

# Package: DACT (via r-universe)

September 28, 2026

**Version** 1.0.0

**Title** Design and Analysis for Clinical Trials

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**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

**Repository** <https://cran.r-universe.dev>

**Date/Publication** 2026-09-28 12:30:08 UTC

**RemoteUrl** <https://github.com/cran/DACT>

**RemoteRef** HEAD

**RemoteSha** 8a5bf927c6e57e1a6dcb29bd98d52e3440e868d4

## Contents

|                                                 |    |
|-------------------------------------------------|----|
| asd_ci_est_back . . . . .                       | 6  |
| asd_ci_est_one_arm_2_stage . . . . .            | 8  |
| asd_ci_est_one_arm_3_stage . . . . .            | 9  |
| asd_new_design . . . . .                        | 10 |
| asd_new_design_survival . . . . .               | 12 |
| asd_new_design_theta . . . . .                  | 13 |
| asd_new_design_theta_survival . . . . .         | 14 |
| asd_power_simu_binary . . . . .                 | 15 |
| asd_power_simu_neg_binomial . . . . .           | 17 |
| asd_power_simu_normal . . . . .                 | 18 |
| asd_power_simu_poisson . . . . .                | 20 |
| asd_power_simu_survival . . . . .               | 21 |
| asd_simu_OC_binary . . . . .                    | 23 |
| asd_simu_OC_neg_binomial . . . . .              | 24 |
| asd_simu_OC_normal . . . . .                    | 26 |
| asd_simu_OC_poisson . . . . .                   | 28 |
| asd_simu_OC_survival . . . . .                  | 30 |
| EXP_3_stg_sz . . . . .                          | 31 |
| fixed_rej_nbgln_simu . . . . .                  | 33 |
| fixed_rej_rate_binary . . . . .                 | 33 |
| fixed_rej_rate_normal . . . . .                 | 34 |
| fixed_rej_rate_poisson . . . . .                | 35 |
| fixed_rej_rate_surv_cox . . . . .               | 36 |
| gsd_ci_est . . . . .                            | 37 |
| gsd_ci_est_2_stage . . . . .                    | 37 |
| gsd_ci_est_3_stage . . . . .                    | 38 |
| gsd_power_simu_binary . . . . .                 | 39 |
| gsd_power_simu_negbinom . . . . .               | 41 |
| gsd_power_simu_normal . . . . .                 | 42 |
| gsd_power_simu_poisson . . . . .                | 44 |
| gsd_power_simu_survival . . . . .               | 45 |
| hybrid_fixed_prior_rej_binary_simu . . . . .    | 46 |
| hybrid_fixed_prior_rej_negbinom_simu . . . . .  | 48 |
| hybrid_fixed_prior_rej_normal_simu . . . . .    | 50 |
| hybrid_fixed_prior_rej_poisson_simu . . . . .   | 51 |
| hybrid_fixed_prior_rej_survival_simu . . . . .  | 53 |
| hybrid_random_prior_rej_binary_simu . . . . .   | 55 |
| hybrid_random_prior_rej_negbinom_simu . . . . . | 56 |
| hybrid_random_prior_rej_normal_simu . . . . .   | 58 |
| hybrid_random_prior_rej_poisson_simu . . . . .  | 60 |
| hybrid_random_prior_rej_survival_simu . . . . . | 61 |
| hybrid_sz . . . . .                             | 63 |

|                                                             |     |
|-------------------------------------------------------------|-----|
| interim_analysis . . . . .                                  | 64  |
| masd_est_back_no_drop . . . . .                             | 65  |
| masd_est_back_with_drop . . . . .                           | 67  |
| masd_est_ci . . . . .                                       | 69  |
| masd_new_samsz . . . . .                                    | 70  |
| masd_new_samsz_survival . . . . .                           | 72  |
| masd_new_samsz_theta . . . . .                              | 73  |
| masd_new_samsz_theta_survival . . . . .                     | 75  |
| masd_power_simu_adapt_binary . . . . .                      | 77  |
| masd_power_simu_adapt_neg_binomial . . . . .                | 78  |
| masd_power_simu_adapt_normal . . . . .                      | 80  |
| masd_power_simu_adapt_poisson . . . . .                     | 81  |
| masd_power_simu_adapt_survival . . . . .                    | 83  |
| masd_simu_OC_binary . . . . .                               | 84  |
| masd_simu_OC_neg_binomial . . . . .                         | 86  |
| masd_simu_OC_normal . . . . .                               | 88  |
| masd_simu_OC_poisson . . . . .                              | 90  |
| masd_simu_OC_survival . . . . .                             | 92  |
| midpnt_sz . . . . .                                         | 94  |
| MSD_power_alsp_boundary_binary_diff . . . . .               | 95  |
| MSD_power_alsp_boundary_neg_binomial . . . . .              | 96  |
| MSD_power_alsp_boundary_normal . . . . .                    | 98  |
| MSD_power_alsp_boundary_poisson . . . . .                   | 100 |
| MSD_power_alsp_boundary_survival_Schoenfeld . . . . .       | 101 |
| MSD_power_OF_boundary_binary_diff . . . . .                 | 103 |
| MSD_power_OF_boundary_neg_binomial . . . . .                | 104 |
| MSD_power_OF_boundary_normal . . . . .                      | 106 |
| MSD_power_OF_boundary_poisson . . . . .                     | 107 |
| MSD_power_OF_boundary_survival_Schoenfeld . . . . .         | 109 |
| msd_power_simu_binary . . . . .                             | 110 |
| msd_power_simu_neg_binomial . . . . .                       | 112 |
| msd_power_simu_normal . . . . .                             | 113 |
| msd_power_simu_poisson . . . . .                            | 115 |
| msd_power_simu_survival . . . . .                           | 116 |
| MSD_Sample_size_alsp_boundary_binary_diff . . . . .         | 117 |
| MSD_Sample_size_alsp_boundary_neg_binomial . . . . .        | 119 |
| MSD_Sample_size_alsp_boundary_normal . . . . .              | 120 |
| MSD_Sample_size_alsp_boundary_poisson . . . . .             | 122 |
| MSD_Sample_size_alsp_boundary_survival_Schoenfeld . . . . . | 124 |
| MSD_Sample_size_OF_boundary_binary_diff . . . . .           | 125 |
| MSD_Sample_size_OF_boundary_neg_binomial . . . . .          | 127 |
| MSD_Sample_size_OF_boundary_normal . . . . .                | 128 |
| MSD_Sample_size_OF_boundary_poisson . . . . .               | 130 |
| MSD_Sample_size_OF_boundary_survival_Schoenfeld . . . . .   | 131 |
| new_sample_size_hybrid . . . . .                            | 133 |
| one_arm_ad_3_stg_binary . . . . .                           | 134 |
| one_arm_ad_two_stg_binary . . . . .                         | 136 |
| one_arm_rej_2_stg_binary . . . . .                          | 137 |

|                                                        |     |
|--------------------------------------------------------|-----|
| one_arm_rej_3_stg_binary . . . . .                     | 138 |
| one_arm_rej_simon_binary . . . . .                     | 140 |
| power_alsp_boundary_binary_diff . . . . .              | 141 |
| power_alsp_boundary_binary_diff_NI . . . . .           | 142 |
| power_alsp_boundary_neg_binomial . . . . .             | 143 |
| power_alsp_boundary_neg_binomial_NI . . . . .          | 144 |
| power_alsp_boundary_normal . . . . .                   | 145 |
| power_alsp_boundary_normal_NI . . . . .                | 146 |
| power_alsp_boundary_poisson . . . . .                  | 147 |
| power_alsp_boundary_poisson_NI . . . . .               | 148 |
| power_alsp_boundary_survival_Schoenfeld . . . . .      | 149 |
| power_alsp_boundary_survival_Schoenfeld_NI . . . . .   | 150 |
| power_binary_diff . . . . .                            | 151 |
| power_binary_diff_NI . . . . .                         | 152 |
| power_OF_boundary_binary_diff . . . . .                | 152 |
| power_OF_boundary_binary_diff_NI . . . . .             | 153 |
| power_OF_boundary_neg_binomial . . . . .               | 154 |
| power_OF_boundary_neg_binomial_NI . . . . .            | 155 |
| power_OF_boundary_normal . . . . .                     | 156 |
| power_OF_boundary_normal_NI . . . . .                  | 157 |
| power_OF_boundary_poisson . . . . .                    | 159 |
| power_OF_boundary_poisson_NI . . . . .                 | 160 |
| power_OF_boundary_survival_Schoenfeld . . . . .        | 161 |
| power_OF_boundary_survival_Schoenfeld_NI . . . . .     | 161 |
| power_pocock_boundary_binary_diff . . . . .            | 162 |
| power_pocock_boundary_binary_diff_NI . . . . .         | 163 |
| power_pocock_boundary_neg_binomial . . . . .           | 164 |
| power_pocock_boundary_neg_binomial_NI . . . . .        | 165 |
| power_pocock_boundary_normal . . . . .                 | 167 |
| power_pocock_boundary_normal_NI . . . . .              | 168 |
| power_pocock_boundary_poisson . . . . .                | 169 |
| power_pocock_boundary_poisson_NI . . . . .             | 170 |
| power_pocock_boundary_survival_Schoenfeld . . . . .    | 171 |
| power_pocock_boundary_survival_Schoenfeld_NI . . . . . | 172 |
| power_two_sample_neg_binomial . . . . .                | 173 |
| power_two_sample_neg_binomial_NI . . . . .             | 174 |
| power_two_sample_normal . . . . .                      | 175 |
| power_two_sample_normal_NI . . . . .                   | 176 |
| power_two_sample_Poisson . . . . .                     | 177 |
| power_two_sample_Poisson_NI . . . . .                  | 177 |
| power_two_sample_surv_Schoenfeld . . . . .             | 178 |
| power_two_sample_surv_Schoenfeld_NI . . . . .          | 179 |
| Sample_size_alsp_boundary_binary_diff . . . . .        | 180 |
| Sample_size_alsp_boundary_binary_diff_NI . . . . .     | 181 |
| Sample_size_alsp_boundary_neg_binomial . . . . .       | 182 |
| Sample_size_alsp_boundary_neg_binomial_NI . . . . .    | 183 |
| Sample_size_alsp_boundary_normal . . . . .             | 184 |
| Sample_size_alsp_boundary_normal_NI . . . . .          | 185 |

