Package 'SSmRCT'

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Type Package

Title Regional sample size allocation for mRCT

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Description Using Japan's Method 1 and Method 2, this package is designed to determine regional sample size allocation strategies based on the marginal, conditional, and joint probabilities of global success, as well as the illustration of efficacy consistency between the target region and globally. It supports a variety of endpoints in superiority, non-inferiority, and equivalence clinical trials, including continuous, binary, survival, and counts endpoints, and simultaneously supports both theoretical calculations and data simulations.

Encoding UTF-8

RoxygenNote 7.2.3

Depends dplyr, furrr, purrr, MASS, mvtnorm, survival

Suggests knitr, rmarkdown

VignetteBuilder knitr

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NeedsCompilation no

R topics documented:

`combine` *Combine vectors or matrices*

Description

Combine two vectors to one vector or two matrices to one matrix

Usage

```
combine(A, B)
```

Arguments

`A`	A vector or matrix
`B`	A vector or matrix

Value

A vector or matrix

Examples

```
combine(c(1, 2, 3), c(4, 5, 6))

combine(
  matrix(c(1, 2, 3, 4), nrow = 2, byrow = TRUE),
  matrix(c(5, 6, 7, 8), nrow = 2, byrow = TRUE)
)
```

`getN_Bin` *Sample size and power for binary endpoints*

Description

Calculating sample size when given power or power when given sample size for binary endpoints.

Usage

```
getN_Bin_Super(p1, p0, alpha = 0.025, beta = NA, N = NA, r = 1, scale = "RD")

getN_Bin_Noninf(
  p1,
  p0,
  cut,
  alpha = 0.025,
  beta = NA,
```

```
  N = NA,
  r = 1,
  scale = "RD",
  direct = 1
)

getN_Bin_Equi(
  p1,
  p0,
  cut,
  alpha = 0.025,
  beta = NA,
  N = NA,
  r = 1,
  scale = "RD",
  maxN = 1e+06
)
```

Arguments

p1	Rate of treatment group.
p0	Rate of control group.
alpha	One-sided type I error rate. The default value is 0.025.
beta	Type II error rate. When beta is NA and N is not NA, the power will be returned.
N	Sample size. When N is NA and beta is not NA, the sample size will be returned.
r	Ratio of the sample sizes of the treatment group to the control group. The default value is 1.
scale	Optional values are "RD" for rate difference, "RR" for relative risk, and "OR" for odds ratio. Default value is "RD".
cut	A positive value for non-inferiority or equivalence margin. For RD, the margin is on the original scale. For RR and OR, the margin is on the log scale. For example, if the non-inferiority margins for RD, RR, OR are 0.2, 0.6, and 1.3, then the cut = 0.2, cut = -log(0.6), and cut = log(1.3), respectively.
direct	If direct = 1, larger values of RD/RR/OR are preferable. If direct = -1, smaller values of RD/RR/OR are preferable.
maxN	Maximum possible sample size(N) in equivalence design. Default value is 1e6.

Details

Taking the larger RD/RR/OR is preferable as an example. Sample size calculation is based on the following Z test, with the success criterion:

in superiority design:

$$Z = \frac{\hat{\delta}}{\sqrt{\frac{\hat{\sigma}_0^2}{N/(r+1)} + \frac{\hat{\sigma}_1^2}{Nr/(r+1)}}} > \Phi^{-1}(1-\alpha)$$

in non-inferiority design:

$$Z = \frac{\hat{\delta} + \Delta}{\sqrt{\frac{\hat{\sigma}_0^2}{N/(r+1)} + \frac{\hat{\sigma}_1^2}{Nr/(r+1)}}} > \Phi^{-1}(1-\alpha)$$

in equivalence design:

$$Z_u = \frac{\hat{\delta} + \Delta}{\sqrt{\frac{\hat{\sigma}_0^2}{N/(r+1)} + \frac{\hat{\sigma}_1^2}{Nr/(r+1)}}} > \Phi^{-1}(1-\alpha) \text{ and } Z_l = \frac{\hat{\delta} - \Delta}{\sqrt{\frac{\hat{\sigma}_0^2}{N/(r+1)} + \frac{\hat{\sigma}_1^2}{Nr/(r+1)}}} < \Phi^{-1}(\alpha)$$

Where $\hat{\delta} = \hat{p}_1 - \hat{p}_0, \hat{\sigma}_0^2 = \hat{p}_0(1-\hat{p}_0), \hat{\sigma}_1^2 = \hat{p}_1(1-\hat{p}_1)$ for RD; $\hat{\delta} = log(\frac{\hat{p}_1}{\hat{p}_0}), \hat{\sigma}_0^2 = \frac{(1-\hat{p}_0)}{\hat{p}_0}, \hat{\sigma}_1^2 = \frac{(1-\hat{p}_1)}{\hat{p}_1}$ for RR; $\hat{\delta} = log(\frac{\hat{p}_1/(1-\hat{p}_1)}{\hat{p}_0/(1-\hat{p}_0)}), \hat{\sigma}_0^2 = \frac{1}{\hat{p}_0(1-\hat{p}_0)}), \hat{\sigma}_1^2 = \frac{1}{\hat{p}_1(1-\hat{p}_1)}$ for OR; and Δ is the non-inferiority or equivalence margin.

Value

A data frame containing input parameters and returned sample size or power.

Examples

```
(v <- getN_Bin_Super(
  p1 = 0.6, p0 = 0.4, alpha = 0.025, beta = 0.2, N = NA, r = 1, scale = "RD"
))
getN_Bin_Super(
  p1 = 0.6, p0 = 0.4, alpha = 0.025, beta = NA, N = v$N, r = 1, scale = "RD"
)

(v <- getN_Bin_Noninf(
  p1 = 0.6, p0 = 0.5, cut = log(1.4),
  alpha = 0.025, beta = 0.2, N = NA, r = 1, scale = "RR", direct = -1
))
getN_Bin_Noninf(
  p1 = 0.6, p0 = 0.5, cut = log(1.4),
  alpha = 0.025, beta = NA, N = v$N, r = 1, scale = "RR", direct = -1
)
```

---

getN_Bin_JM1 *Regional sample size allocation using Japan's Method 1 for binary endpoints*

Description

Based on Japan's Method 1, given the global sample size and marginal probability (power) of efficacy consistency between target region and globally, calculate the required sample size allocated to the target region, in clinical trials using superiority, non-inferiority, and equivalence designs with binary endpoints.

