543406.2024.2342518. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2342518

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
two_stage_power_alsp_boundary_poisson(lambda_t = c(0.2,0.3,0.4), lambda_c = 0.5, margin = 0.12,
direction = 1, s = c(1/3,2/3,1), alpha = c(0.001,0.001,0.023), sampsz_control = 150,
rand_ratio = 1, dist1 = 1, dist2 = 1)
```

---

two_stage_power_alsp_boundary_survival_Schoenfeld

Phase 2/3 seamless combination Group sequential design: Survival analysis, Power calculation, Alpha-spending boundary

---

Description

Phase 2/3 seamless combination Group sequential design: Survival analysis, Power calculation, Alpha-spending boundary

Usage

```
two_stage_power_alsp_boundary_survival_Schoenfeld(
  HR,
  margin,
  direction,
  s,
  alpha,
  events_tot,
  rand_ratio,
  dist1,
  dist2
)
```

Arguments

HR	Hazard ratio (test vs control)
margin	Non-inferiority / superiority margin
direction	Test direction: 1 = larger HR is better, 0 = smaller HR is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha	One-sided significance level (type I error rate)
events_tot	Total number of events
rand_ratio	Randomization ratio, sample size of the test arm over the control arm
dist1	Endpoint / distribution indicator for the first stage
dist2	Endpoint / distribution indicator for the second stage

Value

A named list containing the following elements: 'power', 'type I error control', 'reference'.

References

P. Gao, Y. Li (05 May 2024): Adaptive two-stage seamless sequential design for clinical trials, Journal of Biopharmaceutical Statistics, DOI: 10.1080/10543406.2024.2342518. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2342518

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
two_stage_power_alsp_boundary_survival_Schoenfeld(HR = c(0.2,0.3,0.4), margin = 1.1,
direction = 1, s = c(1/3,2/3,1), alpha = c(0.001,0.001,0.023), events_tot = 20,
rand_ratio = 1, dist1 = 1, dist2 = 1)
```

---

two_stage_power_OF_boundary_binary_diff

Phase 2/3 seamless combination Group sequential design: Binary distribution, Power calculation, O'Brien-Fleming boundary

---

Description

Phase 2/3 seamless combination Group sequential design: Binary distribution, Power calculation, O'Brien-Fleming boundary

Usage

```
two_stage_power_OF_boundary_binary_diff(
  p_t,
  p_c,
  margin,
  direction,
  s,
  alpha,
  sampsz_control,
```

```
  rand_ratio,
  dist1,
  dist2
)
```

Arguments

p_t	Event (response) proportion in the test arm
p_c	Event (response) proportion in the control arm
margin	Non-inferiority / superiority margin
direction	Test direction: 1 = larger p is better, 0 = smaller p is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha	One-sided significance level (type I error rate)
sampsz_control	Control arm sample size
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
dist1	Endpoint / distribution indicator for the first stage
dist2	Endpoint / distribution indicator for the second stage

Value

A named list containing the following elements: 'power', 'type I error control'.

References

P. Gao, Y. Li (05 May 2024): Adaptive two-stage seamless sequential design for clinical trials, Journal of Biopharmaceutical Statistics, DOI: 10.1080/10543406.2024.2342518. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2342518

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
two_stage_power_OF_boundary_binary_diff(p_t = c(0.2,0.3,0.4), p_c = 0.5, margin = 0.15,
direction = 1, s = c(1/3,2/3,1), alpha = 0.025,
sampsz_control = 82, rand_ratio = 1, dist1 = 1, dist2 = 1)
```

`two_stage_power_OF_boundary_neg_binomial`

Phase 2/3 seamless combination Group sequential design: Negative binomial distribution, Power calculation, O'Brien-Fleming boundary

Description

Phase 2/3 seamless combination Group sequential design: Negative binomial distribution, Power calculation, O'Brien-Fleming boundary

Usage

```
two_stage_power_OF_boundary_neg_binomial(
  r_t,
  r_c,
  margin,
  direction,
  s,
  alpha,
  sampsz_control,
  rand_ratio,
  nu_t,
  kappa,
  dist1,
  dist2
)
```

Arguments

`r_t`	Rate parameter of the test arm (negative binomial endpoint)
`r_c`	Rate parameter of the control arm (negative binomial endpoint)
`margin`	Non-inferiority / superiority margin
`direction`	Test direction: 1 = larger r is better, 0 = smaller r is better
`s`	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
`alpha`	One-sided significance level (type I error rate)
`sampsz_control`	Control arm sample size
`rand_ratio`	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
`nu_t`	Follow-up duration of the test arm (negative binomial endpoint)
`kappa`	Dispersion (size) parameter of the negative binomial distribution
`dist1`	Endpoint / distribution indicator for the first stage
`dist2`	Endpoint / distribution indicator for the second stage

Value

A named list containing the following elements: 'power', 'Critical boundaries', 'Critical boundaries for phase 3 only', '1-sided alpha spending', '1-sided cummulative alpha', '2-sided alpha spending', '2-sided cummulative alpha', 'selecting prob at end of phase 2', 'total selection prob at end of phase 2', 'Rejection rate for ech dose', 'total rejection rate', 'conditional rejection rate for each selected dose', 'critical boundary for phase 3 stage', 'Nomimal p-value for phase 3 stage'.

References

P. Gao, Y. Li (05 May 2024): Adaptive two-stage seamless sequential design for clinical trials, Journal of Biopharmaceutical Statistics, DOI: 10.1080/10543406.2024.2342518. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2342518

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
two_stage_power_OF_boundary_neg_binomial(r_t = c(1.1, 1.1, 1.1), r_c = 1.1, margin = 0.1,
direction = 0, s = c(1/3, 2/3, 1), alpha = 0.025, sampsz_control = 100, rand_ratio = 1,
nu_t = 6, kappa = 1, dist1 = 1, dist2 = 1)
```

---

two_stage_power_OF_boundary_normal

Phase 2/3 seamless combination Group sequential design: Normal distribution, Power calculation, O'Brien-Fleming boundary