|                                                              |     |
|--------------------------------------------------------------|-----|
| Sample_size_alsp_boundary_poisson . . . . .                  | 186 |
| Sample_size_alsp_boundary_poisson_NI . . . . .               | 187 |
| Sample_size_alsp_boundary_survival_Schoenfeld . . . . .      | 188 |
| Sample_size_alsp_boundary_survival_Schoenfeld_NI . . . . .   | 189 |
| sample_size_binary_diff . . . . .                            | 190 |
| sample_size_binary_diff_NI . . . . .                         | 190 |
| sample_size_neg_binomial . . . . .                           | 191 |
| sample_size_neg_binomial_NI . . . . .                        | 192 |
| Sample_size_OF_boundary_binary_diff . . . . .                | 193 |
| Sample_size_OF_boundary_binary_diff_NI . . . . .             | 194 |
| Sample_size_OF_boundary_neg_binomial . . . . .               | 195 |
| Sample_size_OF_boundary_neg_binomial_NI . . . . .            | 196 |
| Sample_size_OF_boundary_normal . . . . .                     | 197 |
| Sample_size_OF_boundary_normal_NI . . . . .                  | 198 |
| Sample_size_OF_boundary_poisson . . . . .                    | 199 |
| Sample_size_OF_boundary_poisson_NI . . . . .                 | 200 |
| Sample_size_OF_boundary_survival_Schoenfeld . . . . .        | 201 |
| Sample_size_OF_boundary_survival_Schoenfeld_NI . . . . .     | 202 |
| Sample_size_pocock_boundary_binary_diff . . . . .            | 203 |
| Sample_size_pocock_boundary_binary_diff_NI . . . . .         | 204 |
| Sample_size_pocock_boundary_neg_binomial . . . . .           | 205 |
| Sample_size_pocock_boundary_neg_binomial_NI . . . . .        | 206 |
| Sample_size_pocock_boundary_normal . . . . .                 | 207 |
| Sample_size_pocock_boundary_normal_NI . . . . .              | 208 |
| Sample_size_pocock_boundary_poisson . . . . .                | 209 |
| Sample_size_pocock_boundary_poisson_NI . . . . .             | 210 |
| Sample_size_pocock_boundary_survival_Schoenfeld . . . . .    | 211 |
| Sample_size_pocock_boundary_survival_Schoenfeld_NI . . . . . | 212 |
| sample_size_two_sample_normal . . . . .                      | 213 |
| sample_size_two_sample_normal_NI . . . . .                   | 214 |
| sample_size_two_sample_Poisson . . . . .                     | 215 |
| sample_size_two_sample_Poisson_NI . . . . .                  | 215 |
| sample_size_two_sample_surv_Schoenfeld . . . . .             | 216 |
| sample_size_two_sample_surv_Schoenfeld_NI . . . . .          | 217 |
| simon_ph2_sz . . . . .                                       | 218 |
| Two_stage_asd_simu_OC_binary . . . . .                       | 219 |
| Two_stage_asd_simu_OC_neg_binomial . . . . .                 | 221 |
| Two_stage_asd_simu_OC_normal . . . . .                       | 223 |
| Two_stage_asd_simu_OC_poisson . . . . .                      | 225 |
| Two_stage_asd_simu_OC_survival . . . . .                     | 226 |
| two_stage_ci_0 . . . . .                                     | 228 |
| two_stage_ci_1 . . . . .                                     | 229 |
| two_stage_est_back . . . . .                                 | 231 |
| two_stage_power_alsp_boundary_binary_diff . . . . .          | 233 |
| two_stage_power_alsp_boundary_neg_binomial . . . . .         | 234 |
| two_stage_power_alsp_boundary_normal . . . . .               | 236 |
| two_stage_power_alsp_boundary_poisson . . . . .              | 237 |
| two_stage_power_alsp_boundary_survival_Schoenfeld . . . . .  | 239 |

|                                                                   |     |
|-------------------------------------------------------------------|-----|
| two_stage_power_OF_boundary_binary_diff . . . . .                 | 240 |
| two_stage_power_OF_boundary_neg_binomial . . . . .                | 242 |
| two_stage_power_OF_boundary_normal . . . . .                      | 243 |
| two_stage_power_OF_boundary_poisson . . . . .                     | 245 |
| two_stage_power_OF_boundary_survival_Schoenfeld . . . . .         | 246 |
| two_stage_Sample_size_alsp_boundary_binary_diff . . . . .         | 248 |
| two_stage_Sample_size_alsp_boundary_neg_binomial . . . . .        | 249 |
| two_stage_Sample_size_alsp_boundary_normal . . . . .              | 251 |
| two_stage_Sample_size_alsp_boundary_poisson . . . . .             | 252 |
| two_stage_Sample_size_alsp_boundary_survival_Schoenfeld . . . . . | 254 |
| two_stage_Sample_size_OF_boundary_binary_diff . . . . .           | 255 |
| two_stage_Sample_size_OF_boundary_neg_binomial . . . . .          | 257 |
| two_stage_Sample_size_OF_boundary_normal . . . . .                | 259 |
| two_stage_Sample_size_OF_boundary_poisson . . . . .               | 260 |
| two_stage_Sample_size_OF_boundary_survival_Schoenfeld . . . . .   | 262 |
| two_stg_adapt_power_simu_binary . . . . .                         | 263 |
| two_stg_adapt_power_simu_neg_binomial . . . . .                   | 265 |
| two_stg_adapt_power_simu_normal . . . . .                         | 266 |
| two_stg_adapt_power_simu_poisson . . . . .                        | 268 |
| two_stg_adapt_power_simu_survival . . . . .                       | 270 |
| two_stg_power_simu_binary . . . . .                               | 271 |
| two_stg_power_simu_neg_binomial . . . . .                         | 273 |
| two_stg_power_simu_normal . . . . .                               | 274 |
| two_stg_power_simu_poisson . . . . .                              | 276 |
| two_stg_power_simu_survival . . . . .                             | 277 |

|              |            |
|--------------|------------|
| <b>Index</b> | <b>279</b> |
|--------------|------------|

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|                 |                                                                                                            |
|-----------------|------------------------------------------------------------------------------------------------------------|
| asd_ci_est_back | <i>Group sequential designs / Adaptive sequential designs: Final analysis, With one sample size change</i> |
|-----------------|------------------------------------------------------------------------------------------------------------|