Usage

```
getN_Bin_Super_JM1(
  p1_a,
  p0_a,
  p1_j,
  p0_j,
  pi = 0.5,
  alpha = NA,
```

```
  beta = NA,
  beta1 = 0.2,
  N = NA,
  r = 1,
  scale = "RD"
)

getN_Bin_Noninf_JM1(
  p1_a,
  p0_a,
  p1_j,
  p0_j,
  pi = 0.5,
  cut,
  alpha = NA,
  beta = NA,
  beta1 = 0.2,
  N = NA,
  r = 1,
  scale = "RD",
  direct = 1
)

getN_Bin_Equi_JM1(
  p1_a,
  p0_a,
  p1_j,
  p0_j,
  pi = 0.5,
  cut,
  alpha = NA,
  beta = NA,
  beta1 = 0.2,
  N = NA,
  r = 1,
  scale = "RD",
  maxN = 1e+06
)
```

Arguments

p1_a	Rate of treatment group globally.
p0_a	Rate of the control group globally.
p1_j	Rate of treatment group in target region.
p0_j	Rate of control group in target region.
pi	Proportion of global efficacy to retain. The default value is 0.5, which means retaining half of the efficacy.
alpha	One-sided type I error rate for global success, which is used to calculate global sample size only when N is NA. The default value is 0.025.
beta	Type II error rate for global success, which is used to calculate global sample size only when N is missing.

beta1	Type II error rate for efficacy consistency between target region and globally. The default value is 0.2.
N	Global sample size. When N is NA and alpha and beta are not NAs, N will be calculated automatically.
r	Ratio of the sample sizes of the treatment group to the control group. The default value is 1.
scale	Optional values are "RD" for rate difference, "RR" for relative risk, and "OR" for odds ratio. Default value is "RD".
cut	A positive value for non-inferiority or equivalence margin. For RD, the margin is on the original scale. For RR and OR, the margin is on the log scale. For example, if the non-inferiority margins for RD, RR, OR are 0.2, 0.6, and 1.3, then the cut = 0.2, cut = -log(0.6), and cut = log(1.3), respectively.
direct	If direct = 1, larger values of RD/RR/OR are preferable. If direct = -1, smaller values of RD/RR/OR are preferable.
maxN	Maximum possible sample size (N) in equivalence design. Default value is 1e6.

Details

The global success criterion and the efficacy consistency criterion between target region and globally could be found in getPwr_Bin_Super_JM1.

Value

A data frame where f is required proportion of sample size allocated to the target region, and Nj is required sample size for the target region, calculated as Nj = N * f.

References

1. Quan H, Li M, Chen J, et al. Assessment of Consistency of Treatment Effects in Multiregional Clinical Trials. Drug Information J. 2010;44(5):617-632. doi:10.1177/009286151004400509

2. Liao JJZ, Yu Z, Li Y. Sample size allocation in multiregional equivalence studies. Pharm Stat. 2018;17(5):570-577. doi:10.1002/pst.1871

See Also

getPwr_Bin_Super_JM1, getN_Bin_Super.

Examples

```
getN_Bin_Super_JM1(
  p1_a = 0.75, p0_a = 0.5, p1_j = 0.7, p0_j = 0.5, pi = 0.5, beta1 = 0.2,
  N = 200, r = 1, scale = "RD"
)

getN_Bin_Noninf_JM1(
  p1_a = 0.5, p0_a = 0.5, p1_j = 0.6, p0_j = 0.5, pi = 0.5, cut = log(1.6),
  alpha = 0.025, beta = 0.2, beta1 = 0.2, N = NA, r = 1, scale = "RR",
  direct = -1
)
```

getN_Con *Sample size and power for continuous endpoints*

Description

Calculating sample size when given power or power when given sample size for continuous endpoints.

Usage

```
getN_Con_Super(delta, sigma, alpha = 0.025, beta = NA, N = NA, r = 1)

getN_Con_Noninf(
  delta,
  sigma,
  cut,
  alpha = 0.025,
  beta = NA,
  N = NA,
  r = 1,
  direct = 1
)

getN_Con_Equi(
  delta,
  sigma,
  cut,
  alpha = 0.025,
  beta = NA,
  N = NA,
  r = 1,
  maxN = 1e+06
)
```

Arguments

delta	Mean difference between treatment and control groups.
sigma	Common standard deviation.
alpha	One-sided type I error rate. The default value is 0.025.
beta	Type II error rate. When beta is NA and N is not NA, the power will be returned.
N	Sample size. When N is NA and beta is not NA, the sample size will be returned.
r	Ratio of the sample sizes of the treatment group to the control group. The default value is 1.
cut	A positive value for non-inferiority or equivalence margin.
direct	direct = 1 indicates that a larger mean difference is preferable, while direct = -1 indicates that a smaller mean difference is preferable.
maxN	Maximum possible sample size(N) in equivalence design. Default value is 1e6.

Details

Taking the larger mean difference is preferable as an example. Sample size calculation is based on the following Z test, with the success criterion:

in superiority design:

$$Z = \frac{\hat{\delta}}{\hat{\sigma}\sqrt{\frac{1}{N/(r+1)} + \frac{1}{Nr/(r+1)}}} > \Phi^{-1}(1-\alpha)$$

in non-inferiority design:

$$Z = \frac{\hat{\delta} + \Delta}{\hat{\sigma}\sqrt{\frac{1}{N/(r+1)} + \frac{1}{Nr/(r+1)}}} > \Phi^{-1}(1-\alpha)$$

in equivalence design:

$$Z_u = \frac{\hat{\delta} + \Delta}{\hat{\sigma}\sqrt{\frac{1}{N/(r+1)} + \frac{1}{Nr/(r+1)}}} > \Phi^{-1}(1-\alpha) \text{ and } Z_l = \frac{\hat{\delta} - \Delta}{\hat{\sigma}\sqrt{\frac{1}{N/(r+1)} + \frac{1}{Nr/(r+1)}}} < \Phi^{-1}(\alpha)$$

Where $\hat{\delta}$ is the mean difference between treatment and control groups, and Δ is the non-inferiority or equivalence margin.

Value

A data frame containing input parameters and returned sample size or power.

Examples

```
(v <- getN_Con_Super(delta = 1.5, sigma = 4, alpha = 0.025, beta = 0.2, N = NA, r = 1))
getN_Con_Super(delta = 1.5, sigma = 4, alpha = 0.025, beta = NA, N = v$N, r = 1)

(v <- getN_Con_Noninf(
  delta = 1, sigma = 4, cut = 2, alpha = 0.025, beta = 0.2, N = NA, r = 1, direct = -1
))
getN_Con_Noninf(
  delta = 1, sigma = 4, cut = 2, alpha = 0.025, beta = NA, N = v$N, r = 1, direct = -1
)
```

---

getN_Con_JM1 *Regional sample size allocation using Japan's Method 1 for continuous endpoints*

Description

Based on Japan's Method 1, given the global sample size and marginal probability (power) of efficacy consistency between target region and globally, calculate the required sample size allocated to the target region, in clinical trials using superiority, non-inferiority, and equivalence designs with continuous endpoints.

Usage

```
getN_Con_Super_JM1(
  delta_a,
  delta_j,
  sigma,
  pi = 0.5,
  alpha = NA,
  beta = NA,
  beta1 = 0.2,
  N = NA,
  r = 1
)

getN_Con_Noninf_JM1(
  delta_a,
  delta_j,
  sigma,
  pi = 0.5,
  cut,
  alpha = NA,
  beta = NA,
  beta1 = 0.2,
  N = NA,
  r = 1,
  direct = 1
)

getN_Con_Equi_JM1(
  delta_a,
  delta_j,
  sigma,
  pi = 0.5,
  cut,
  alpha = NA,
  beta = NA,
  beta1 = 0.2,
  N = NA,
  r = 1,
  maxN = 1e+06
)
```

Arguments

delta_a	Mean difference between treatment and control groups globally.
delta_j	Mean difference between treatment and control groups in target region.
sigma	Common standard deviation.
pi	Proportion of global efficacy to retain. The default value is 0.5, which means retaining half of the efficacy.
alpha	One-sided type I error rate for global success, which is used to calculate global sample size only when N is NA. The default value is 0.025.

beta	Type II error rate for global success, which is used to calculate global sample size only when N is NA.
beta1	Type II error rate for efficacy consistency between target region and globally. The default value is 0.2.
N	Global sample size. When N is NA and alpha and beta are not NAs, N will be calculated automatically.
r	Ratio of the sample sizes of the treatment group to the control group. The default value is 1.
cut	A positive value for non-inferiority or equivalence margin.
direct	direct = 1 indicates that a larger mean difference is preferable, while direct = -1 indicates that a smaller mean difference is preferable.
maxN	Maximum possible sample size (N) in equivalence design. Default value is 1e6.