---

Description

Phase 2/3 seamless combination Group sequential design: Normal distribution, Power calculation, O'Brien-Fleming boundary

Usage

```
two_stage_power_OF_boundary_normal(
  mu_t,
  mu_c,
  std_t,
```

```
  std_c,
  margin,
  direction,
  s,
  alpha,
  sampsz_control,
  rand_ratio,
  dist1,
  dist2
)
```

Arguments

mu_t	Means of the test arm
mu_c	Means of the control arm
std_t	Standard deviation of the test arm
std_c	Standard deviation of the control arm
margin	Non-inferiority / superiority margin
direction	Test direction: 1 = larger mu is better, 0 = smaller mu is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha	One-sided significance level (type I error rate)
sampsz_control	Control arm sample size
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
dist1	Endpoint / distribution indicator for the first stage
dist2	Endpoint / distribution indicator for the second stage

Value

A named list containing the following elements: 'power', 'type I error control'.

References

P. Gao, Y. Li (05 May 2024): Adaptive two-stage seamless sequential design for clinical trials, Journal of Biopharmaceutical Statistics, DOI: 10.1080/10543406.2024.2342518. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2342518

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
two_stage_power_OF_boundary_normal(mu_t = c(0.2,0.3,0.4), mu_c = 0, std_t = 1, std_c = 1,
margin = 0.01, direction = 1, s = c(1/3,2/3,1), alpha = 0.025, sampsz_control = 180,
rand_ratio = 1, dist1 = 1, dist2 = 1)
```

---

two_stage_power_OF_boundary_poisson

Phase 2/3 seamless combination Group sequential design: Poisson distribution, Power calculation, O'Brien-Fleming boundary

---

Description

Phase 2/3 seamless combination Group sequential design: Poisson distribution, Power calculation, O'Brien-Fleming boundary

Usage

```
two_stage_power_OF_boundary_poisson(
  lambda_t,
  lambda_c,
  margin,
  direction,
  s,
  alpha,
  sampsz_control,
  rand_ratio,
  dist1,
  dist2
)
```

Arguments

lambda_t	Event rate in the test arm (Poisson / negative binomial endpoint)
lambda_c	Event rate in the control arm (Poisson / negative binomial endpoint)
margin	Non-inferiority / superiority margin
direction	Test direction: 1 = larger lambda is better, 0 = smaller lambda is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha	One-sided significance level (type I error rate)
sampsz_control	Control arm sample size
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
dist1	Endpoint / distribution indicator for the first stage
dist2	Endpoint / distribution indicator for the second stage

Value

A named list containing the following elements: 'power', 'type I error control'.

References

P. Gao, Y. Li (05 May 2024): Adaptive two-stage seamless sequential design for clinical trials, Journal of Biopharmaceutical Statistics, DOI: 10.1080/10543406.2024.2342518. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2342518

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
two_stage_power_OF_boundary_poisson(lambda_t = c(0.2,0.3,0.4), lambda_c = 0.5, margin = 0.12,
direction = 1, s = c(1/3,2/3,1), alpha = 0.025, sampsz_control = 150, rand_ratio = 1,
dist1 = 1, dist2 = 1)
```

---

two_stage_power_OF_boundary_survival_Schoenfeld

Phase 2/3 seamless combination Group sequential design: Survival analysis, Power calculation, O'Brien-Fleming boundary

---

Description

Phase 2/3 seamless combination Group sequential design: Survival analysis, Power calculation, O'Brien-Fleming boundary

Usage

```
two_stage_power_OF_boundary_survival_Schoenfeld(
  HR,
  margin,
  direction,
  s,
  alpha,
  events_tot,
  rand_ratio,
```

```
  dist1,
  dist2
)
```

Arguments

HR	Hazard ratio (test vs control)
margin	Non-inferiority / superiority margin
direction	Test direction: 1 = larger HR is better, 0 = smaller HR is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha	One-sided significance level (type I error rate)
events_tot	Total number of events
rand_ratio	Randomization ratio, sample size of the test arm over the control arm
dist1	Endpoint / distribution indicator for the first stage
dist2	Endpoint / distribution indicator for the second stage

Value

A named list containing the following elements: 'power', 'type I error control', 'reference'.

References

P. Gao, Y. Li (05 May 2024): Adaptive two-stage seamless sequential design for clinical trials, Journal of Biopharmaceutical Statistics, DOI: 10.1080/10543406.2024.2342518. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2342518

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
two_stage_power_OF_boundary_survival_Schoenfeld(HR = c(0.55,0.55), margin = 1, direction = 2,
s = c(1/3,2/3,1), alpha = 0.025,
events_tot = 137, rand_ratio = 1, dist1 = 2, dist2 = 1)
```

`two_stage_Sample_size_alsp_boundary_binary_diff` *Phase 2/3 seamless combination Group sequential design: Binary distribution, Sample size calculation, Alpha-spending boundary*

Description

Phase 2/3 seamless combination Group sequential design: Binary distribution, Sample size calculation, Alpha-spending boundary

Usage

```
two_stage_Sample_size_alsp_boundary_binary_diff(
  p_t,
  p_c,
  margin,
  direction,
  s,
  alpha,
  beta,
  rand_ratio,
  dist1,
  dist2
)
```

Arguments

`p_t`	Event (response) proportion in the test arm
`p_c`	Event (response) proportion in the control arm
`margin`	Non-inferiority / superiority margin
`direction`	Test direction: 1 = larger p is better, 0 = smaller p is better
`s`	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
`alpha`	One-sided significance level (type I error rate)
`beta`	Type II error rate, i.e. 1 - power
`rand_ratio`	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
`dist1`	Endpoint / distribution indicator for the first stage
`dist2`	Endpoint / distribution indicator for the second stage

Value

A named list containing the following elements: 'test arm sample size', 'control arm sample size', 'sample size for each dose in a two arm study with same critical boudary', 'sample size for control arm in a two arm study with same critical boudary', 'type I error control', 'exit probabilities'.

References

P. Gao, Y. Li (05 May 2024): Adaptive two-stage seamless sequential design for clinical trials, Journal of Biopharmaceutical Statistics, DOI: 10.1080/10543406.2024.2342518. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2342518

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
two_stage_Sample_size_alsp_boundary_binary_diff(p_t = 0.4, p_c = 0.3, margin = 0.1,
direction = 0, s = c(1/3, 2/3, 1), alpha = 0.025,
beta = 0.1, rand_ratio = 1, dist1 = 1, dist2 = 1)
```