---

## Description

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

## Usage

```
asd_ci_est_back(
  s,
  c_bry,
  snw,
  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

|                                   |                                                                                                                 |
|-----------------------------------|-----------------------------------------------------------------------------------------------------------------|
| <code>s</code>                    | Vector of information fractions of each analysis, e.g. <code>c(1/3, 2/3, 1)</code> ; the last element must be 1 |
| <code>c_bry</code>                | Vector of critical boundaries for each analysis                                                                 |
| <code>snew</code>                 | Vector of new information fractions after the sample size is changed                                            |
| <code>c_bry_new</code>            | Critical boundaries after the sample size is changed                                                            |
| <code>theta_hat_inter</code>      | Treatment effect estimate observed at the interim analysis                                                      |
| <code>theta_hat_inter_sd</code>   | Standard error of <code>'theta_hat_inter'</code>                                                                |
| <code>inter_vt</code>             | Index of the interim analysis at which the sample size is re-estimated (1-based)                                |
| <code>theta_hat_last_ad</code>    | Treatment effect estimate observed at the last analysis after the sample size change                            |
| <code>theta_hat_last_ad_sd</code> | Standard error of <code>'theta_hat_last_ad'</code>                                                              |
| <code>last_vt_ad</code>           | Index of the last analysis after the sample size change                                                         |
| <code>alpha_2</code>              | 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. Schöfer. 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                                         |
| <i>Final analysis: three stage design, with sample size change</i> |

---

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 | <i>Group sequential designs / Adaptive sequential designs: Interim analysis, Non-survival analysis, Use theta_interim</i> |
|----------------|---------------------------------------------------------------------------------------------------------------------------|

---

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. $1 - \text{power}$                                                          |

**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. <code>c(1/3, 2/3, 1)</code> ; 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 | <i>Group sequential designs / Adaptive sequential designs: Interim analysis, Non-survival analysis, Input theta</i> |
|----------------------|---------------------------------------------------------------------------------------------------------------------|

---

**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. Schöfer. 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. Schfer. 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

|                        |                                                                                                                 |
|------------------------|-----------------------------------------------------------------------------------------------------------------|
| <code>mu_t</code>      | Mean of the test arm                                                                                            |
| <code>mu_c</code>      | Mean of the control arm                                                                                         |
| <code>sigma_t</code>   | Standard deviation of the test arm                                                                              |
| <code>sigma_c</code>   | Standard deviation of the control arm                                                                           |
| <code>direction</code> | Test direction: 1 = larger mu is better, 0 = smaller mu is better                                               |
| <code>s</code>         | Vector of information fractions of each analysis, e.g. <code>c(1/3, 2/3, 1)</code> ; the last element must be 1 |
| <code>bry_type</code>  | Critical boundary type: 1 = O'Brien-Fleming, 2 = Pocock, 3 = alpha-spending                                     |
| <code>alpha_2</code>   | Type I error for the two-sided test                                                                             |
| <code>samsz</code>     | Planned sample size of the control arm used in the simulation                                                   |
| <code>N_max</code>     | Maximum allowed sample size (control arm)                                                                       |
| <code>theta_cut</code> | Efficacy cut-off on the effect-size scale applied at the interim analysis                                       |
| <code>beta</code>      | Type II error rate, i.e. 1 - power                                                                              |
| <code>sim_num</code>   | 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. Schfer. 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. Schaffer. 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 | <i>Group sequential designs / Adaptive sequential designs: Simulations, Binary distribution, Optimizing adaptive sequential design</i> |
|--------------------|----------------------------------------------------------------------------------------------------------------------------------------|

---

## 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 | <i>Group sequential designs / Adaptive sequential designs: Simulations, Negative binomial distribution, Optimizing adaptive sequential design</i> |
|--------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------|

---

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 | <i>Group sequential designs / Adaptive sequential designs: Simulations, Normal distribution, Optimizing adaptive sequential design</i> |
|--------------------|----------------------------------------------------------------------------------------------------------------------------------------|

---

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. Schfer. 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 | <i>Group sequential designs / Adaptive sequential designs: Simulations, Poisson distribution, Optimizing adaptive sequential design</i> |
|---------------------|-----------------------------------------------------------------------------------------------------------------------------------------|

---

## 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. Schfer. 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 | <i>Group sequential designs / Adaptive sequential designs: Simulations, Survival analysis, Optimizing adaptive sequential design</i> |
|----------------------|--------------------------------------------------------------------------------------------------------------------------------------|

---

## 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 | <i>Three-stage design</i> |
|--------------|---------------------------|

---

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**

$n_1$ : Number of patients at first look.  $n_1$  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  $n_1$  from Simon's design with  $p=p_{\text{low}}$ .

$r_1$ : If no more than  $r_1$  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.

$EN(p_0)$  is the expected sample size under the null hypothesis.

$PET(p_0)$  is the probability of early termination under the null hypothesis.

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

$PET_{p_{\text{low}}}$  is the probability of early termination under  $p=p_{\text{low}}$ .

$\text{power}_{p_1}$  is the power under  $p=p_1$ .

$\text{power}_{p_{\text{low}}}$  is the power under  $p=p_{\text{low}}$ .

Type I error is the probability of rejecting the null hypothesis under  $p \leq p_0$ .

The minimax design has the smallest  $n_2$  among all possible choices of  $(n_1, r_1, n_2, r_2)$ .

The optimal design has the smallest  $EN(p_0)$  among all possible choices of  $(n_1, r_1, n_2, r_2)$ .

The  $n_1$  and  $n_2$  for the average design is the average of  $n_1$ '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 | <i>Group sequential designs / Adaptive sequential designs: Final analysis, Without sample size change</i> |
|------------|-----------------------------------------------------------------------------------------------------------|

---

**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 | <i>Final analysis: two stage design, no sample size change</i> |
|--------------------|----------------------------------------------------------------|

---

**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 | <i>Final analysis: three stage design, no sample size change</i> |
|--------------------|------------------------------------------------------------------|

---

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**

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

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

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

|                        |                                                                                                                 |
|------------------------|-----------------------------------------------------------------------------------------------------------------|
| <code>mu_t</code>      | Mean of the test arm                                                                                            |
| <code>mu_c</code>      | Mean of the control arm                                                                                         |
| <code>sigma_t</code>   | Standard deviation of the test arm                                                                              |
| <code>sigma_c</code>   | Standard deviation of the control arm                                                                           |
| <code>direction</code> | Test direction: 1 = larger mu is better, 0 = smaller mu is better                                               |
| <code>s</code>         | Vector of information fractions of each analysis, e.g. <code>c(1/3, 2/3, 1)</code> ; the last element must be 1 |
| <code>bry_type</code>  | Critical boundary type: 1 = O'Brien-Fleming, 2 = Pocock, 3 = alpha-spending                                     |
| <code>alpha_2</code>   | Type I error for the two-sided test                                                                             |
| <code>samsz</code>     | Planned sample size of the control arm used in the simulation                                                   |
| <code>sim_num</code>   | 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. Schöfer. 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. Schaffer. 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. $1 - \text{power}$                                                          |
| 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*. Volume 30, Issue 28, 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*. Volume 30, Issue 28, 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. $1 - \text{power}$                                                          |

### 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                                                                              |
| <i>Hybrid: Simulations, Negative binomial distribution, Using random<br/>informative prior from previous trial</i> |

---

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

|                         |                                                                                                      |
|-------------------------|------------------------------------------------------------------------------------------------------|
| <code>r_t_0</code>      | Event rate for test arm - previous trial                                                             |
| <code>r_c_0</code>      | Event rate for control arm - previous trial                                                          |
| <code>sampsz_0</code>   | Sample size from previous trial                                                                      |
| <code>r_t</code>        | Event rate for test arm - current trial                                                              |
| <code>r_c</code>        | Event rate for control arm - current trial                                                           |
| <code>kappa</code>      | dispersion parameter                                                                                 |
| <code>nu_t</code>       | exposure time                                                                                        |
| <code>rand_ratio</code> | Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm        |
| <code>s</code>          | Vector of information fractions of each analysis, e.g. $c(1/3, 2/3, 1)$ ; the last element must be 1 |
| <code>sampsz</code>     | Planned sample size: the planned sample size at the final analysis                                   |
| <code>N_max</code>      | Maximum sample size: a user chosen , maximum allowable sample size for sample size modification      |
| <code>theta_cut</code>  | Efficacy cut-off on the effect-size scale applied at the interim analysis                            |
| <code>cp_min</code>     | Promising zone <code>cp_min</code>                                                                   |
| <code>gamma</code>      | Parameter chosen for the credible interval modified predictive power (CI_MPP)                        |
| <code>alpha_2</code>    | Type I error for the two-sided test                                                                  |
| <code>beta</code>       | Type II error rate, i.e. $1 - \text{power}$                                                          |
| <code>sim_num</code>    | 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*. Volume 30, Issue 28, 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**

|                        |                                                                                                                 |
|------------------------|-----------------------------------------------------------------------------------------------------------------|
| <code>mu_0</code>      | Effect size from previous trial                                                                                 |
| <code>sigma_0</code>   | Common standard deviation from previous trial                                                                   |
| <code>sampsz_0</code>  | Sample size from previous trial                                                                                 |
| <code>mu</code>        | Effect size used when calibrating the boundaries                                                                |
| <code>sigma</code>     | Futility threshold                                                                                              |
| <code>s</code>         | Vector of information fractions of each analysis, e.g. <code>c(1/3, 2/3, 1)</code> ; the last element must be 1 |
| <code>sampsz</code>    | Planned sample size: the planned sample size at the final analysis                                              |
| <code>N_max</code>     | Maximum sample size: a user chosen , maximum allowable sample size for sample size modification                 |
| <code>theta_cut</code> | Efficacy cut-off on the effect-size scale applied at the interim analysis                                       |
| <code>cp_min</code>    | Promising zone <code>cp_min</code>                                                                              |
| <code>gamma</code>     | Parameter chosen for the credible interval modified predictive power (CI_MPP)                                   |
| <code>alpha_2</code>   | Type I error for the two-sided test                                                                             |
| <code>beta</code>      | Type II error rate, i.e. 1 - power                                                                              |
| <code>sim_num</code>   | 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*. Volume 30, Issue 28, 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                                                             |
| <i>Hybrid: Simulations, Survival analysis, Using random informative prior from previous trial</i> |

---

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  $p \leq p_0$ .  
The minimax design has the smallest  $n_2$  among all possible choices of  $(n_1, r_1, n_2, r_2)$ .  
The optimal design has the smallest  $EN(p_0)$  among all possible choices of  $(n_1, r_1, n_2, r_2)$ .  
The  $n_1$  for the average design is the average of  $n_1$ '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 | <i>The interim analysis can be conducted for both two-stage and three-stage designs</i> |
|------------------|-----------------------------------------------------------------------------------------|

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, $r_{final}=r_2$ . For the three-stage design, $r_{final}=r_3$ .                                         |
| n_inter | Number of patients at the interim look. For two-stage designs, $n_{inter}=n_1$ . For the three-stage design, $n_{inter}=n_2$ . |
| n_final | For two-stage designs, $n_{inter}=n_2$ . For the three-stage design, $n_{inter}=n_3$ .                                         |
| 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, `origin_comp==comp2`*

---

**Description**

Multiple comparisons Group sequential design: Final analysis, With one sample size change, `origin_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**

|                                      |                                                                                                      |
|--------------------------------------|------------------------------------------------------------------------------------------------------|
| <code>s</code>                       | Vector of information fractions of each analysis, e.g. $c(1/3, 2/3, 1)$ ; the last element must be 1 |
| <code>c_bry</code>                   | Vector of critical boundaries for each analysis                                                      |
| <code>snew</code>                    | Vector of new information fractions after the sample size is changed                                 |
| <code>c_bry_new</code>               | Critical boundaries after the sample size is changed                                                 |
| <code>theta_hat_inter_m1</code>      | 'theta_hat_inter_m1' as used by this function; see Examples.                                         |
| <code>theta_hat_inter_m1_sd</code>   | 'theta_hat_inter_m1_sd' as used by this function; see Examples.                                      |
| <code>inter_vt</code>                | Index of the interim analysis at which the sample size is re-estimated (1-based)                     |
| <code>theta_hat_last_ad_m1</code>    | 'theta_hat_last_ad_m1' as used by this function; see Examples.                                       |
| <code>theta_hat_last_ad_m1_sd</code> | 'theta_hat_last_ad_m1_sd' as used by this function; see Examples.                                    |