Details

The global success criterion and the efficacy consistency criterion between target region and globally could be found in getPwr_Con_Super_JM1.

Value

A data frame where f is required proportion of sample size allocated to the target region, and Nj is the required sample size for the target region, calculated as Nj = N * f.

References

1. Quan H, Li M, Chen J, et al. Assessment of Consistency of Treatment Effects in Multiregional Clinical Trials. Drug Information J. 2010;44(5):617-632. doi:10.1177/009286151004400509

2. Liao JJZ, Yu Z, Li Y. Sample size allocation in multiregional equivalence studies. Pharm Stat. 2018;17(5):570-577. doi:10.1002/pst.1871

See Also

getPwr_Con_Super_JM1, getN_Con_Super.

Examples

```
getN_Con_Super_JM1(
  delta_a = 0.7, delta_j = 0.5, sigma = 1, pi = 0.5, beta1 = 0.2, N = 100,
  r = 1
)

getN_Con_Noninf_JM1(
  delta_a = 0, delta_j = 0.5, sigma = 4, pi = 0.5, cut = 2, alpha = 0.025,
  beta = 0.2, beta1 = 0.2, N = NA, r = 1, direct = -1
)
```

getN_Count *Sample size and power for count endpoints*

Description

Calculating sample size when given power or power when given sample size for count endpoints.

Usage

```
getN_Count_Super(
  delta,
  lambda0,
  t,
  k = 0,
  alpha = 0.025,
  beta = NA,
  N = NA,
  r = 1
)

getN_Count_Noninf(
  delta,
  lambda0,
  t,
  k = 0,
  cut,
  alpha = 0.025,
  beta = NA,
  N = NA,
  r = 1,
  direct = 1
)

getN_Count_Equi(
  delta,
  lambda0,
  t,
  k = 0,
  cut,
  alpha = 0.025,
  beta = NA,
  N = NA,
  r = 1,
  maxN = 1e+06
)
```

Arguments

delta	log(RR) between treatment and control groups.
lambda0	Baseline hazard of control group.

t	Average exposure time.
k	The over-dispersion parameter for negative binomial distribution, which is 0 for poisson distribution. The default value is 0.
alpha	One-sided type I error rate. The default value is 0.025.
beta	Type II error rate. When beta is NA and N is not NA, the power will be returned.
N	Sample size. When N is NA and beta is not NA, the sample size will be returned.
r	Ratio of the sample sizes of the treatment group to the control group. The default value is 1.
cut	A positive value for non-inferiority or equivalence margin. For example, if the non-inferiority margin for RR is 0.6, then cut = -log(0.6). If the non-inferiority margin for RR is 1.3, then cut = log(1.3).
direct	direct = 1 indicates that a larger RR is preferable, while direct = -1 indicates that a smaller RR is preferable.
maxN	Maximum possible sample size(N) in equivalence design. Default value is 1e6.

Details

Taking the larger RR is preferable as an example. Sample size calculation is based on the following Z test, with the success criterion:

in superiority design:

$$Z = \frac{\hat{\delta}}{\sqrt{\frac{\hat{\sigma}_0^2}{N/(r+1)} + \frac{\hat{\sigma}_1^2}{Nr/(r+1)}}} \Phi^{-1}(1-\alpha)$$

in non-inferiority design:

$$Z = \frac{\hat{\delta} + \Delta}{\sqrt{\frac{\hat{\sigma}_0^2}{N/(r+1)} + \frac{\hat{\sigma}_1^2}{Nr/(r+1)}}} \Phi^{-1}(1-\alpha)$$

in equivalence design:

$$Z_u = \frac{\hat{\delta} + \Delta}{\sqrt{\frac{\hat{\sigma}_0^2}{N/(r+1)} + \frac{\hat{\sigma}_1^2}{Nr/(r+1)}}} \Phi^{-1}(1-\alpha) \text{ and } Z_l = \frac{\hat{\delta} - \Delta}{\sqrt{\frac{\hat{\sigma}_0^2}{N/(r+1)} + \frac{\hat{\sigma}_1^2}{Nr/(r+1)}}} < \Phi^{-1}(\alpha)$$

Where $\hat{\delta} = log(\hat{RR})$ between treatment and control groups, $\hat{\sigma}_0^2 = \frac{1}{\hat{\lambda}_0 t} + \hat{k}, \sigma_1^2 = \frac{1}{e^{\hat{\delta}} \hat{\lambda}_0 t} + \hat{k}$, and Δ is the non-inferiority or equivalence margin (cut).

Value

A data frame containing input parameters and returned sample size or power.

Examples

```
(v <- getN_Count_Super(
  delta = log(1.2),
  lambda0 = 0.5, t = 5, k = 0, alpha = 0.025, beta = 0.2, N = NA, r = 1
))
getN_Count_Super(
  delta = log(1.2),
  lambda0 = 0.5, t = 5, k = 0, alpha = 0.025, beta = NA, N = v$N, r = 1
```

```
)

(v <- getN_Count_Noninf(
  delta = log(1.1),
  lambda0 = 0.1, t = 5, k = 1, cut = log(1.4),
  alpha = 0.025, beta = 0.2, N = NA, r = 1, direct = -1
))
getN_Count_Noninf(
  delta = log(1.1),
  lambda0 = 0.1, t = 5, k = 1, cut = log(1.4),
  alpha = 0.025, beta = NA, N = v$N, r = 1, direct = -1
)
```

`getN_Count_JM1` *Regional sample size allocation using Japan's Method 1 for count endpoints*

Description

Based on Japan's Method 1, given the global sample size and marginal probability (power) of efficacy consistency between target region and globally, calculate the required sample size allocated to the target region, in clinical trials using superiority, non-inferiority, and equivalence designs with count endpoints.

Usage

```
getN_Count_Super_JM1(
  delta_a,
  delta_j,
  lambda0_a,
  lambda0_j,
  t,
  k = 0,
  pi = 0.5,
  alpha = NA,
  beta = NA,
  beta1 = 0.2,
  N = NA,
  r = 1
)

getN_Count_Noninf_JM1(
  delta_a,
  delta_j,
  lambda0_a,
  lambda0_j,
  t,
  k = 0,
  pi = 0.5,
  cut,
  alpha = NA,
  beta = NA,
```

```
  beta1 = 0.2,
  N = NA,
  r = 1,
  direct = 1
)

getN_Count_Equi_JM1(
  delta_a,
  delta_j,
  lambda0_a,
  lambda0_j,
  t,
  k = 0,
  pi = 0.5,
  cut,
  alpha = NA,
  beta = NA,
  beta1 = 0.2,
  N = NA,
  r = 1,
  maxN = 1e+06
)
```

Arguments

delta_a	log(RR) between treatment and control groups globally.
delta_j	log(RR) between treatment and control groups for target region.
lambda0_a	Baseline hazard of control group globally.
lambda0_j	Baseline hazard of control group for target region.
t	Average exposure time.
k	The over-dispersion parameter for negative binomial distribution, which is 0 for poisson distribution. The default value is 0.
pi	Proportion of global efficacy to retain. The default value is 0.5, which means retaining half of the efficacy.
alpha	One-sided type I error rate for global success, which is used to calculate global sample size only when N is NA. The default value is 0.025.
beta	Type II error rate for global success, which is used to calculate global sample size only when N is NA.
beta1	Type II error rate for efficacy consistency between target region and globally. The default value is 0.2.
N	Global sample size. When N is NA and alpha and beta are not NAs, N will be calculated automatically.
r	Ratio of the sample sizes of the treatment group to the control group. The default value is 1.
cut	A positive value for non-inferiority or equivalence margin. For example, if the non-inferiority margin for RR is 0.6, then cut = -log(0.6). If the non-inferiority margin for RR is 1.3, then cut = log(1.3).
direct	direct = 1 indicates that a larger RR is preferable, while direct = -1 indicates that a smaller RR is preferable.
maxN	Maximum possible sample size (N) in equivalence design. Default value is 1e6.