---

two_stage_Sample_size_alsp_boundary_neg_binomial

Phase 2/3 seamless combination Group sequential design: Negative binomial distribution, Sample size calculation, Alpha-spending boundary

---

Description

Phase 2/3 seamless combination Group sequential design: Negative binomial distribution, Sample size calculation, Alpha-spending boundary

Usage

```
two_stage_Sample_size_alsp_boundary_neg_binomial(
  r_t,
  r_c,
  margin,
  direction,
  s,
  alpha,
  beta,
  rand_ratio,
  nu_t,
  kappa,
```

```
  dist1,
  dist2
)
```

Arguments

r_t	Rate parameter of the test arm (negative binomial endpoint)
r_c	Rate parameter of the control arm (negative binomial endpoint)
margin	Non-inferiority / superiority margin
direction	Test direction: 1 = larger r is better, 0 = smaller r is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha	One-sided significance level (type I error rate)
beta	Type II error rate, i.e. 1 - power
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
nu_t	Follow-up duration of the test arm (negative binomial endpoint)
kappa	Dispersion (size) parameter of the negative binomial distribution
dist1	Endpoint / distribution indicator for the first stage
dist2	Endpoint / distribution indicator for the second stage

Value

A named list containing the following elements: 'test arm sample size', 'control arm sample size', 'sample size for each dose in a two arm study with same critical boudary', 'Critical boundaries', 'Critical boundaries for phase 3 only', '1-sided alpha spending', '1-sided cummulative alpha', '2-sided alpha spending', '2-sided cummulative alpha', 'selecting prob at end of phase 2', 'total selection prob at end of phase 2', 'Rejection rate for ech dose', 'total rejection rate', 'conditional rejection rate for each selected dose', 'critical boundary for phase 3 stage', 'Nomimal p-value for phase 3 stage'.

References

P. Gao, Y. Li (05 May 2024): Adaptive two-stage seamless sequential design for clinical trials, Journal of Biopharmaceutical Statistics, DOI: 10.1080/10543406.2024.2342518. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2342518

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
two_stage_Sample_size_alsp_boundary_neg_binomial(r_t = c(0.2,0.3,0.4), r_c = 0.6, margin = 0.1,
direction = 1, s = c(1/3,2/3,1), alpha = c(0.001,0.001,0.023), beta = 0.1, rand_ratio = 1,
nu_t = 1, kappa = 1, dist1 = 1, dist2 = 1)
```

---

two_stage_Sample_size_alsp_boundary_normal

Phase 2/3 seamless combination Group sequential design: Normal distribution, Sample size calculation, Alpha-spending boundary

---

Description

Phase 2/3 seamless combination Group sequential design: Normal distribution, Sample size calculation, Alpha-spending boundary

Usage

```
two_stage_Sample_size_alsp_boundary_normal(
  mu_t,
  mu_c,
  std_t,
  std_c,
  margin,
  direction,
  s,
  alpha,
  beta,
  rand_ratio,
  dist1,
  dist2
)
```

Arguments

mu_t	Means of the test arm
mu_c	Means of the control arm
std_t	Standard deviation of the test arm
std_c	Standard deviation of the control arm
margin	Non-inferiority / superiority margin
direction	Test direction: 1 = larger mu is better, 0 = smaller mu is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha	One-sided significance level (type I error rate)

beta	Type II error rate, i.e. 1 - power
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
dist1	Endpoint / distribution indicator for the first stage
dist2	Endpoint / distribution indicator for the second stage

Value

A named list containing the following elements: 'test arm sample size', 'control arm sample size', 'sample size for each dose in a two arm study with same critical boudary', 'sample size for control arm in a two arm study with same critical boudary', 'type I error control', 'exit probabilities'.

References

P. Gao, Y. Li (05 May 2024): Adaptive two-stage seamless sequential design for clinical trials, Journal of Biopharmaceutical Statistics, DOI: 10.1080/10543406.2024.2342518. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2342518

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
two_stage_Sample_size_alsp_boundary_normal(mu_t = 2.6, mu_c = 0.6, std_t = 9.43, std_c = 9.86,
margin = 0.1, direction = 0, s = c(1/3, 2/3, 1), alpha = 0.025, beta = 0.1, rand_ratio = 1,
dist1 = 1, dist2 = 1)
```

---

two_stage_Sample_size_alsp_boundary_poisson

Phase 2/3 seamless combination Group sequential design: Poisson distribution, Sample size calculation, Alpha-spending boundary

---

Description

Phase 2/3 seamless combination Group sequential design: Poisson distribution, Sample size calculation, Alpha-spending boundary

Usage

```
two_stage_Sample_size_alsp_boundary_poisson(
  lambda_t,
  lambda_c,
  margin,
  direction,
  s,
  alpha,
  beta,
  rand_ratio,
  dist1,
  dist2
)
```

Arguments

lambda_t	Event rate in the test arm (Poisson / negative binomial endpoint)
lambda_c	Event rate in the control arm (Poisson / negative binomial endpoint)
margin	Non-inferiority / superiority margin
direction	Test direction: 1 = larger lambda is better, 0 = smaller lambda is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha	One-sided significance level (type I error rate)
beta	Type II error rate, i.e. 1 - power
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
dist1	Endpoint / distribution indicator for the first stage
dist2	Endpoint / distribution indicator for the second stage

Value

A named list containing the following elements: 'test arm sample size', 'control arm sample size', 'sample size for each dose in a two arm study with same critical boudary', 'sample size for control arm in a two arm study with same critical boudary', 'type I error control', 'exit probabilities'.