| <code>last_vt_ad</code>              | Index of the last analysis after the sample size change                                              |
| <code>alpha_2</code>                 | Type I error for the two-sided test                                                                  |
| <code>dist</code>                    | 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. Schfer. 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, origin\_comp>comp2*

---

## Description

Multiple comparisons Group sequential design: Final analysis, With one sample size change, origin\_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. Schaffer. 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), snw = 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 | <i>Multiple comparisons Group sequential design: Final analysis, Without sample size change</i> |
|-------------|-------------------------------------------------------------------------------------------------|

---

**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

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

H.H. Müller, H. Schöfer. 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_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 | <i>Multiple comparisons Group sequential design: Interim analysis, Non-survival analysis, Use theta_interim</i> |
|----------------|-----------------------------------------------------------------------------------------------------------------|

---

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>
- 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. Schaffer. 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_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>

H.H. Müller, H. Schfer. 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_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 | <i>Multiple comparisons Group sequential design: Interim analysis, Non-survival analysis, Input theta</i> |
|----------------------|-----------------------------------------------------------------------------------------------------------|

---

**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. $1 - \text{power}$                                                          |
| 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

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

H.H. Müller, H. Schöfer. 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_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), snw = 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,
  snw,
  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. $1 - \text{power}$                                                          |
| 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>
- H.H. Müller, H. Schfer. 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_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>

H.H. Müller, H. Schfer. 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_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. Schöfer. 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>

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_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 | <i>Multiple comparisons Group sequential design: Simulations, Poisson distribution, Operating characteristics</i> |
|-------------------------------|-------------------------------------------------------------------------------------------------------------------|

---

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. Schöfer. 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 |                                                                                                                |
|                                | <i>Multiple comparisons Group sequential design: Simulations, Survival analysis, Operating characteristics</i> |

---

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. Schöfer. 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 | <i>Multiple comparisons Group sequential design: Simulations, Binary distribution, Optimizing adaptive sequential design</i> |
|---------------------|------------------------------------------------------------------------------------------------------------------------------|

---

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. Schaffer. 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. Schfer. 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 | <i>Multiple comparisons Group sequential design: Simulations, Normal distribution, Optimizing adaptive sequential design</i> |
|---------------------|------------------------------------------------------------------------------------------------------------------------------|

---

### 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. Schöfer. 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 | <i>Multiple comparisons Group sequential design: Simulations, Poisson distribution, Optimizing adaptive sequential design</i> |
|----------------------|-------------------------------------------------------------------------------------------------------------------------------|

---

## 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. Schfer. 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. Schfer. 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 | $\text{Min}(n_2 - n_1)$ sets the minimal difference between $n_2$ and $n_1$ for the design. |

**Value**

$n_1$ : Number of patients at first look.

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

$r_1$ : If no more than  $r_1$  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.

$EN(p_0)$  is the expected sample size under the null hypothesis.

$PET(p_0)$  is the probability of early termination under the null hypothesis.

$PET_p$  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  $p \leq p_0$ .

The minimax design has the smallest  $n_2$  among all possible choices of  $(n_1, r_1, n_2, r_2)$ .

The optimal design has the smallest  $EN(p_0)$  among all possible choices of  $(n_1, r_1, n_2, r_2)$ .

The  $n_1$  for the average design is the average of  $n_1$ '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                                                                                  |
| <i>Multiple comparisons Group sequential design: Binary distribution, Power calculation, Alpha-spending boundary</i> |

---

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. Schfer. 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                                                                                            |
| <i>Multiple comparisons Group sequential design: Negative binomial distribution, Power calculation, Alpha-spending boundary</i> |

---

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**

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

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

H.H. Müller, H. Schfer. 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_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. Schöfer. 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. Schfer. 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. Schöfer. 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. Schfer. 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. Schfer. 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. Schfer. 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                                                                                          |
| <i>Multiple comparisons Group sequential design: Poisson distribution, Power calculation, O'Brien-Fleming boundary</i> |

---

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                                                                           |
| <i>Multiple comparisons Group sequential design: Survival analysis, Power calculation, O'Brien-Fleming boundary</i> |

---

**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. Schaffer. 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 | <i>Multiple comparisons Group sequential design: Simulations, Binary distribution, Type I error and power</i> |
|-----------------------|---------------------------------------------------------------------------------------------------------------|

---

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. Schöfer. 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**

|                        |                                                                                                                 |
|------------------------|-----------------------------------------------------------------------------------------------------------------|
| <code>r_t</code>       | Rate parameter of the test arm (negative binomial endpoint)                                                     |
| <code>r_c</code>       | Rate parameter of the control arm (negative binomial endpoint)                                                  |
| <code>kappa</code>     | Dispersion (size) parameter of the negative binomial distribution                                               |
| <code>direction</code> | Test direction: 1 = larger r is better, 0 = smaller r is better                                                 |
| <code>s</code>         | Vector of information fractions of each analysis, e.g. <code>c(1/3, 2/3, 1)</code> ; the last element must be 1 |
| <code>bry_type</code>  | Critical boundary type: 1 = O'Brien-Fleming, 2 = Pocock, 3 = alpha-spending                                     |
| <code>alpha_2</code>   | Type I error for the two-sided test                                                                             |
| <code>samsz</code>     | Planned sample size of the control arm used in the simulation                                                   |
| <code>sim_num</code>   | 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. Schfer. 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_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. Schfer. 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. Schfer. 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 | <i>Multiple comparisons Group sequential design: Simulations, Survival analysis, Type I error and power</i> |
|-------------------------|-------------------------------------------------------------------------------------------------------------|

---

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. Schfer. 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. Schfer. 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**

|                         |                                                                                                                 |
|-------------------------|-----------------------------------------------------------------------------------------------------------------|
| <code>r_t</code>        | Rate parameter of the test arm (negative binomial endpoint)                                                     |
| <code>r_c</code>        | Rate parameter of the control arm (negative binomial endpoint)                                                  |
| <code>margin</code>     | Non-inferiority / superiority margin                                                                            |
| <code>direction</code>  | Test direction: 1 = larger r is better, 0 = smaller r is better                                                 |
| <code>s</code>          | Vector of information fractions of each analysis, e.g. <code>c(1/3, 2/3, 1)</code> ; the last element must be 1 |
| <code>alpha</code>      | One-sided significance level (type I error rate)                                                                |
| <code>beta</code>       | Type II error rate, i.e. 1 - power                                                                              |
| <code>rand_ratio</code> | 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                                                                                           |
| <i>Multiple comparisons Group sequential design: Normal distribution,<br/>Sample size calculation, Alpha-spending boundary</i> |

---

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. Schöfer. 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. Schfer. 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>
- H.H. Müller, H. Schöfer. 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_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. Schfer. 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

|                         |                                                                                                                 |
|-------------------------|-----------------------------------------------------------------------------------------------------------------|
| <code>r_t</code>        | Rate parameter of the test arm (negative binomial endpoint)                                                     |
| <code>r_c</code>        | Rate parameter of the control arm (negative binomial endpoint)                                                  |
| <code>margin</code>     | Non-inferiority / superiority margin                                                                            |
| <code>direction</code>  | Test direction: 1 = larger r is better, 0 = smaller r is better                                                 |
| <code>s</code>          | Vector of information fractions of each analysis, e.g. <code>c(1/3, 2/3, 1)</code> ; the last element must be 1 |
| <code>alpha</code>      | One-sided significance level (type I error rate)                                                                |
| <code>beta</code>       | Type II error rate, i.e. 1 - power                                                                              |
| <code>rand_ratio</code> | Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm                   |
| <code>nu_t</code>       | exposure time                                                                                                   |
| <code>kappa</code>      | dispersion parameter                                                                                            |
| <code>dist1</code>      | Endpoint / distribution indicator for the first stage                                                           |
| <code>dist2</code>      | 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. Schöfer. 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. Schfer. 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                                                                               |
| <i>Multiple comparisons Group sequential design: Survival analysis,<br/>Sample size calculation, O'Brien-Fleming boundary</i> |

---

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                    |
| <i>Hybrid: New sample size estimation</i> |

---

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*. Volume 30, Issue 28, 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                         |
| <i>Simulations: adaptive three stage design</i> |

---

**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 | <i>Simulations: Two stage fixed expanded Simon’s design: either hybrid or mid-point design</i> |
|--------------------------|------------------------------------------------------------------------------------------------|

---

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 | <i>Simulations: Expanded Simon’s design: the three stage design, no sample size change</i> |
|--------------------------|--------------------------------------------------------------------------------------------|

---

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                           |
| <i>Simulations: two stage fixed Simon’s design</i> |

---

**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 | <i>Group sequential designs / Adaptive sequential designs: Binary distribution, Superiority trial, Power calculation, Alpha-spending boundary</i> |
|---------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------|

---

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**

|                             |                                                                                                                 |
|-----------------------------|-----------------------------------------------------------------------------------------------------------------|
| <code>r_t</code>            | Mean of the test arm                                                                                            |
| <code>r_c</code>            | Mean of the control arm                                                                                         |
| <code>s</code>              | Vector of information fractions of each analysis, e.g. <code>c(1/3, 2/3, 1)</code> ; the last element must be 1 |
| <code>alpha_2</code>        | Type I error for the two-sided test                                                                             |
| <code>sampsz_control</code> | Control arm sample size                                                                                         |
| <code>rand_ratio</code>     | Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm                   |
| <code>nu_t</code>           | exposure time                                                                                                   |
| <code>kappa</code>          | 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 |                                                                                                                                                                  |
|                                     | <i>Group sequential designs / Adaptive sequential designs: Negative binomial distribution, Non-inferiority trial, Power calculation, Alpha-spending boundary</i> |

---

**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 |

|                             |                                                                                                                 |
|-----------------------------|-----------------------------------------------------------------------------------------------------------------|
| <code>s</code>              | Vector of information fractions of each analysis, e.g. <code>c(1/3, 2/3, 1)</code> ; the last element must be 1 |
| <code>sampsz_control</code> | Control arm sample size                                                                                         |
| <code>rand_ratio</code>     | Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm                   |
| <code>alpha_2</code>        | 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                                                                                                          |
| <i>Group sequential designs / Adaptive sequential designs: Survival analysis, Non-inferiority trial, Power calculation, Alpha-spending boundary</i> |

---

**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 | <i>Fixed sample designs: Binary distribution, Superiority trial, Power calculation</i> |
|-------------------|----------------------------------------------------------------------------------------|

---

**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 | <i>Fixed sample designs: Binary distribution, Non-inferiority trial, Power calculation</i> |
|----------------------|--------------------------------------------------------------------------------------------|

---

**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 | <i>Group sequential designs / Adaptive sequential designs: Binary distribution, Superiority trial, Power calculation, O’Brien-Fleming boundary</i> |
|-------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------|