Details

The global success criterion and the efficacy consistency criterion between target region and globally could be found in `getPwr_Count_Super_JM1`.

Value

A data frame where `f` is required proportion of sample size allocated to the target region, and `Nj` is required sample size for the target region, calculated as `Nj = N * f`.

References

1. Quan H, Li M, Chen J, et al. Assessment of Consistency of Treatment Effects in Multiregional Clinical Trials. Drug Information J. 2010;44(5):617-632. doi:10.1177/009286151004400509

2. Liao JJZ, Yu Z, Li Y. Sample size allocation in multiregional equivalence studies. Pharm Stat. 2018;17(5):570-577. doi:10.1002/pst.1871

See Also

`getPwr_Count_Super_JM1`, `getN_Count_Super`.

Examples

```
getN_Count_Super_JM1(
  delta_a = log(1.4),
  delta_j = log(1.3),
  lambda0_a = 0.1, lambda0_j = 0.1, t = 5, k = 0, pi = 0.5, beta1 = 0.2,
  N = 300, r = 1
)

getN_Count_Noninf_JM1(
  delta_a = log(1.0),
  delta_j = log(1.1),
  lambda0_a = 0.1, lambda0_j = 0.1, t = 5, k = 0, pi = 0.5, cut = log(1.3),
  alpha = 0.025, beta = 0.2, beta1 = 0.2, N = NA, r = 1, direct = -1
)
```

---

getN_Surv *Sample size and power for survival endpoints*

Description

Calculating sample size when given power or power when given sample size for survival endpoints.

Usage

```
getN_Surv_Super(delta, alpha = 0.025, beta = NA, N = NA, r = 1, criterion = 1)

getN_Surv_Noninf(
  delta,
  cut,
  alpha = 0.025,
  beta = NA,
```

```
  N = NA,
  r = 1,
  criterion = 1,
  direct = 1
)

getN_Surv_Equi(
  delta,
  cut,
  alpha = 0.025,
  beta = NA,
  N = NA,
  r = 1,
  criterion = 1,
  maxN = 1e+06
)
```

Arguments

delta	log(HR) between treatment and control groups.
alpha	One-sided type I error rate. The default value is 0.025.
beta	Type II error rate. When beta is NA and N is not NA, the power will be returned.
N	Sample size. When N is NA and beta is not NA, the sample size will be returned.
r	Ratio of the sample sizes of the treatment group to the control group. The default value is 1.
criterion	If criterion = 1, the success criterion defined on the log(HR) scale will be used. If criterion = 2, the success criterion defined on the HR scale will be used. See details for more information.
cut	A positive value for non-inferiority or equivalence margin. For example, if the non-inferiority margin for HR is 0.6, then cut = -log(0.6). If the non-inferiority margin for HR is 1.3, then cut = log(1.3).
direct	direct = 1 indicates that a larger HR is preferable, while direct = -1 indicates that a smaller HR is preferable.
maxN	Maximum possible sample size(N) in equivalence design. Default value is 1e6.

Details

Taking the larger HR is preferable as an example. Sample size calculation is based on the following Z test, with the success criterion:

criterion = 1 in superiority design:

$$Z = \frac{\hat{\delta}}{\sqrt{\frac{1}{N/(r+1)} + \frac{1}{Nr/(r+1)}}} > \Phi^{-1}(1-\alpha)$$

criterion = 2 in superiority design:

$$Z = \frac{1 - e^{\hat{\delta}}}{e^{\hat{\delta}}\sqrt{\frac{1}{N/(r+1)} + \frac{1}{Nr/(r+1)}}} > \Phi^{-1}(\alpha)$$

`criterion` = 1 in non-inferiority design:

$$Z = \frac{\hat{\delta} + \Delta}{\sqrt{\frac{1}{N/(r+1)} + \frac{1}{Nr/(r+1)}}} > \Phi^{-1}(1-\alpha)$$

`criterion` = 2 in non-inferiority design:

$$Z = \frac{\frac{1}{e^{\Delta}} - e^{\hat{\delta}}}{e^{\hat{\delta}}\sqrt{\frac{1}{N/(r+1)} + \frac{1}{Nr/(r+1)}}} > \Phi^{-1}(\alpha)$$

`criterion` = 1 in equivalence design:

$$Z_u = \frac{\hat{\delta} + \Delta}{\sqrt{\frac{1}{N/(r+1)} + \frac{1}{Nr/(r+1)}}} > \Phi^{-1}(1-\alpha) \text{ and } Z_l = \frac{\hat{\delta} - \Delta}{\sqrt{\frac{1}{N/(r+1)} + \frac{1}{Nr/(r+1)}}} > \Phi^{-1}(\alpha)$$

`criterion` = 2 in equivalence design:

$$Z_l = \frac{\frac{1}{e^{\Delta}} - e^{\hat{\delta}}}{e^{\hat{\delta}}\sqrt{\frac{1}{N/(r+1)} + \frac{1}{Nr/(r+1)}}} > \Phi^{-1}(\alpha) \text{ and } Z_u = \frac{e^{\Delta} - e^{\hat{\delta}}}{e^{\hat{\delta}}\sqrt{\frac{1}{N/(r+1)} + \frac{1}{Nr/(r+1)}}} > \Phi^{-1}(1-\alpha)$$

Where $\hat{\delta} = log(\hat{HR})$ between treatment and control groups, and Δ is the non-inferiority or equivalence margin (`cut`).

For `criterion` = 2, by delta method, $e^{\hat{\delta}}$ approximately follows a distribution of $N(e^{\delta}, (e^{\delta}\sqrt{\frac{1}{N/(r+1)} + \frac{1}{Nr/(r+1)}})^2)$

Value

A data frame containing input parameters and returned sample size or power.

Examples

```
(v <- getN_Surv_Super(
  delta = log(1.2),
  alpha = 0.025, beta = 0.2, N = NA, r = 1, criterion = 1
))
getN_Surv_Super(
  delta = log(1.2),
  alpha = 0.025, beta = NA, N = v$N, r = 1, criterion = 1
)

(v <- getN_Surv_Noninf(
  delta = log(1.1),
  cut = log(1.3),
  alpha = 0.025, beta = 0.2, N = NA, r = 1, criterion = 2, direct = -1
))
getN_Surv_Noninf(
  delta = log(1.1),
  cut = log(1.3),
  alpha = 0.025, beta = NA, N = v$N, r = 1, criterion = 2, direct = -1
)
```

getN_Surv_JM1 *Regional sample size allocation using Japan's Method 1 for survival endpoints*

Description

Based on Japan's Method 1, given the global sample size and marginal probability (power) of efficacy consistency between target region and globally, calculate the required sample size allocated to the target region, in clinical trials using superiority, non-inferiority, and equivalence designs with survival endpoints.