References

P. Gao, Y. Li (05 May 2024): Adaptive two-stage seamless sequential design for clinical trials, Journal of Biopharmaceutical Statistics, DOI: 10.1080/10543406.2024.2342518. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2342518

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
two_stage_Sample_size_alsp_boundary_poisson(lambda_t = 1.1, lambda_c = 1.0, margin = 0.1,
direction = 0, s = c(1/3, 2/3, 1), alpha = 0.025,
beta = 0.1, rand_ratio = 1, dist1 = 1, dist2 = 1)
```

---

two_stage_Sample_size_alsp_boundary_survival_Schoenfeld

Phase 2/3 seamless combination Group sequential design: Survival analysis, Sample size calculation, Alpha-spending boundary

---

Description

Phase 2/3 seamless combination Group sequential design: Survival analysis, Sample size calculation, Alpha-spending boundary

Usage

```
two_stage_Sample_size_alsp_boundary_survival_Schoenfeld(
  HR,
  margin,
  direction,
  s,
  alpha,
  beta,
  rand_ratio,
  dist1,
  dist2
)
```

Arguments

HR	Hazard ratio (test vs control)
margin	Non-inferiority / superiority margin
direction	Test direction: 1 = larger HR is better, 0 = smaller HR is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha	One-sided significance level (type I error rate)
beta	Type II error rate, i.e. 1 - power

rand_ratio	Randomization ratio, sample size of the test arm over the control arm
dist1	Endpoint / distribution indicator for the first stage
dist2	Endpoint / distribution indicator for the second stage

Value

A named list containing the following elements: 'Combined number of events between a dose and control', 'total number of events from all doses and control', 'combined number of events in each dose and control in a two arm study with same critical boudary', 'type I error control', 'exit probabilities', 'reference'.

References

P. Gao, Y. Li (05 May 2024): Adaptive two-stage seamless sequential design for clinical trials, Journal of Biopharmaceutical Statistics, DOI: 10.1080/10543406.2024.2342518. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2342518

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
two_stage_Sample_size_alsp_boundary_survival_Schoenfeld(HR = 0.7, margin = 0.1, direction = 0,
s = c(1/3, 2/3, 1), alpha = 0.025, beta = 0.1, rand_ratio = 1, dist1 = 1, dist2 = 1)
```

---

two_stage_Sample_size_OF_boundary_binary_diff

Phase 2/3 seamless combination Group sequential design: Binary distribution, Sample size calculation, O'Brien-Fleming boundary

---

Description

Phase 2/3 seamless combination Group sequential design: Binary distribution, Sample size calculation, O'Brien-Fleming boundary

Usage

```
two_stage_Sample_size_OF_boundary_binary_diff(
  p_t,
  p_c,
  margin,
  direction,
  s,
  alpha,
  beta,
  rand_ratio,
  dist1,
  dist2
)
```

Arguments

p_t	Event (response) proportion in the test arm
p_c	Event (response) proportion in the control arm
margin	Non-inferiority / superiority margin
direction	Test direction: 1 = larger p is better, 0 = smaller p is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha	One-sided significance level (type I error rate)
beta	Type II error rate, i.e. 1 - power
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
dist1	Endpoint / distribution indicator for the first stage
dist2	Endpoint / distribution indicator for the second stage

Value

A named list containing the following elements: 'test arm sample size', 'control arm sample size', 'sample size for each dose in a two arm study with same critical boudary', 'sample size for control arm in a two arm study with same critical boudary', 'type I error control', 'exit probabilities'.

References

P. Gao, Y. Li (05 May 2024): Adaptive two-stage seamless sequential design for clinical trials, Journal of Biopharmaceutical Statistics, DOI: 10.1080/10543406.2024.2342518. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2342518

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
two_stage_Sample_size_OF_boundary_binary_diff(p_t = 0.4, p_c = 0.3, margin = 0.1, direction = 0,
s = c(1/3, 2/3, 1), alpha = 0.025, beta = 0.1, rand_ratio = 1, dist1 = 1, dist2 = 1)
```

---

two_stage_Sample_size_OF_boundary_neg_binomial

Phase 2/3 seamless combination Group sequential design: Negative binomial distribution, Sample size calculation, O'Brien-Fleming boundary

---

Description

Phase 2/3 seamless combination Group sequential design: Negative binomial distribution, Sample size calculation, O'Brien-Fleming boundary

Usage

```
two_stage_Sample_size_OF_boundary_neg_binomial(
  r_t,
  r_c,
  margin,
  direction,
  s,
  alpha,
  beta,
  rand_ratio,
  nu_t,
  kappa,
  dist1,
  dist2
)
```

Arguments

r_t	Rate parameter of the test arm (negative binomial endpoint)
r_c	Rate parameter of the control arm (negative binomial endpoint)
margin	Non-inferiority / superiority margin
direction	Test direction: 1 = larger r is better, 0 = smaller r is better

s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha	One-sided significance level (type I error rate)
beta	Type II error rate, i.e. 1 - power
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
nu_t	Follow-up duration of the test arm (negative binomial endpoint)
kappa	Dispersion (size) parameter of the negative binomial distribution
dist1	Endpoint / distribution indicator for the first stage
dist2	Endpoint / distribution indicator for the second stage

Value

A named list containing the following elements: 'test arm sample size', 'control arm sample size', 'sample size for each dose in a two arm study with same critical boudary', 'sample size for control arm in a two arm study with same critical boudary', 'type I error control', 'exit probabilities', 'Reference'.

References

P. Gao, Y. Li (05 May 2024): Adaptive two-stage seamless sequential design for clinical trials, Journal of Biopharmaceutical Statistics, DOI: 10.1080/10543406.2024.2342518. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2342518

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
two_stage_Sample_size_OF_boundary_neg_binomial(r_t = c(1.1, 1.1, 1.1), r_c = 1.1, margin = 0.1,
direction = 0, s = c(1/3, 2/3, 1), alpha = 0.025, beta = 0.1, rand_ratio = 1, nu_t = 6,
kappa = 1, dist1 = 1, dist2 = 1)
```

two_stage_Sample_size_OF_boundary_normal

Phase 2/3 seamless combination Group sequential design: Normal distribution, Sample size calculation, O'Brien-Fleming boundary