---

**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 | <i>Group sequential designs / Adaptive sequential designs: Normal distribution, Superiority trial, Power calculation, O'Brien-Fleming boundary</i> |
|--------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------|

---

**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**

|                             |                                                                                                                 |
|-----------------------------|-----------------------------------------------------------------------------------------------------------------|
| <code>mu_t</code>           | Mean of the test arm                                                                                            |
| <code>mu_c</code>           | Mean of the control arm                                                                                         |
| <code>std_t</code>          | Standard deviation of the test arm                                                                              |
| <code>std_c</code>          | Standard deviation of the control arm                                                                           |
| <code>margin</code>         | Non-inferiority margin                                                                                          |
| <code>direction</code>      | Test direction: 1 = larger mu is better, 0 = smaller mu is better                                               |
| <code>s</code>              | Vector of information fractions of each analysis, e.g. <code>c(1/3, 2/3, 1)</code> ; the last element must be 1 |
| <code>sampsz_control</code> | Control arm sample size                                                                                         |
| <code>rand_ratio</code>     | Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm                   |
| <code>alpha</code>          | 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**

|                             |                                                                                                                 |
|-----------------------------|-----------------------------------------------------------------------------------------------------------------|
| <code>lambda_t</code>       | Mean of the test arm                                                                                            |
| <code>lambda_c</code>       | Mean of the control arm                                                                                         |
| <code>s</code>              | Vector of information fractions of each analysis, e.g. <code>c(1/3, 2/3, 1)</code> ; the last element must be 1 |
| <code>alpha_2</code>        | Type I error for the two-sided test                                                                             |
| <code>sampsz_control</code> | Control arm sample size                                                                                         |
| <code>rand_ratio</code>     | 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                                                                                                         |
| <i>Group sequential designs / Adaptive sequential designs: Binary distribution, Superiority trial, Power calculation, Pocock boundary</i> |

---

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                                                                                                                   |
| <i>Group sequential designs / Adaptive sequential designs: Negative binomial distribution, Superiority trial, Power calculation, Pocock boundary</i> |

---

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**

|                             |                                                                                                                 |
|-----------------------------|-----------------------------------------------------------------------------------------------------------------|
| <code>r_t</code>            | Mean of the test arm                                                                                            |
| <code>r_c</code>            | Mean of the control arm                                                                                         |
| <code>s</code>              | Vector of information fractions of each analysis, e.g. <code>c(1/3, 2/3, 1)</code> ; the last element must be 1 |
| <code>alpha_2</code>        | Type I error for the two-sided test                                                                             |
| <code>sampsz_control</code> | Control arm sample size                                                                                         |
| <code>rand_ratio</code>     | Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm                   |
| <code>nu_t</code>           | exposure time                                                                                                   |
| <code>kappa</code>          | 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**

|                             |                                                                                                                 |
|-----------------------------|-----------------------------------------------------------------------------------------------------------------|
| <code>r_t</code>            | Mean of the test arm                                                                                            |
| <code>r_c</code>            | Mean of the control arm                                                                                         |
| <code>margin</code>         | Non-inferiority margin                                                                                          |
| <code>direction</code>      | Test direction: 1 = larger <code>r_t</code> is better, 0 = smaller <code>r_t</code> is better                   |
| <code>s</code>              | Vector of information fractions of each analysis, e.g. <code>c(1/3, 2/3, 1)</code> ; the last element must be 1 |
| <code>alpha</code>          | One-sided significance level (type I error rate)                                                                |
| <code>sampsz_control</code> | Control arm sample size                                                                                         |
| <code>rand_ratio</code>     | Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm                   |
| <code>nu_t</code>           | exposure time                                                                                                   |
| <code>kappa</code>          | 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. <code>c(1/3, 2/3, 1)</code> ; 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                                                                                                |
| <i>Group sequential designs / Adaptive sequential designs: Survival analysis, Non-inferiority trial, Power calculation, Pocock boundary</i> |

---

**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**

|                         |                                                                                                   |
|-------------------------|---------------------------------------------------------------------------------------------------|
| <code>r_t</code>        | The event rate of the test arm                                                                    |
| <code>r_c</code>        | The event rate of the control arm                                                                 |
| <code>alpha_2</code>    | The type I error for the two-sided test                                                           |
| <code>n_control</code>  | Sample size of the control arm                                                                    |
| <code>rand_ratio</code> | The ratio of the number of subjects in the test arm vs. the number of subjects in the control arm |
| <code>nu_t</code>       | The exposure time                                                                                 |
| <code>kappa</code>      | 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

|                         |                                                                                                                                       |
|-------------------------|---------------------------------------------------------------------------------------------------------------------------------------|
| <code>r_t</code>        | The event rate of the test arm                                                                                                        |
| <code>r_c</code>        | The event rate of the control arm                                                                                                     |
| <code>margin</code>     | The non-inferiority margin                                                                                                            |
| <code>direction</code>  | Test direction: 1 = larger <code>r_t</code> , <code>r_c</code> are better, 0 = smaller <code>r_t</code> , <code>r_c</code> are better |
| <code>alpha</code>      | The type I error for the one-sided test                                                                                               |
| <code>n_control</code>  | Sample size of the control arm                                                                                                        |
| <code>rand_ratio</code> | The ratio of the number of subjects in the test arm vs. the number of subjects in the control arm                                     |
| <code>nu_t</code>       | The exposure time                                                                                                                     |
| <code>kappa</code>      | 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

|                         |                                                  |
|-------------------------|--------------------------------------------------|
| <code>mu_t</code>       | The mean of the test arm.                        |
| <code>mu_c</code>       | The mean of the control arm.                     |
| <code>sigma_t</code>    | The standard deviation for the test arm.         |
| <code>sigma_c</code>    | The standard deviation for the control arm.      |
| <code>alpha_2</code>    | The type I error for the two-sided test.         |
| <code>n_control</code>  | The sample size for the control arm.             |
| <code>rand_ratio</code> | 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**

|                         |                                                  |
|-------------------------|--------------------------------------------------|
| <code>mu_t</code>       | The mean of the test arm.                        |
| <code>mu_c</code>       | The mean of the control arm.                     |
| <code>sigma_t</code>    | The standard deviation for the test arm.         |
| <code>sigma_c</code>    | The standard deviation for the control arm.      |
| <code>margin</code>     | The non-inferiority margin                       |
| <code>direction</code>  | If larger mu is better                           |
| <code>alpha</code>      | The type I error for the two-sided test.         |
| <code>n_control</code>  | The sample size for the control arm.             |
| <code>rand_ratio</code> | 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**

|                         |                                                                                                   |
|-------------------------|---------------------------------------------------------------------------------------------------|
| <code>lambda_t</code>   | The event rate of the test arm                                                                    |
| <code>lambda_c</code>   | The event rate of the control arm                                                                 |
| <code>alpha_2</code>    | The type I error for the two-sided test                                                           |
| <code>n_control</code>  | Sample size of the control arm                                                                    |
| <code>rand_ratio</code> | 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                                                                                                                   |
| <i>Group sequential designs / Adaptive sequential designs: Binary distribution, Superiority trial, Sample size calculation, Alpha-spending boundary</i> |

---

**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 | <i>Group sequential designs / Adaptive sequential designs: Poisson distribution, Superiority trial, Sample size calculation, Alpha-spending boundary</i> |
|-----------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------|

---

**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                                                                                                         |
| <i>Group sequential designs / Adaptive sequential designs: Survival analysis, Superiority trial, Sample size calculation, Alpha-spending boundary</i> |

---

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                                                                                                          |
| <i>Group sequential designs / Adaptive sequential designs: Survival analysis, Non-inferiority trial, Sample size calculation, Alpha-spending boundary</i> |

---

**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                                                                                                                       |
| <i>Group sequential designs / Adaptive sequential designs: Binary distribution, Non-inferiority trial, Sample size calculation, O'Brien-Fleming boundary</i> |

---

**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**

|                         |                                                                                                                 |
|-------------------------|-----------------------------------------------------------------------------------------------------------------|
| <code>mu_t</code>       | Mean of the test arm                                                                                            |
| <code>mu_c</code>       | Mean of the control arm                                                                                         |
| <code>std_t</code>      | Standard deviation of the test arm                                                                              |
| <code>std_c</code>      | Standard deviation of the control arm                                                                           |
| <code>margin</code>     | Non-inferiority margin                                                                                          |
| <code>direction</code>  | Test direction: 1 = larger mu is better, 0 = smaller mu is better                                               |
| <code>s</code>          | Vector of information fractions of each analysis, e.g. <code>c(1/3, 2/3, 1)</code> ; the last element must be 1 |
| <code>alpha</code>      | One-sided significance level (type I error rate)                                                                |
| <code>beta</code>       | Type II error rate, i.e. 1 - power                                                                              |
| <code>rand_ratio</code> | 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                                                                                                         |
| <i>Group sequential designs / Adaptive sequential designs: Binary distribution, Superiority trial, Sample size calculation, Pocock boundary</i> |

---

**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                                                                                                                   |
| <i>Group sequential designs / Adaptive sequential designs: Negative binomial distribution, Superiority trial, Sample size calculation, Pocock boundary</i> |

---

**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                                                                                                              |
| <i>Group sequential designs / Adaptive sequential designs: Poisson distribution, Superiority trial, Sample size calculation, Pocock boundary</i> |

---

**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                                                                                               |
| <i>Group sequential designs / Adaptive sequential designs: Survival analysis, Superiority trial, Sample size calculation, Pocock boundary</i> |

---

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

|                         |                                                  |
|-------------------------|--------------------------------------------------|
| <code>mu_t</code>       | The mean of the test arm.                        |
| <code>mu_c</code>       | The mean of the control arm.                     |
| <code>sigma_t</code>    | The standard deviation for the test arm.         |
| <code>sigma_c</code>    | The standard deviation for the control arm.      |
| <code>alpha_2</code>    | The type I error for the two-sided test.         |
| <code>beta</code>       | Type II error.                                   |
| <code>rand_ratio</code> | 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**

|                         |                                                                                                   |
|-------------------------|---------------------------------------------------------------------------------------------------|
| <code>lambda_t</code>   | The event rate of the test arm                                                                    |
| <code>lambda_c</code>   | The event rate of the control arm                                                                 |
| <code>alpha_2</code>    | The type I error for the two-sided test                                                           |
| <code>beta</code>       | Type II error rate, i.e. 1 - power                                                                |
| <code>rand_ratio</code> | 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 | <i>Two-stage design: Simon’s design</i> |
|--------------|-----------------------------------------|

---

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  $p \leq p_0$ .

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 | <i>Phase 2/3 seamless combination Group sequential design: Simulations, Binary distribution, Optimizing adaptive sequential design</i> |
|------------------------------|----------------------------------------------------------------------------------------------------------------------------------------|

---

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. Schfer. 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. Schfer. 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 | <i>Phase 2/3 seamless combination Group sequential design: Simulations, Normal distribution, Optimizing adaptive sequential design</i> |
|------------------------------|----------------------------------------------------------------------------------------------------------------------------------------|

---