Usage

```
getN_Surv_Super_JM1(
  delta_a,
  delta_j,
  pi = 0.5,
  alpha = NA,
  beta = NA,
  beta1 = 0.2,
  N = NA,
  r = 1,
  criterion = 1
)

getN_Surv_Noninf_JM1(
  delta_a,
  delta_j,
  pi = 0.5,
  cut,
  alpha = NA,
  beta = NA,
  beta1 = 0.2,
  N = NA,
  r = 1,
  criterion = 1,
  direct = 1
)

getN_Surv_Equi_JM1(
  delta_a,
  delta_j,
  pi = 0.5,
  cut,
  alpha = NA,
  beta = NA,
  beta1 = 0.2,
  N = NA,
  r = 1,
  criterion = 1,
  maxN = 1e+06
```

)

Arguments

delta_a	log(HR) between treatment and control groups globally.
delta_j	log(HR) between treatment and control groups in target region.
pi	Proportion of global efficacy to retain. The default value is 0.5, which means retaining half of the efficacy.
alpha	One-sided type I error rate for global success, which is used to calculate global sample size only when N is NA. The default value is 0.025.
beta	Type II error rate for global success, which is used to calculate global sample size only when N is NA.
beta1	Type II error rate for efficacy consistency between target region and globally. The default value is 0.2.
N	Global sample size. When N is NA and alpha and beta are not NAs, N will be calculated automatically.
r	Ratio of the sample sizes of the treatment group to the control group. The default value is 1.
criterion	If criterion = 1, the consistency criterion defined on the log(HR) scale will be used. If criterion = 2, the consistency criterion defined on the HR scale will be used. See details for more information.
cut	A positive value for non-inferiority or equivalence margin. For example, if the non-inferiority margin for HR is 0.6, then cut = -log(0.6). If the non-inferiority margin for HR is 1.3, then cut = log(1.3).
direct	direct = 1 indicates that a larger HR is preferable, while direct = -1 indicates that a smaller HR is preferable.
maxN	Maximum possible sample size (N) in equivalence design. Default value is 1e6.

Details

The global success criterion and the efficacy consistency criterion between target region and globally could be found in getPwr_Surv_Super_JM1.

Value

A data frame where f is required proportion of sample size allocated to the target region, and Nj is required sample size for the target region, calculated as Nj = N * f.

References

1. Quan H, Li M, Chen J, et al. Assessment of Consistency of Treatment Effects in Multiregional Clinical Trials. Drug Information J. 2010;44(5):617-632. doi:10.1177/009286151004400509

2. Liao JJZ, Yu Z, Li Y. Sample size allocation in multiregional equivalence studies. Pharm Stat. 2018;17(5):570-577. doi:10.1002/pst.1871

See Also

getPwr_Surv_Super_JM1, getN_Surv_Super.

Examples

```
getN_Surv_Super_JM1(
  delta_a = log(1.4),
  delta_j = log(1.3),
  pi = 0.5, beta1 = 0.2, N = 200, r = 1, criterion = 1
)

getN_Surv_Noninf_JM1(
  delta_a = log(1.0),
  delta_j = log(1.1),
  pi = 0.5, cut = log(1.4),
  alpha = 0.025, beta = 0.2, beta1 = 0.2, N = NA, r = 1, criterion = 2,
  direct = -1
)
```

---

getPwr_Bin_JM1 *Power of mRCT using Japan's Method 1 for binary endpoints*

Description

Based on Japan's Method 1, given the global and target region sample sizes, calculate and simulate the marginal probabilities, conditional probabilities, and joint probabilities of global success and efficacy consistency between target region and globally, in clinical trials using superiority, non-inferiority, and equivalence designs with binary endpoints.

Usage

```
getPwr_Bin_Super_JM1(
  p1_j,
  p0_j,
  p1_nj = NA,
  p0_nj = NA,
  p1_a = NA,
  p0_a = NA,
  f,
  pi = 0.5,
  alpha = 0.025,
  beta = NA,
  N = NA,
  r = 1,
  scale = "RD",
  sim = FALSE,
  nsim = 1000,
  seed = 0,
  numcore = 4
)

getPwr_Bin_Noninf_JM1(
  p1_j,
  p0_j,
  p1_nj = NA,
```

```
  p0_nj = NA,
  p1_a = NA,
  p0_a = NA,
  f,
  pi = 0.5,
  cut,
  alpha = 0.025,
  beta = NA,
  N = NA,
  r = 1,
  scale = "RD",
  direct = 1,
  sim = FALSE,
  nsim = 1000,
  seed = 0,
  numcore = 4
)

getPwr_Bin_Equi_JM1(
  p1_j,
  p0_j,
  p1_nj = NA,
  p0_nj = NA,
  p1_a = NA,
  p0_a = NA,
  f,
  pi = 0.5,
  cut,
  alpha,
  beta = NA,
  N = NA,
  r = 1,
  scale = "RD",
  sim = FALSE,
  nsim = 1000,
  seed = 0,
  numcore = 4
)
```

Arguments

p1_j	Rate of treatment group in target region.
p0_j	Rate of control group in target region.
p1_nj	Rate of treatment group in other regions. When p1_nj is not NA, p1_a will be calculated automatically.
p0_nj	Rate of control group in other regions. When p0_nj is not NA, p0_a will be calculated automatically.
p1_a	Rate of treatment group globally.
p0_a	Rate of the control group globally.
f	Proportion of sample size allocated to target region.

pi	Proportion of global efficacy to retain. The default value is 0.5, which means retaining half of the efficacy.
alpha	One-sided type I error rate for global success. The default value is 0.025.
beta	Type II error rate for global success, which is used to calculate global sample size only when N is NA.
N	Global sample size. When N is NA and alpha and beta are not NA, N will be calculated automatically.
r	Ratio of the sample sizes of the treatment group to the control group. The default value is 1.
scale	Optional values are "RD" for rate difference, "RR" for relative risk, and "OR" for odds ratio. Default value is "RD".
sim	Logical value. When set to FALSE, theoretical calculation is performed. When set to TRUE, simulation is used, which is more time-consuming.
nsim	Number of simulations.
seed	Random seed for simulation.
numcore	Number of CPU cores to use during simulation.
cut	A positive value for non-inferiority or equivalence margin. For RD, the margin is on the original scale. For RR and OR, the margin is on the log scale. For example, if the non-inferiority margins for RD, RR, OR are 0.2, 0.6, and 1.3, then the cut = 0.2, cut = -log(0.6), and cut = log(1.3), respectively.
direct	If direct = 1, larger values of RD/RR/OR are preferable. If direct = -1, smaller values of RD/RR/OR are preferable.