Description

Phase 2/3 seamless combination Group sequential design: Normal distribution, Sample size calculation, O'Brien-Fleming boundary

Usage

```
two_stage_Sample_size_OF_boundary_normal(
  mu_t,
  mu_c,
  std_t,
  std_c,
  margin,
  direction,
  s,
  alpha,
  beta,
  rand_ratio,
  dist1,
  dist2
)
```

Arguments

mu_t	Means of the test arm
mu_c	Means of the control arm
std_t	Standard deviation of the test arm
std_c	Standard deviation of the control arm
margin	Non-inferiority / superiority margin
direction	Test direction: 1 = larger mu is better, 0 = smaller mu is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha	One-sided significance level (type I error rate)
beta	Type II error rate, i.e. 1 - power
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
dist1	Endpoint / distribution indicator for the first stage
dist2	Endpoint / distribution indicator for the second stage

Value

A named list containing the following elements: 'test arm sample size', 'control arm sample size', 'sample size for each dose in a two arm study with same critical boudary', 'sample size for control arm in a two arm study with same critical boudary', 'type I error control', 'exit probabilities'.

References

P. Gao, Y. Li (05 May 2024): Adaptive two-stage seamless sequential design for clinical trials, Journal of Biopharmaceutical Statistics, DOI: 10.1080/10543406.2024.2342518. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2342518

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
two_stage_Sample_size_OF_boundary_normal(mu_t = 2.6, mu_c = 0.6, std_t = 9.43, std_c = 9.86,
margin = 0.1, direction = 0, s = c(1/3, 2/3, 1), alpha = 0.025, beta = 0.1, rand_ratio = 1,
dist1 = 1, dist2 = 1)
```

---

two_stage_Sample_size_OF_boundary_poisson

Phase 2/3 seamless combination Group sequential design: Poisson distribution, Sample size calculation, O'Brien-Fleming boundary

---

Description

Phase 2/3 seamless combination Group sequential design: Poisson distribution, Sample size calculation, O'Brien-Fleming boundary

Usage

```
two_stage_Sample_size_OF_boundary_poisson(
  lambda_t,
  lambda_c,
  margin,
  direction,
  s,
```

```
  alpha,
  beta,
  rand_ratio,
  dist1,
  dist2
)
```

Arguments

lambda_t	Event rate in the test arm (Poisson / negative binomial endpoint)
lambda_c	Event rate in the control arm (Poisson / negative binomial endpoint)
margin	Non-inferiority / superiority margin
direction	Test direction: 1 = larger lambda is better, 0 = smaller lambda is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha	One-sided significance level (type I error rate)
beta	Type II error rate, i.e. 1 - power
rand_ratio	Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm
dist1	Endpoint / distribution indicator for the first stage
dist2	Endpoint / distribution indicator for the second stage

Value

A named list containing the following elements: 'test arm sample size', 'control arm sample size', 'sample size for each dose in a two arm study with same critical boudary', 'sample size for control arm in a two arm study with same critical boudary', 'type I error control', 'exit probabilities'.

References

P. Gao, Y. Li (05 May 2024): Adaptive two-stage seamless sequential design for clinical trials, Journal of Biopharmaceutical Statistics, DOI: 10.1080/10543406.2024.2342518. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2342518

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
two_stage_Sample_size_OF_boundary_poisson(lambda_t = 1.1, lambda_c = 1.0, margin = 0.1,
direction = 0, s = c(1/3, 2/3, 1), alpha = 0.025,
beta = 0.1, rand_ratio = 1, dist1 = 1, dist2 = 1)
```

---

two_stage_Sample_size_OF_boundary_survival_Schoenfeld

Phase 2/3 seamless combination Group sequential design: Survival analysis, Sample size calculation, O'Brien-Fleming boundary

---

Description

Phase 2/3 seamless combination Group sequential design: Survival analysis, Sample size calculation, O'Brien-Fleming boundary

Usage

```
two_stage_Sample_size_OF_boundary_survival_Schoenfeld(
  HR,
  margin,
  direction,
  s,
  alpha,
  beta,
  rand_ratio,
  dist1,
  dist2
)
```

Arguments

HR	Hazard ratio (test vs control)
margin	Non-inferiority / superiority margin
direction	Test direction: 1 = larger HR is better, 0 = smaller HR is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
alpha	One-sided significance level (type I error rate)
beta	Type II error rate, i.e. 1 - power
rand_ratio	Randomization ratio, sample size of the test arm over the control arm
dist1	Endpoint / distribution indicator for the first stage
dist2	Endpoint / distribution indicator for the second stage

Value

A named list containing the following elements: 'Combined number of events between a dose and control', 'total number of events from all doses and control', 'combined number of events in each dose and control in a two arm study with same critical boudary', 'type I error control', 'exit probabilities', 'reference'.