**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. Schfer. 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>

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. Schfer. 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_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                                                                                                       |
| <i>Phase 2/3 seamless combination Group sequential design: Simulations, Survival analysis, Optimizing adaptive sequential design</i> |

---

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. Schfer. 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 | <i>Phase 2/3 seamless combination Group sequential design: Final analysis, Without sample size change, last_vt == 1</i> |
|----------------|-------------------------------------------------------------------------------------------------------------------------|

---

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>

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_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 | <i>Phase 2/3 seamless combination Group sequential design: Final analysis, Without sample size change, last_vt &gt; 1</i> |
|----------------|---------------------------------------------------------------------------------------------------------------------------|

---

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

|                                |                                                                                                                 |
|--------------------------------|-----------------------------------------------------------------------------------------------------------------|
| <code>s</code>                 | Vector of information fractions of each analysis, e.g. <code>c(1/3, 2/3, 1)</code> ; the last element must be 1 |
| <code>c_bry_two_stg</code>     | Critical boundaries of the two-stage design                                                                     |
| <code>c_bry_p3</code>          | Critical boundaries of the prior (phase 3) study                                                                |
| <code>comp</code>              | Type of comparison between arms                                                                                 |
| <code>theta_hat_p3</code>      | Treatment effect estimate from the prior (phase 3) study                                                        |
| <code>theta_hat_p3_sd</code>   | Standard error of 'theta_hat_p3'                                                                                |
| <code>theta_hat_last</code>    | Treatment effect estimate observed at the final analysis                                                        |
| <code>theta_hat_last_sd</code> | Standard error of 'theta_hat_last'                                                                              |
| <code>last_vt</code>           | Index of the analysis at which the trial stopped                                                                |
| <code>alpha_2</code>           | Type I error for the two-sided test                                                                             |
| <code>dist</code>              | 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. Schöfer. 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 | <i>Phase 2/3 seamless combination Group sequential design: Final analysis, With one sample size change</i> |
|--------------------|------------------------------------------------------------------------------------------------------------|

---

## 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>
- H.H. Müller, H. Schaffer. 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_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

|                             |                                                                                                                 |
|-----------------------------|-----------------------------------------------------------------------------------------------------------------|
| <code>p_t</code>            | Event (response) proportion in the test arm                                                                     |
| <code>p_c</code>            | Event (response) proportion in the control arm                                                                  |
| <code>margin</code>         | Non-inferiority / superiority margin                                                                            |
| <code>direction</code>      | Test direction: 1 = larger p is better, 0 = smaller p is better                                                 |
| <code>s</code>              | Vector of information fractions of each analysis, e.g. <code>c(1/3, 2/3, 1)</code> ; the last element must be 1 |
| <code>alpha</code>          | One-sided significance level (type I error rate)                                                                |
| <code>sampsz_control</code> | Control arm sample size                                                                                         |
| <code>rand_ratio</code>     | Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm                   |
| <code>dist1</code>          | Endpoint / distribution indicator for the first stage                                                           |
| <code>dist2</code>          | 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. Schaffer. 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_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                                                                                                |
| <i>Phase 2/3 seamless combination Group sequential design: Negative binomial distribution, Power calculation, Alpha-spending boundary</i> |

---

**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

|                             |                                                                                                                 |
|-----------------------------|-----------------------------------------------------------------------------------------------------------------|
| <code>r_t</code>            | Rate parameter of the test arm (negative binomial endpoint)                                                     |
| <code>r_c</code>            | Rate parameter of the control arm (negative binomial endpoint)                                                  |
| <code>margin</code>         | Non-inferiority / superiority margin                                                                            |
| <code>direction</code>      | Test direction: 1 = larger r is better, 0 = smaller r is better                                                 |
| <code>s</code>              | Vector of information fractions of each analysis, e.g. <code>c(1/3, 2/3, 1)</code> ; the last element must be 1 |
| <code>alpha</code>          | One-sided significance level (type I error rate)                                                                |
| <code>sampsz_control</code> | Control arm sample size                                                                                         |
| <code>rand_ratio</code>     | Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm                   |
| <code>nu_t</code>           | Follow-up duration of the test arm (negative binomial endpoint)                                                 |
| <code>kappa</code>          | Dispersion (size) parameter of the negative binomial distribution                                               |
| <code>dist1</code>          | Endpoint / distribution indicator for the first stage                                                           |
| <code>dist2</code>          | 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 cumulative alpha', '2-sided alpha spending', '2-sided cumulative alpha', 'selecting prob at end of phase 2', 'total selection prob at end of phase 2', 'Rejection rate for each 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. Schöfer. 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. Schöfer. 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 | <i>Phase 2/3 seamless combination Group sequential design: Poisson distribution, Power calculation, Alpha-spending boundary</i> |
|---------------------------------------|---------------------------------------------------------------------------------------------------------------------------------|

---

**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. Schfer. 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. Schfer. 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

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

|                         |                                                                                                                 |
|-------------------------|-----------------------------------------------------------------------------------------------------------------|
| <code>r_t</code>        | Rate parameter of the test arm (negative binomial endpoint)                                                     |
| <code>r_c</code>        | Rate parameter of the control arm (negative binomial endpoint)                                                  |
| <code>margin</code>     | Non-inferiority / superiority margin                                                                            |
| <code>direction</code>  | Test direction: 1 = larger r is better, 0 = smaller r is better                                                 |
| <code>s</code>          | Vector of information fractions of each analysis, e.g. <code>c(1/3, 2/3, 1)</code> ; the last element must be 1 |
| <code>alpha</code>      | One-sided significance level (type I error rate)                                                                |
| <code>beta</code>       | Type II error rate, i.e. 1 - power                                                                              |
| <code>rand_ratio</code> | Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm                   |
| <code>nu_t</code>       | Follow-up duration of the test arm (negative binomial endpoint)                                                 |
| <code>kappa</code>      | Dispersion (size) parameter of the negative binomial distribution                                               |
| <code>dist1</code>      | Endpoint / distribution indicator for the first stage                                                           |
| <code>dist2</code>      | 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. Schfer. 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 | <i>Phase 2/3 seamless combination Group sequential design: Normal distribution, Sample size calculation, Alpha-spending boundary</i> |
|--------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------|

---

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>

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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_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                                                                                           |
| <i>Phase 2/3 seamless combination Group sequential design: Poisson distribution, Sample size calculation, Alpha-spending boundary</i> |

---

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>

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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_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                                                                            |
| <i>Phase 2/3 seamless combination Group sequential design: Survival analysis, Sample size calculation, Alpha-spending boundary</i> |

---

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>

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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\_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 | <i>Phase 2/3 seamless combination Group sequential design: Binary distribution, Sample size calculation, O'Brien-Fleming boundary</i> |
|-----------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------|

---

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>

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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_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

|                        |                                                                 |
|------------------------|-----------------------------------------------------------------|
| <code>r_t</code>       | Rate parameter of the test arm (negative binomial endpoint)     |
| <code>r_c</code>       | Rate parameter of the control arm (negative binomial endpoint)  |
| <code>margin</code>    | Non-inferiority / superiority margin                            |
| <code>direction</code> | Test direction: 1 = larger r is better, 0 = smaller r is better |

|                         |                                                                                                                 |
|-------------------------|-----------------------------------------------------------------------------------------------------------------|
| <code>s</code>          | Vector of information fractions of each analysis, e.g. <code>c(1/3, 2/3, 1)</code> ; the last element must be 1 |
| <code>alpha</code>      | One-sided significance level (type I error rate)                                                                |
| <code>beta</code>       | Type II error rate, i.e. 1 - power                                                                              |
| <code>rand_ratio</code> | Ratio of the number of subjects in the test arm vs. the number of subjects in the control arm                   |
| <code>nu_t</code>       | Follow-up duration of the test arm (negative binomial endpoint)                                                 |
| <code>kappa</code>      | Dispersion (size) parameter of the negative binomial distribution                                               |
| <code>dist1</code>      | Endpoint / distribution indicator for the first stage                                                           |
| <code>dist2</code>      | 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>

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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_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>

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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_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>
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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_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. Schöfer. 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**

|                        |                                                                                                                 |
|------------------------|-----------------------------------------------------------------------------------------------------------------|
| <code>r_t</code>       | Rate parameter of the test arm (negative binomial endpoint)                                                     |
| <code>r_c</code>       | Rate parameter of the control arm (negative binomial endpoint)                                                  |
| <code>kappa</code>     | Dispersion (size) parameter of the negative binomial distribution                                               |
| <code>direction</code> | Test direction: 1 = larger r is better, 0 = smaller r is better                                                 |
| <code>s</code>         | Vector of information fractions of each analysis, e.g. <code>c(1/3, 2/3, 1)</code> ; the last element must be 1 |
| <code>bry_type</code>  | Critical boundary type: 1 = O'Brien-Fleming, 2 = Pocock, 3 = alpha-spending                                     |
| <code>alpha_2</code>   | Type I error for the two-sided test                                                                             |
| <code>theta_cut</code> | 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 | <i>Phase 2/3 seamless combination Group sequential design: Simulations, Normal distribution, Operating characteristics</i> |
|---------------------------------|----------------------------------------------------------------------------------------------------------------------------|

---

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**

|                        |                                                                                                                 |
|------------------------|-----------------------------------------------------------------------------------------------------------------|
| <code>mu_t</code>      | Means of the test arm                                                                                           |
| <code>mu_c</code>      | Means of the control arm                                                                                        |
| <code>sigma_t</code>   | Standard deviation of the test arm                                                                              |
| <code>sigma_c</code>   | Standard deviation of the control arm                                                                           |
| <code>direction</code> | Test direction: 1 = larger mu is better, 0 = smaller mu is better                                               |
| <code>s</code>         | Vector of information fractions of each analysis, e.g. <code>c(1/3, 2/3, 1)</code> ; the last element must be 1 |
| <code>bry_type</code>  | Critical boundary type: 1 = O'Brien-Fleming, 2 = Pocock, 3 = alpha-spending                                     |
| <code>alpha_2</code>   | Type I error for the two-sided test                                                                             |
| <code>theta_cut</code> | Efficacy cut-off on the effect-size scale applied at the interim analysis                                       |
| <code>samsz</code>     | Planned sample size of the control arm used in the simulation                                                   |
| <code>N_max</code>     | Maximum allowed sample size (control arm)                                                                       |
| <code>beta</code>      | Type II error rate, i.e. 1 - power                                                                              |
| <code>sim_num</code>   | 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. Schöfer. 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_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>

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. Schfer. 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_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>

H.H. Müller, H. Schöfer. 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_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>

H.H. Müller, H. Schfer. 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_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

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

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

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

H.H. Müller, H. Schöfer. 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_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. <code>c(1/3, 2/3, 1)</code> ; 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>

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. Schaffer. 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)
```