Details

Taking the larger RD/RR/OR is preferable as an example. The global success criterion and the efficacy consistency criterion between target region and globally

in superiority design:

$$Z_a = \frac{\hat{\delta}_a}{\sqrt{Var(\hat{\delta}_a)}} > \Phi^{-1}(1-\alpha)$$

$$\hat{\delta}_j - \pi\hat{\delta}_a > 0$$

in non-inferiority design:

$$Z_a = \frac{\hat{\delta}_a + \Delta}{\sqrt{Var(\hat{\delta}_a)}} > \Phi^{-1}(1-\alpha)$$

$$\hat{\delta}_j - \hat{\delta}_a + \pi\Delta > 0$$

in equivalence design:

$$Z_{a_u} = \frac{\hat{\delta}_a + \Delta}{\sqrt{Var(\hat{\delta}_a)}} > \Phi^{-1}(1-\alpha) \text{ and } Z_{a_l} = \frac{\hat{\delta}_a - \Delta}{\sqrt{Var(\hat{\delta}_a)}} < \Phi^{-1}(\alpha)$$

$$\hat{\delta}_j - \hat{\delta}_a + \pi\Delta > 0 \text{ and } \hat{\delta}_j - \hat{\delta}_a - \pi\Delta < 0$$

Where $\hat{\delta} = \hat{p}_1 - \hat{p}_0$ for RD, $\hat{\delta} = log(\frac{\hat{p}_1}{\hat{p}_0})$ for RR, and $\hat{\delta} = log(\frac{\hat{p}_1/(1-\hat{p}_1)}{\hat{p}_0/(1-\hat{p}_0)})$ for OR. Δ is the non-inferiority or equivalence margin (cut).

Value

A data frame containing input parameters and returned power.

pwr1 The marginal probability of global success.

pwr2 The marginal probability that the target region efficacy is consistent with the global efficacy.

pwr3 The conditional probability that the target region efficacy is consistent with the global efficacy given global success.

pwr4 The joint probability of global success and the target region efficacy being consistent with the global efficacy.

References

1. Quan H, Li M, Chen J, et al. Assessment of Consistency of Treatment Effects in Multiregional Clinical Trials. Drug Information J. 2010;44(5):617-632. doi:10.1177/009286151004400509

2. Liao JJZ, Yu Z, Li Y. Sample size allocation in multiregional equivalence studies. Pharm Stat. 2018;17(5):570-577. doi:10.1002/pst.1871

Examples

```
getPwr_Bin_Super_JM1(
  p1_j = 0.7, p0_j = 0.5, p1_a = 0.75, p0_a = 0.5, f = seq(0.1, 0.9, 0.1),
  pi = 0.5, alpha = 0.025, beta = NA, N = 200, r = 1, scale = "RD", sim = FALSE
)

# p1_a and p0_a will be calculated based on p1_j and p1_nj, p0_j and p0_nj, respectively.
# Global sample size will be calculated based on beta.
getPwr_Bin_Noninf_JM1(
  p1_j = 0.6, p0_j = 0.5, p1_nj = 0.5, p0_nj = 0.5, f = seq(0.1, 0.9, 0.1),
  pi = 0.5, cut = log(1.4),
  alpha = 0.025, beta = 0.2, N = NA, r = 1, scale = "RR", direct = -1,
  sim = FALSE
)
```

---

getPwr_Bin_JM2 *Power of mRCT using Japan's Method 2 for binary endpoints*

Description

Based on Japan's Method 2, given the global and target region sample sizes, calculate and simulate the marginal probabilities, conditional probabilities, and joint probabilities of global success and efficacy consistency between target region and globally, in clinical trials using superiority, non-inferiority, and equivalence designs with binary endpoints.

Usage

```
getPwr_Bin_Super_JM2(
  p1_i,
  p0_i,
  fi,
  alpha = 0.025,
  beta = NA,
```

```
  N = NA,
  r = 1,
  scale = "RD",
  sim = FALSE,
  nsim = 1000,
  seed = 0
)

getPwr_Bin_Noninf_JM2(
  p1_i,
  p0_i,
  fi,
  cut,
  alpha = 0.025,
  beta = NA,
  N = NA,
  r = 1,
  scale = "RD",
  direct = 1,
  sim = FALSE,
  nsim = 1000,
  seed = 0
)

getPwr_Bin_Equi_JM2(
  p1_i,
  p0_i,
  fi,
  cut,
  alpha = 0.025,
  beta = NA,
  N = NA,
  r = 1,
  scale = "RD",
  sim = FALSE,
  nsim = 1000,
  seed = 0
)
```

Arguments

p1_i	A vector. Rate of treatment group in each region.
p0_i	A vector. Rate of control group in each region.
fi	A vector. Proportion of sample size allocated to each region.
alpha	One-sided type I error rate for global success. The default value is 0.025.
beta	Type II error rate for global success, which is used to calculate global sample size only when N is NA.
N	Global sample size. Global sample size. When N is NA and beta is not NA, N will be calculated automatically.
r	Ratio of the sample sizes of the treatment group to the control group. The default value is 1.

scale	Optional values are "RD" for rate difference, "RR" for relative risk, and "OR" for odds ratio. Default value is "RD".
sim	Logical value. When set to FALSE, theoretical calculation is performed. When set to TRUE, simulation is used, which is more time-consuming.
nsim	Number of simulations.
seed	Random seed for simulation.
cut	A positive value for non-inferiority or equivalence margin. For RD, the margin is on the original scale. For RR and OR, the margin is on the log scale. For example, if the non-inferiority margins for RD, RR, and OR are 0.2, 0.6, and 1.3, then the cut = 0.2, cut = -log(0.6), and cut = log(1.3), respectively.
direct	If direct = 1, larger values of RD/RR/OR are preferable. If direct = -1, smaller values of RD/RR/OR are preferable.

Details

Taking the larger RD/RR/OR is preferable as an example. The global success criterion and the efficacy consistency criterion between target region and globally

in superiority design:

$$Z_a = \frac{\hat{\delta}_a}{\sqrt{Var(\hat{\delta}_a)}} > \Phi^{-1}(1-\alpha)$$

$$\hat{\delta}_i > 0 \text{ for i = 1, 2, .., m}$$

in non-inferiority design:

$$Z_a = \frac{\hat{\delta}_a + \Delta}{\sqrt{Var(\hat{\delta}_a)}} > \Phi^{-1}(1-\alpha)$$

$$\hat{\delta}_i + \Delta > 0 \text{ for i = 1, 2, .., m}$$

in equivalence design:

$$Z_{a_u} = \frac{\hat{\delta}_a + \Delta}{\sqrt{Var(\hat{\delta}_a)}} > \Phi^{-1}(1-\alpha) \text{ and } Z_{a_l} = \frac{\hat{\delta}_a - \Delta}{\sqrt{Var(\hat{\delta}_a)}} < \Phi^{-1}(\alpha)$$

$$\hat{\delta}_i + \Delta > 0 \text{ and } \hat{\delta}_i - \Delta < 0 \text{ for i = 1, 2, .., m}$$

Where $\hat{\delta} = \hat{p}_1 - \hat{p}_0$ for RD, $\hat{\delta} = log(\frac{\hat{p}_1}{\hat{p}_0})$ for RR, and $\hat{\delta} = log(\frac{\hat{p}_1/(1-\hat{p}_1)}{\hat{p}_0/(1-\hat{p}_0)})$ for OR. Δ is the non-inferiority or equivalence margin (cut).

Value

A list where:

- overall
  - pwr1 The marginal probability of global success.
  - pwr2 The marginal probability that all region's efficacy is consistent with the global efficacy.
  - pwr3 The conditional probability that all region's efficacy is consistent with the global efficacy given global success.

  - pwr4 The joint probability of global success and all region's efficacy being consistent with the global efficacy.