References

P. Gao, Y. Li (05 May 2024): Adaptive two-stage seamless sequential design for clinical trials, Journal of Biopharmaceutical Statistics, DOI: 10.1080/10543406.2024.2342518. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2342518

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
two_stage_Sample_size_OF_boundary_survival_Schoenfeld(HR = 0.7, margin = 0.1, direction = 0,
s = c(1/3, 2/3, 1), alpha = 0.025, beta = 0.1,
rand_ratio = 1, dist1 = 1, dist2 = 1)
```

---

two_stg_adapt_power_simu_binary

Phase 2/3 seamless combination Group sequential design: Simulations, Binary distribution, Operating characteristics

---

Description

Phase 2/3 seamless combination Group sequential design: Simulations, Binary distribution, Operating characteristics

Usage

```
two_stg_adapt_power_simu_binary(
  p_t,
  p_c,
  direction,
  s,
```

```
  bry_type,
  alpha_2,
  theta_cut,
  N_max,
  samsz,
  beta,
  sim_num
)
```

Arguments

p_t	Event (response) proportion in the test arm
p_c	Event (response) proportion in the control arm
direction	Test direction: 1 = larger p is better, 0 = smaller p is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
bry_type	Critical boundary type: 1 = O'Brien-Fleming, 2 = Pocock, 3 = alpha-spending
alpha_2	Type I error for the two-sided test
theta_cut	Efficacy cut-off on the effect-size scale applied at the interim analysis
N_max	Maximum allowed sample size (control arm)
samsz	Planned sample size of the control arm used in the simulation
beta	Type II error rate, i.e. 1 - power
sim_num	Number of simulation replicates

Value

A matrix in which each row corresponds to one simulation replicate and the columns hold the simulated operating characteristics (e.g. rejection indicators, sample sizes and stopping stages).

References

P. Gao, Y. Li (05 May 2024): Adaptive two-stage seamless sequential design for clinical trials, Journal of Biopharmaceutical Statistics, DOI: 10.1080/10543406.2024.2342518. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2342518

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
two_stg_adapt_power_simu_binary(p_t = c(0.4,0.5), p_c = 0.3, direction = 1, s = c(1/3,2/3,1),
bry_type = 1, alpha_2 = 0.05, theta_cut = 0.05, N_max = 1000, samsz = 100,
beta = 0.1, sim_num = 20)
```

---

two_stg_adapt_power_simu_neg_binomial

Phase 2/3 seamless combination Group sequential design: Simulations, Negative binomial distribution, Operating characteristics

---

Description

Phase 2/3 seamless combination Group sequential design: Simulations, Negative binomial distribution, Operating characteristics

Usage

```
two_stg_adapt_power_simu_neg_binomial(
  r_t,
  r_c,
  kappa,
  direction,
  s,
  bry_type,
  alpha_2,
  theta_cut,
  samsz,
  N_max,
  beta,
  sim_num
)
```

Arguments

r_t	Rate parameter of the test arm (negative binomial endpoint)
r_c	Rate parameter of the control arm (negative binomial endpoint)
kappa	Dispersion (size) parameter of the negative binomial distribution
direction	Test direction: 1 = larger r is better, 0 = smaller r is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
bry_type	Critical boundary type: 1 = O'Brien-Fleming, 2 = Pocock, 3 = alpha-spending
alpha_2	Type I error for the two-sided test
theta_cut	Efficacy cut-off on the effect-size scale applied at the interim analysis

samsz	Planned sample size of the control arm used in the simulation
N_max	Maximum allowed sample size (control arm)
beta	Type II error rate, i.e. 1 - power
sim_num	Number of simulation replicates

Value

A matrix in which each row corresponds to one simulation replicate and the columns hold the simulated operating characteristics (e.g. rejection indicators, sample sizes and stopping stages).

References

P. Gao, Y. Li (05 May 2024): Adaptive two-stage seamless sequential design for clinical trials, Journal of Biopharmaceutical Statistics, DOI: 10.1080/10543406.2024.2342518. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2342518

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
two_stg_adapt_power_simu_neg_binomial(
r_t = c(1.1,1.1,1.1), r_c = 1.1, kappa = 1, direction = 1,
s = c(1/3,1), bry_type = 1, alpha_2 = 0.05, theta_cut = 0.05, samsz = 100, N_max = 1000,
beta = 0.1, sim_num = 20)
```

---

two_stg_adapt_power_simu_normal

Phase 2/3 seamless combination Group sequential design: Simulations, Normal distribution, Operating characteristics

---

Description

Phase 2/3 seamless combination Group sequential design: Simulations, Normal distribution, Operating characteristics

Usage

```
two_stg_adapt_power_simu_normal(
  mu_t,
  mu_c,
  sigma_t,
  sigma_c,
  direction,
  s,
  bry_type,
  alpha_2,
  theta_cut,
  samsz,
  N_max,
  beta,
  sim_num
)
```

Arguments

mu_t	Means of the test arm
mu_c	Means of the control arm
sigma_t	Standard deviation of the test arm
sigma_c	Standard deviation of the control arm
direction	Test direction: 1 = larger mu is better, 0 = smaller mu is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
bry_type	Critical boundary type: 1 = O'Brien-Fleming, 2 = Pocock, 3 = alpha-spending
alpha_2	Type I error for the two-sided test
theta_cut	Efficacy cut-off on the effect-size scale applied at the interim analysis
samsz	Planned sample size of the control arm used in the simulation
N_max	Maximum allowed sample size (control arm)
beta	Type II error rate, i.e. 1 - power
sim_num	Number of simulation replicates

Value

A matrix in which each row corresponds to one simulation replicate and the columns hold the simulated operating characteristics (e.g. rejection indicators, sample sizes and stopping stages).

References

P. Gao, Y. Li (05 May 2024): Adaptive two-stage seamless sequential design for clinical trials, Journal of Biopharmaceutical Statistics, DOI: 10.1080/10543406.2024.2342518. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2342518

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

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P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
two_stg_adapt_power_simu_normal(mu_t = c(0,0.4,0.5), mu_c = 0, sigma_t = 1, sigma_c = 1,
direction = 1, s = c(1/3,2/3,1), bry_type = 1, alpha_2 = 0.05, theta_cut = 0.05, samsz = 100,
N_max = 1000, beta = 0.1, sim_num = 20)
```

---

two_stg_adapt_power_simu_poisson

Phase 2/3 seamless combination Group sequential design: Simulations, Poisson distribution, Operating characteristics

---

Description

Phase 2/3 seamless combination Group sequential design: Simulations, Poisson distribution, Operating characteristics