# Index

asd\_ci\_est\_back, [6](#)  
asd\_ci\_est\_one\_arm\_2\_stage, [8](#)  
asd\_ci\_est\_one\_arm\_3\_stage, [9](#)  
asd\_new\_design, [10](#)  
asd\_new\_design\_survival, [12](#)  
asd\_new\_design\_theta, [13](#)  
asd\_new\_design\_theta\_survival, [14](#)  
asd\_power\_simu\_binary, [15](#)  
asd\_power\_simu\_neg\_binomial, [17](#)  
asd\_power\_simu\_normal, [18](#)  
asd\_power\_simu\_poisson, [20](#)  
asd\_power\_simu\_survival, [21](#)  
asd\_simu\_OC\_binary, [23](#)  
asd\_simu\_OC\_neg\_binomial, [24](#)  
asd\_simu\_OC\_normal, [26](#)  
asd\_simu\_OC\_poisson, [28](#)  
asd\_simu\_OC\_survival, [30](#)  
  
EXP\_3\_stg\_sz, [31](#)  
  
fixed\_rej\_nbglm\_simu, [33](#)  
fixed\_rej\_rate\_binary, [33](#)  
fixed\_rej\_rate\_normal, [34](#)  
fixed\_rej\_rate\_poisson, [35](#)  
fixed\_rej\_rate\_surv\_cox, [36](#)  
  
gsd\_ci\_est, [37](#)  
gsd\_ci\_est\_2\_stage, [37](#)  
gsd\_ci\_est\_3\_stage, [38](#)  
gsd\_power\_simu\_binary, [39](#)  
gsd\_power\_simu\_negbinom, [41](#)  
gsd\_power\_simu\_normal, [42](#)  
gsd\_power\_simu\_poisson, [44](#)  
gsd\_power\_simu\_survival, [45](#)  
  
hybrid\_fixed\_prior\_rej\_binary\_simu, [46](#)  
hybrid\_fixed\_prior\_rej\_negbinom\_simu, [48](#)  
hybrid\_fixed\_prior\_rej\_normal\_simu, [50](#)  
hybrid\_fixed\_prior\_rej\_poisson\_simu, [51](#)  
  
hybrid\_fixed\_prior\_rej\_survival\_simu, [53](#)  
hybrid\_random\_prior\_rej\_binary\_simu, [55](#)  
hybrid\_random\_prior\_rej\_negbinom\_simu, [56](#)  
hybrid\_random\_prior\_rej\_normal\_simu, [58](#)  
hybrid\_random\_prior\_rej\_poisson\_simu, [60](#)  
hybrid\_random\_prior\_rej\_survival\_simu, [61](#)  
hybrid\_sz, [63](#)  
  
interim\_analysis, [64](#)  
  
masd\_est\_back\_no\_drop, [65](#)  
masd\_est\_back\_with\_drop, [67](#)  
masd\_est\_ci, [69](#)  
masd\_new\_samsz, [70](#)  
masd\_new\_samsz\_survival, [72](#)  
masd\_new\_samsz\_theta, [73](#)  
masd\_new\_samsz\_theta\_survival, [75](#)  
masd\_power\_simu\_adapt\_binary, [77](#)  
masd\_power\_simu\_adapt\_neg\_binomial, [78](#)  
masd\_power\_simu\_adapt\_normal, [80](#)  
masd\_power\_simu\_adapt\_poisson, [81](#)  
masd\_power\_simu\_adapt\_survival, [83](#)  
masd\_simu\_OC\_binary, [84](#)  
masd\_simu\_OC\_neg\_binomial, [86](#)  
masd\_simu\_OC\_normal, [88](#)  
masd\_simu\_OC\_poisson, [90](#)  
masd\_simu\_OC\_survival, [92](#)  
midpnt\_sz, [94](#)  
MSD\_power\_alsp\_boundary\_binary\_diff, [95](#)  
MSD\_power\_alsp\_boundary\_neg\_binomial, [96](#)  
MSD\_power\_alsp\_boundary\_normal, [98](#)  
MSD\_power\_alsp\_boundary\_poisson, [100](#)