- pwr_margin The marginal probability that the ith region efficacy is consistent with the global efficacy.
- pwr_condition The conditional probability that the ith region efficacy is consistent with the global efficacy given global success.
- pwr_joint The joint probability of global success and the ith region efficacy being consistent with the global efficacy.

References

1. Quan H, Li M, Chen J, et al. Assessment of Consistency of Treatment Effects in Multiregional Clinical Trials. Drug Information J. 2010;44(5):617-632. doi:10.1177/009286151004400509

2. Liao JJZ, Yu Z, Li Y. Sample size allocation in multiregional equivalence studies. Pharm Stat. 2018;17(5):570-577. doi:10.1002/pst.1871

Examples

```
f_set <- seq(0.1, 0.9, 0.1)
map_dfr(
  .x = 1:length(f_set),
  .f = function(i) {
    f <- f_set[i]
    res <- getPwr_Bin_Super_JM2(
      p1_i = c(0.7, 0.75),
      p0_i = c(0.5, 0.5),
      fi = c(f, 1 - f),
      alpha = 0.025, beta = NA, N = 100, r = 1, scale = "RD", sim = FALSE
    )$overall
    res$f <- f
    res
  }
)

# Global rates of treatment and control groups will be calculated based on p1_i, p0_i, and fi.
# Global sample size will be calculated based on beta.
f_set <- seq(0.1, 0.9, 0.1)
map_dfr(
  .x = 1:length(f_set),
  .f = function(i) {
    f <- f_set[i]
    res <- getPwr_Bin_Noninf_JM2(
      p1_i = c(0.6, 0.5),
      p0_i = c(0.5, 0.5),
      fi = c(f, 1 - f),
      cut = log(1.4),
      alpha = 0.025, beta = 0.2, N = NA, r = 1, scale = "RR", direct = -1,
      sim = FALSE
    )$overall
    res$f <- f
    res
  }
)
```

getPwr_Con_JM1 *Power of mRCT using Japan's Method 1 for continuous endpoints*

Description

Based on Japan's Method 1, given the global and target region sample sizes, calculate and simulate the marginal probabilities, conditional probabilities, and joint probabilities of global success and efficacy consistency between target region and globally, in clinical trials using superiority, non-inferiority, and equivalence designs with continuous endpoints.

Usage

```
getPwr_Con_Super_JM1(
  delta_j,
  delta_nj = NA,
  delta_a = NA,
  sigma,
  f,
  pi = 0.5,
  alpha = 0.025,
  beta = NA,
  N = NA,
  r = 1,
  sim = FALSE,
  nsim = 1000,
  seed = 0,
  numcore = 4
)

getPwr_Con_Noninf_JM1(
  delta_j,
  delta_nj = NA,
  delta_a = NA,
  sigma,
  f,
  pi = 0.5,
  cut,
  alpha = 0.025,
  beta = NA,
  N = NA,
  r = 1,
  direct = 1,
  sim = FALSE,
  nsim = 1000,
  seed = 0,
  numcore = 4
)

getPwr_Con_Equi_JM1(
  delta_j,
  delta_nj = NA,
```

```
  delta_a = NA,
  sigma,
  f,
  pi = 0.5,
  cut,
  alpha = 0.025,
  beta = NA,
  N = NA,
  r = 1,
  sim = FALSE,
  nsim = 1000,
  seed = 0,
  numcore = 4
)
```

Arguments

delta_j	Mean difference between treatment and control groups in target region.
delta_nj	Mean difference between treatment and control groups in other regions. When delta_nj is not NA, delta_a will be calculated automatically.
delta_a	Mean difference between treatment and control groups globally.
sigma	Common standard deviation.
f	Proportion of sample size allocated to target region.
pi	Proportion of global efficacy to retain. The default value is 0.5, which means retaining half of the efficacy.
alpha	One-sided type I error rate for global success. The default value is 0.025.
beta	Type II error rate for global success, which is used to calculate global sample size only when N is NA.
N	Global sample size. When N is NA and beta is not NA, N will be calculated automatically.
r	Ratio of the sample sizes of the treatment group to the control group. The default value is 1.
sim	Logical value. When set to FALSE, theoretical calculation is performed. When set to TRUE, simulation is used, which is more time-consuming.
nsim	Number of simulations.
seed	Random seed for simulation.
numcore	Number of CPU cores to use during simulation.
cut	A positive value for non-inferiority or equivalence margin.
direct	direct = 1 indicates that a larger mean difference is preferable, while direct = -1 indicates that a smaller mean difference is preferable.

Details

Taking the larger mean difference is preferable as an example. The global success criterion and the efficacy consistency criterion between target region and globally

in superiority design:

$$Z_a = \frac{\hat{\delta}_a}{\sqrt{Var(\hat{\delta}_a)}} > \Phi^{-1}(1-\alpha)$$

$$\hat{\delta}_j - \pi\hat{\delta}_a > 0$$

in non-inferiority design:

$$Z_a = \frac{\hat{\delta}_a + \Delta}{\sqrt{Var(\hat{\delta}_a)}} > \Phi^{-1}(1-\alpha)$$

$$\hat{\delta}_j - \hat{\delta}_a + \pi\Delta > 0$$

in equivalence design:

$$Z_{a_u} = \frac{\hat{\delta}_a + \Delta}{\sqrt{Var(\hat{\delta}_a)}} > \Phi^{-1}(1-\alpha) \text{ and } Z_{a_l} = \frac{\hat{\delta}_a - \Delta}{\sqrt{Var(\hat{\delta}_a)}} < \Phi^{-1}(\alpha)$$

$$\hat{\delta}_j - \hat{\delta}_a + \pi\Delta > 0 \text{ and } \hat{\delta}_j - \hat{\delta}_a - \pi\Delta < 0$$

Where $\hat{\delta}$ is the mean difference between treatment and control groups, and Δ is the non-inferiority or equivalence margin.

Value

A data frame containing input parameters and returned power.

`pwr1` The marginal probability of global success.

`pwr2` The marginal probability that the target region efficacy is consistent with the global efficacy.

`pwr3` The conditional probability that the target region efficacy is consistent with the global efficacy given global success.

`pwr4` The joint probability of global success and the target region efficacy being consistent with the global efficacy.

References

1. Quan H, Li M, Chen J, et al. Assessment of Consistency of Treatment Effects in Multiregional Clinical Trials. Drug Information J. 2010;44(5):617-632. doi:10.1177/009286151004400509

2. Liao JJZ, Yu Z, Li Y. Sample size allocation in multiregional equivalence studies. Pharm Stat. 2018;17(5):570-577. doi:10.1002/pst.1871

Examples

```
getPwr_Con_Super_JM1(
  delta_j = 0.5, delta_a = 0.7, sigma = 1, f = seq(0.1, 0.9, 0.1),
  pi = 0.5, alpha = 0.025, beta = NA, N = 100, r = 1, sim = FALSE
)

# delta_a will be calculated based on delta_j and delta_nj.
# Global sample size will be calculated based on beta.
getPwr_Con_Noninf_JM1(
  delta_j = 0.2, delta_nj = 0.1, sigma = 1, f = seq(0.1, 0.9, 0.1),
  pi = 0.5, cut = 0.4, alpha = 0.025, beta = 0.2, N = NA, r = 1, direct = -1,
  sim = FALSE
)
```

getPwr_Con_JM2 *Power of mRCT using Japan's Method 2 for continuous endpoints*

Description

Based on Japan's Method 2, given the global and target region sample sizes, calculate and simulate the marginal probabilities, conditional probabilities, and joint probabilities of global success and efficacy consistency between target region and globally, in clinical trials using superiority, non-inferiority, and equivalence designs with continuous endpoints.