Usage

```
two_stg_adapt_power_simu_poisson(
  lambda_t,
  lambda_c,
  direction,
  s,
  bry_type,
  alpha_2,
  theta_cut,
  N_max,
  samsz,
  beta,
  sim_num
)
```

Arguments

lambda_t	Event rate in the test arm (Poisson / negative binomial endpoint)
lambda_c	Event rate in the control arm (Poisson / negative binomial endpoint)
direction	Test direction: 1 = larger lambda is better, 0 = smaller lambda is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
bry_type	Critical boundary type: 1 = O'Brien-Fleming, 2 = Pocock, 3 = alpha-spending
alpha_2	Type I error for the two-sided test
theta_cut	Efficacy cut-off on the effect-size scale applied at the interim analysis
N_max	Maximum allowed sample size (control arm)
samsz	Planned sample size of the control arm used in the simulation
beta	Type II error rate, i.e. 1 - power
sim_num	Number of simulation replicates

Value

A matrix in which each row corresponds to one simulation replicate and the columns hold the simulated operating characteristics (e.g. rejection indicators, sample sizes and stopping stages).

References

P. Gao, Y. Li (05 May 2024): Adaptive two-stage seamless sequential design for clinical trials, Journal of Biopharmaceutical Statistics, DOI: 10.1080/10543406.2024.2342518. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2342518

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P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
two_stg_adapt_power_simu_poisson(lambda_t = c(1.1,1.1,1.1), lambda_c = 1.1, direction = 1,
s = c(1/3,1), bry_type = 1, alpha_2 = 0.05,
theta_cut = 0.05, N_max = 1000, samsz = 100, beta = 0.1, sim_num = 20)
```

two_stg_adapt_power_simu_survival *Phase 2/3 seamless combination Group sequential design: Simulations, Survival analysis, Operating characteristics*

Description

Phase 2/3 seamless combination Group sequential design: Simulations, Survival analysis, Operating characteristics

Usage

```
two_stg_adapt_power_simu_survival(
  HR,
  s,
  bry_type,
  alpha_2,
  evt_num,
  evt_max,
  HR_cut,
  surv_rate,
  beta,
  sim_num
)
```

Arguments

HR	Hazard ratio (test vs control)
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
bry_type	Critical boundary type: 1 = O'Brien-Fleming, 2 = Pocock, 3 = alpha-spending
alpha_2	Type I error for the two-sided test
evt_num	Total number of events at the final analysis
evt_max	Maximum number of events
HR_cut	Hazard-ratio cut-off for early stopping at the interim analysis
surv_rate	Survival rate used to translate the number of events into a sample size
beta	Type II error rate, i.e. 1 - power
sim_num	Number of simulation replicates

Value

A matrix in which each row corresponds to one simulation replicate and the columns hold the simulated operating characteristics (e.g. rejection indicators, sample sizes and stopping stages).

References

P. Gao, Y. Li (05 May 2024): Adaptive two-stage seamless sequential design for clinical trials, Journal of Biopharmaceutical Statistics, DOI: 10.1080/10543406.2024.2342518. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2342518

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

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P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
two_stg_adapt_power_simu_survival(HR = rep(1,2), s = c(1/3,2/3,1), bry_type = 1, alpha_2 = 0.05,
evt_num = 150, evt_max = 1500, HR_cut = 0.95, surv_rate = 0.5, beta = 0.1, sim_num = 20)
```

---

two_stg_power_simu_binary

Phase 2/3 seamless combination Group sequential design: Simulations, Binary distribution, Type I error and power

---

Description

Phase 2/3 seamless combination Group sequential design: Simulations, Binary distribution, Type I error and power

Usage

```
two_stg_power_simu_binary(
  p_t,
  p_c,
  direction,
  s,
  bry_type,
  alpha_2,
  samsz,
  sim_num
)
```

Arguments

p_t	Event (response) proportion in the test arm
p_c	Event (response) proportion in the control arm
direction	Test direction: 1 = larger p is better, 0 = smaller p is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
bry_type	Critical boundary type: 1 = O'Brien-Fleming, 2 = Pocock, 3 = alpha-spending
alpha_2	Type I error for the two-sided test
samsz	Planned sample size of the control arm used in the simulation
sim_num	Number of simulation replicates

Value

A matrix in which each row corresponds to one simulation replicate and the columns hold the simulated operating characteristics (e.g. rejection indicators, sample sizes and stopping stages).

References

P. Gao, Y. Li (05 May 2024): Adaptive two-stage seamless sequential design for clinical trials, Journal of Biopharmaceutical Statistics, DOI: 10.1080/10543406.2024.2342518. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2342518

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

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P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
two_stg_power_simu_binary(p_t = c(0.4,0.4,0.4), p_c = 0.4, direction = 1, s = c(1/3,2/3,1),
bry_type = 1, alpha_2 = 0.05, samsz = 100, sim_num = 20)
```

`two_stg_power_simu_neg_binomial` *Phase 2/3 seamless combination Group sequential design: Simulations, Negative binomial distribution, Type I error and power*

Description

Phase 2/3 seamless combination Group sequential design: Simulations, Negative binomial distribution, Type I error and power

Usage

```
two_stg_power_simu_neg_binomial(
  r_t,
  r_c,
  kappa,
  direction,
  s,
  bry_type,
  alpha_2,
  samsz,
  sim_num
)
```

Arguments

`r_t`	Rate parameter of the test arm (negative binomial endpoint)
`r_c`	Rate parameter of the control arm (negative binomial endpoint)
`kappa`	Dispersion (size) parameter of the negative binomial distribution
`direction`	Test direction: 1 = larger r is better, 0 = smaller r is better
`s`	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
`bry_type`	Critical boundary type: 1 = O'Brien-Fleming, 2 = Pocock, 3 = alpha-spending
`alpha_2`	Type I error for the two-sided test
`samsz`	Planned sample size of the control arm used in the simulation
`sim_num`	Number of simulation replicates

Value

A matrix in which each row corresponds to one simulation replicate and the columns hold the simulated operating characteristics (e.g. rejection indicators, sample sizes and stopping stages).

References

P. Gao, Y. Li (05 May 2024): Adaptive two-stage seamless sequential design for clinical trials, Journal of Biopharmaceutical Statistics, DOI: 10.1080/10543406.2024.2342518. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2342518

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

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P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
two_stg_power_simu_neg_binomial(r_t = c(1.1,1.1,1.1), r_c = 1.1, kappa = 1, direction = 1,
s = c(1/3,1), bry_type = 1, alpha_2 = 0.05, samsz = 100, sim_num = 20)
```