- MSD\_power\_alsp\_boundary\_survival\_Schoenfeld, 101
- MSD\_power\_OF\_boundary\_binary\_diff, 103
- MSD\_power\_OF\_boundary\_neg\_binomial, 104
- MSD\_power\_OF\_boundary\_normal, 106
- MSD\_power\_OF\_boundary\_poisson, 107
- MSD\_power\_OF\_boundary\_survival\_Schoenfeld, 109
- msd\_power\_simu\_binary, 110
- msd\_power\_simu\_neg\_binomial, 112
- msd\_power\_simu\_normal, 113
- msd\_power\_simu\_poisson, 115
- msd\_power\_simu\_survival, 116
- MSD\_Sample\_size\_alsp\_boundary\_binary\_diff, 117
- MSD\_Sample\_size\_alsp\_boundary\_neg\_binomial, 119
- MSD\_Sample\_size\_alsp\_boundary\_normal, 120
- MSD\_Sample\_size\_alsp\_boundary\_poisson, 122
- MSD\_Sample\_size\_alsp\_boundary\_survival\_Schoenfeld, 124
- MSD\_Sample\_size\_OF\_boundary\_binary\_diff, 125
- MSD\_Sample\_size\_OF\_boundary\_neg\_binomial, 127
- MSD\_Sample\_size\_OF\_boundary\_normal, 128
- MSD\_Sample\_size\_OF\_boundary\_poisson, 130
- MSD\_Sample\_size\_OF\_boundary\_survival\_Schoenfeld, 131
- new\_sample\_size\_hybrid, 133
- one\_arm\_ad\_3\_stg\_binary, 134
- one\_arm\_ad\_two\_stg\_binary, 136
- one\_arm\_rej\_2\_stg\_binary, 137
- one\_arm\_rej\_3\_stg\_binary, 138
- one\_arm\_rej\_simon\_binary, 140
- power\_alsp\_boundary\_binary\_diff, 141
- power\_alsp\_boundary\_binary\_diff\_NI, 142
- power\_alsp\_boundary\_neg\_binomial, 143
- power\_alsp\_boundary\_neg\_binomial\_NI, 144
- power\_alsp\_boundary\_normal, 145
- power\_alsp\_boundary\_normal\_NI, 146
- power\_alsp\_boundary\_poisson, 147
- power\_alsp\_boundary\_poisson\_NI, 148
- power\_alsp\_boundary\_survival\_Schoenfeld, 149
- power\_alsp\_boundary\_survival\_Schoenfeld\_NI, 150
- power\_binary\_diff, 151
- power\_binary\_diff\_NI, 152
- power\_OF\_boundary\_binary\_diff, 152
- power\_OF\_boundary\_binary\_diff\_NI, 153
- power\_OF\_boundary\_neg\_binomial, 154
- power\_OF\_boundary\_neg\_binomial\_NI, 155
- power\_OF\_boundary\_normal, 156
- power\_OF\_boundary\_normal\_NI, 157
- power\_OF\_boundary\_poisson, 159
- power\_OF\_boundary\_poisson\_NI, 160
- power\_OF\_boundary\_survival\_Schoenfeld, 161
- power\_OF\_boundary\_survival\_Schoenfeld\_NI, 161
- power\_pocock\_boundary\_binary\_diff, 162
- power\_pocock\_boundary\_binary\_diff\_NI, 163
- power\_pocock\_boundary\_neg\_binomial, 164
- power\_pocock\_boundary\_neg\_binomial\_NI, 165
- power\_pocock\_boundary\_normal, 167
- power\_pocock\_boundary\_normal\_NI, 168
- power\_pocock\_boundary\_poisson, 169
- power\_pocock\_boundary\_poisson\_NI, 170
- power\_pocock\_boundary\_survival\_Schoenfeld, 171
- power\_pocock\_boundary\_survival\_Schoenfeld\_NI, 172
- power\_two\_sample\_neg\_binomial, 173
- power\_two\_sample\_neg\_binomial\_NI, 174
- power\_two\_sample\_normal, 175
- power\_two\_sample\_normal\_NI, 176
- power\_two\_sample\_Poisson, 177
- power\_two\_sample\_Poisson\_NI, 177
- power\_two\_sample\_surv\_Schoenfeld, 178
- power\_two\_sample\_surv\_Schoenfeld\_NI, 179
- Sample\_size\_alsp\_boundary\_binary\_diff, 180

- Sample\_size\_alsp\_boundary\_binary\_diff\_NI, 181
- Sample\_size\_alsp\_boundary\_neg\_binomial, 182
- Sample\_size\_alsp\_boundary\_neg\_binomial\_NI, 183
- Sample\_size\_alsp\_boundary\_normal, 184
- Sample\_size\_alsp\_boundary\_normal\_NI, 185
- Sample\_size\_alsp\_boundary\_poisson, 186
- Sample\_size\_alsp\_boundary\_poisson\_NI, 187
- Sample\_size\_alsp\_boundary\_survival\_Schoenfeld, 188
- Sample\_size\_alsp\_boundary\_survival\_Schoenfeld\_NI, 189
- sample\_size\_binary\_diff, 190
- sample\_size\_binary\_diff\_NI, 190
- sample\_size\_neg\_binomial, 191
- sample\_size\_neg\_binomial\_NI, 192
- Sample\_size\_OF\_boundary\_binary\_diff, 193
- Sample\_size\_OF\_boundary\_binary\_diff\_NI, 194
- Sample\_size\_OF\_boundary\_neg\_binomial, 195
- Sample\_size\_OF\_boundary\_neg\_binomial\_NI, 196
- Sample\_size\_OF\_boundary\_normal, 197
- Sample\_size\_OF\_boundary\_normal\_NI, 198
- Sample\_size\_OF\_boundary\_poisson, 199
- Sample\_size\_OF\_boundary\_poisson\_NI, 200
- Sample\_size\_OF\_boundary\_survival\_Schoenfeld, 201
- Sample\_size\_OF\_boundary\_survival\_Schoenfeld\_NI, 202
- Sample\_size\_pocock\_boundary\_binary\_diff, 203
- Sample\_size\_pocock\_boundary\_binary\_diff\_NI, 204
- Sample\_size\_pocock\_boundary\_neg\_binomial, 205
- Sample\_size\_pocock\_boundary\_neg\_binomial\_NI, 206
- Sample\_size\_pocock\_boundary\_normal, 207
- Sample\_size\_pocock\_boundary\_normal\_NI, 208
- Sample\_size\_pocock\_boundary\_poisson, 209
- Sample\_size\_pocock\_boundary\_poisson\_NI, 210
- Sample\_size\_pocock\_boundary\_survival\_Schoenfeld, 211
- Sample\_size\_pocock\_boundary\_survival\_Schoenfeld\_NI, 212
- sample\_size\_two\_sample\_normal, 213
- sample\_size\_two\_sample\_normal\_NI, 214
- sample\_size\_two\_sample\_Poisson, 215
- sample\_size\_two\_sample\_Poisson\_NI, 215
- sample\_size\_two\_sample\_surv\_Schoenfeld, 216
- sample\_size\_two\_sample\_surv\_Schoenfeld\_NI, 217
- simon\_ph2\_sz, 218
- Two\_stage\_asd\_simu\_OC\_binary, 219
- Two\_stage\_asd\_simu\_OC\_neg\_binomial, 221
- Two\_stage\_asd\_simu\_OC\_normal, 223
- Two\_stage\_asd\_simu\_OC\_poisson, 225
- Two\_stage\_asd\_simu\_OC\_survival, 226
- two\_stage\_ci\_0, 228
- two\_stage\_ci\_1, 229
- two\_stage\_est\_back, 231
- two\_stage\_power\_alsp\_boundary\_binary\_diff, 233
- two\_stage\_power\_alsp\_boundary\_neg\_binomial, 234
- two\_stage\_power\_alsp\_boundary\_normal, 236
- two\_stage\_power\_alsp\_boundary\_poisson, 237
- two\_stage\_power\_alsp\_boundary\_survival\_Schoenfeld, 239
- two\_stage\_power\_OF\_boundary\_binary\_diff, 240
- two\_stage\_power\_OF\_boundary\_neg\_binomial, 242
- two\_stage\_power\_OF\_boundary\_normal, 243
- two\_stage\_power\_OF\_boundary\_poisson, 245
- two\_stage\_power\_OF\_boundary\_survival\_Schoenfeld, 246

two\_stage\_Sample\_size\_alsp\_boundary\_binary\_diff,  
248

two\_stage\_Sample\_size\_alsp\_boundary\_neg\_binomial,  
249

two\_stage\_Sample\_size\_alsp\_boundary\_normal,  
251

two\_stage\_Sample\_size\_alsp\_boundary\_poisson,  
252

two\_stage\_Sample\_size\_alsp\_boundary\_survival\_Schoenfeld,  
254

two\_stage\_Sample\_size\_OF\_boundary\_binary\_diff,  
255

two\_stage\_Sample\_size\_OF\_boundary\_neg\_binomial,  
257

two\_stage\_Sample\_size\_OF\_boundary\_normal,  
259

two\_stage\_Sample\_size\_OF\_boundary\_poisson,  
260

two\_stage\_Sample\_size\_OF\_boundary\_survival\_Schoenfeld,  
262

two\_stg\_adapt\_power\_simu\_binary, 263

two\_stg\_adapt\_power\_simu\_neg\_binomial,  
265

two\_stg\_adapt\_power\_simu\_normal, 266

two\_stg\_adapt\_power\_simu\_poisson, 268

two\_stg\_adapt\_power\_simu\_survival, 270

two\_stg\_power\_simu\_binary, 271

two\_stg\_power\_simu\_neg\_binomial, 273

two\_stg\_power\_simu\_normal, 274

two\_stg\_power\_simu\_poisson, 276

two\_stg\_power\_simu\_survival, 277