---

two_stg_power_simu_normal

Phase 2/3 seamless combination Group sequential design: Simulations, Normal distribution, Type I error and power

---

Description

Phase 2/3 seamless combination Group sequential design: Simulations, Normal distribution, Type I error and power

Usage

```
two_stg_power_simu_normal(
  mu_t,
  mu_c,
  sigma_t,
  sigma_c,
  direction,
  s,
  bry_type,
  alpha_2,
  samsz,
  sim_num
)
```

Arguments

mu_t	Means of the test arm
mu_c	Means of the control arm
sigma_t	Standard deviation of the test arm
sigma_c	Standard deviation of the control arm
direction	Test direction: 1 = larger mu is better, 0 = smaller mu is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
bry_type	Critical boundary type: 1 = O'Brien-Fleming, 2 = Pocock, 3 = alpha-spending
alpha_2	Type I error for the two-sided test
samsz	Planned sample size of the control arm used in the simulation
sim_num	Number of simulation replicates

Value

A named list containing the following elements: 'simulation summary', 'planned control sample size', 'planned total sample size'.

References

P. Gao, Y. Li (05 May 2024): Adaptive two-stage seamless sequential design for clinical trials, Journal of Biopharmaceutical Statistics, DOI: 10.1080/10543406.2024.2342518. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2342518

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

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P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
two_stg_power_simu_normal(mu_t = c(0,0,0), mu_c = 0, sigma_t = 1, sigma_c = 1, direction = 1,
s = c(1/3,1), bry_type = 1, alpha_2 = 0.05, samsz = 100, sim_num = 20)
```

two_stg_power_simu_poisson *Phase 2/3 seamless combination Group sequential design: Simulations, Poisson distribution, Type I error and power*

Description

Phase 2/3 seamless combination Group sequential design: Simulations, Poisson distribution, Type I error and power

Usage

```
two_stg_power_simu_poisson(
  lambda_t,
  lambda_c,
  direction,
  s,
  bry_type,
  alpha_2,
  samsz,
  sim_num
)
```

Arguments

lambda_t	Event rate in the test arm (Poisson / negative binomial endpoint)
lambda_c	Event rate in the control arm (Poisson / negative binomial endpoint)
direction	Test direction: 1 = larger lambda is better, 0 = smaller lambda is better
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
bry_type	Critical boundary type: 1 = O'Brien-Fleming, 2 = Pocock, 3 = alpha-spending
alpha_2	Type I error for the two-sided test
samsz	Planned sample size of the control arm used in the simulation
sim_num	Number of simulation replicates

Value

A named list containing the following elements: 'simulation summary', 'planned control sample size ', 'planned total sample size'.

References

P. Gao, Y. Li (05 May 2024): Adaptive two-stage seamless sequential design for clinical trials, Journal of Biopharmaceutical Statistics, DOI: 10.1080/10543406.2024.2342518. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2342518

Gao, P., Zhang, W. (2024). A systematic approach to adaptive sequential design for clinical trials: using simulations to select a design with desired operating characteristics. Journal of Biopharmaceutical Statistics,2024 Aug;34(5):737-752. doi:10.1080/10543406.2024.2358796. Epub 2024 May 30. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2358796

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P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
two_stg_power_simu_poisson(lambda_t = c(1.1,1.3,1.4), lambda_c = 1.1, direction = 1,
s = c(1/3,1), bry_type = 1, alpha_2 = 0.05,
samsz = 100, sim_num = 20)
```

---

two_stg_power_simu_survival

Phase 2/3 seamless combination Group sequential design: Simulations, Survival analysis, Type I error and power

---

Description

Phase 2/3 seamless combination Group sequential design: Simulations, Survival analysis, Type I error and power

Usage

```
two_stg_power_simu_survival(
  HR,
  s,
  bry_type,
  alpha_2,
  surv_rate,
  evt_num,
  sim_num
)
```

Arguments

HR	Hazard ratio (test vs control)
s	Vector of information fractions of each analysis, e.g. c(1/3, 2/3, 1); the last element must be 1
bry_type	Critical boundary type: 1 = O'Brien-Fleming, 2 = Pocock, 3 = alpha-spending
alpha_2	Type I error for the two-sided test
surv_rate	Survival rate used to translate the number of events into a sample size
evt_num	Total number of events at the final analysis
sim_num	Number of simulation replicates

Value

A named list containing the following elements: 'simulation summary', 'planned number of events', 'planned total number of events'.

References

P. Gao, Y. Li (05 May 2024): Adaptive two-stage seamless sequential design for clinical trials, Journal of Biopharmaceutical Statistics, DOI: 10.1080/10543406.2024.2342518. To link to this article: https://www.tandfonline.com/doi/full/10.1080/10543406.2024.2342518

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H.H. Müller, H. Sch?fer. Adaptive Group Sequential Designs for Clinical Trials: Combining the Advantages of Adaptive and of Classical Group Sequential Approaches. BIOMETRICs 57, 886-891. September 2001.

P. Gao, J. H. Ware, C. Mehta. Sample size re-estimation for adaptive sequential design in clinical trials. J Biopharm Stat. 2008;18(6):1184-96.

Examples

```
two_stg_power_simu_survival(HR = c(0.8,0.8), s = c(1/3,2/3,1), bry_type = 1, alpha_2 = 0.05,
surv_rate = 0.5, evt_num = 800, sim_num = 20)
```

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