Usage

```
getPwr_Con_Super_JM2(
  delta_i,
  sigma,
  fi,
  alpha = 0.025,
  beta = NA,
  N = NA,
  r = 1,
  sim = FALSE,
  nsim = 1000,
  seed = 0
)

getPwr_Con_Noninf_JM2(
  delta_i,
  sigma,
  fi,
  cut,
  alpha = 0.025,
  beta = NA,
  N = NA,
  r = 1,
  direct = 1,
  sim = FALSE,
  nsim = 1000,
  seed = 0
)

getPwr_Con_Equi_JM2(
  delta_i,
  sigma,
  fi,
  cut,
  alpha = 0.025,
  beta = NA,
  N = NA,
  r = 1,
  sim = FALSE,
  nsim = 1000,
```

```
  seed = 0
)
```

Arguments

delta_i	A vector. Mean difference between treatment and control groups in each region.
sigma	Common standard deviation.
fi	A vector. Proportion of sample size allocated to each region.
alpha	One-sided type I error rate for global success. The default value is 0.025.
beta	Type II error rate for global success, which is used to calculate global sample size only when N is NA.
N	Global sample size. Global sample size. When N is NA and beta is not NA, N will be calculated automatically.
r	Ratio of the sample sizes of the treatment group to the control group. The default value is 1.
sim	Logical value. When set to FALSE, theoretical calculation is performed. When set to TRUE, simulation is used, which is more time-consuming.
nsim	Number of simulations.
seed	Random seed for simulation.
cut	A positive value for non-inferiority or equivalence margin.
direct	direct = 1 indicates that a larger mean difference is preferable, while direct = -1 indicates that a smaller mean difference is preferable.

Details

Taking the larger mean difference is preferable as an example. The global success criterion and the efficacy consistency criterion between target region and globally

in superiority design:

$$Z_a = \frac{\hat{\delta}_a}{\sqrt{Var(\hat{\delta}_a)}} > \Phi^{-1}(1-\alpha)$$

$$\hat{\delta}_i > 0 \text{ for i = 1, 2, .., m}$$

in non-inferiority design:

$$Z_a = \frac{\hat{\delta}_a + \Delta}{\sqrt{Var(\hat{\delta}_a)}} > \Phi^{-1}(1-\alpha)$$

$$\hat{\delta}_i + \Delta > 0 \text{ for i = 1, 2, .., m}$$

in equivalence design:

$$Z_{a_u} = \frac{\hat{\delta}_a + \Delta}{\sqrt{Var(\hat{\delta}_a)}} > \Phi^{-1}(1-\alpha) \text{ and } Z_{a_l} = \frac{\hat{\delta}_a - \Delta}{\sqrt{Var(\hat{\delta}_a)}} < \Phi^{-1}(\alpha)$$

$$\hat{\delta}_i + \Delta > 0 \text{ and } \hat{\delta}_i - \Delta < 0 \text{ for i = 1, 2, .., m}$$

Where $\hat{\delta}$ is the mean difference between treatment and control groups, and Δ is the non-inferiority or equivalence margin.

Value

A list where:

- overall
  - pwr1 The marginal probability of global success.
  - pwr2 The marginal probability that all region's efficacy is consistent with the global efficacy.
  - pwr3 The conditional probability that all region's efficacy is consistent with the global efficacy given global success.
  - pwr4 The joint probability of global success and all region's efficacy being consistent with the global efficacy.
- pwr_margin The marginal probability that the ith region efficacy is consistent with the global efficacy.
- pwr_condition The conditional probability that the ith region efficacy is consistent with the global efficacy given global success.
- pwr_joint The joint probability of global success and the ith region efficacy being consistent with the global efficacy.

References

1. Quan H, Li M, Chen J, et al. Assessment of Consistency of Treatment Effects in Multiregional Clinical Trials. Drug Information J. 2010;44(5):617-632. doi:10.1177/009286151004400509

2. Liao JJZ, Yu Z, Li Y. Sample size allocation in multiregional equivalence studies. Pharm Stat. 2018;17(5):570-577. doi:10.1002/pst.1871

Examples

```
f_set <- seq(0.1, 0.9, 0.1)
map_dfr(
  .x = 1:length(f_set),
  .f = function(i) {
    f <- f_set[i]
    res <- getPwr_Con_Super_JM2(
      delta_i = c(1, 0.8),
      sigma = 4, fi = c(f, 1 - f),
      alpha = 0.025, beta = NA, N = 200, r = 1, sim = FALSE
    )$overall
    res$f <- f
    res
  }
)

# Global mean difference will be calculated based on delta_i and fi.
# Global sample size will be calculated based on beta.
f_set <- seq(0.1, 0.9, 0.1)
map_dfr(
  .x = 1:length(f_set),
  .f = function(i) {
    f <- f_set[i]
    res <- getPwr_Con_Noninf_JM2(
      delta_i = c(1, 0),
      sigma = 4, fi = c(f, 1 - f),
      cut = 2, alpha = 0.025, beta = 0.2, N = NA, r = 1, direct = -1,
```

```
      sim = FALSE
    )$overall
    res$f <- f
    res
  }
)
```

---

getPwr_Count_JM1 *Power of mRCT using Japan's Method 1 for count endpoints*

Description

Based on Japan's Method 1, given the global and target region sample sizes, calculate and simulate the marginal probabilities, conditional probabilities, and joint probabilities of global success and efficacy consistency between target region and globally, in clinical trials using superiority, non-inferiority, and equivalence designs with count endpoints.

Usage

```
getPwr_Count_Super_JM1(
  delta_j,
  delta_nj = NA,
  delta_a = NA,
  lambda0_j,
  lambda0_nj = NA,
  lambda0_a = NA,
  t,
  k = 0,
  f,
  pi = 0.5,
  alpha = 0.025,
  beta = NA,
  N = NA,
  r = 1,
  sim = FALSE,
  nsim = 1000,
  seed = 0,
  numcore = 4
)

getPwr_Count_Noninf_JM1(
  delta_j,
  delta_nj = NA,
  delta_a = NA,
  lambda0_j,
  lambda0_nj = NA,
  lambda0_a = NA,
  t,
  k = 0,
  f,
  pi = 0.5,
```

```
  cut,
  alpha = 0.025,
  beta = NA,
  N = NA,
  r = 1,
  direct = 1,
  sim = FALSE,
  nsim = 1000,
  seed = 0,
  numcore = 4
)

getPwr_Count_Equi_JM1(
  delta_j,
  delta_nj = NA,
  delta_a = NA,
  lambda0_j,
  lambda0_nj = NA,
  lambda0_a = NA,
  t,
  k = 0,
  f,
  pi = 0.5,
  cut,
  alpha = 0.025,
  beta = NA,
  N = NA,
  r = 1,
  sim = FALSE,
  nsim = 1000,
  seed = 0,
  numcore = 4
)
```

Arguments

delta_j	log(RR) between treatment and control groups for target region.
delta_nj	log(RR) between treatment and control groups for other regions. When delta_nj is not NA, delta_a will be calculated automatically.
delta_a	log(RR) between treatment and control groups globally.
lambda0_j	Baseline hazard of control group for target region.
lambda0_nj	Baseline hazard of control group for other regions. When lambda0_nj is not NA, lambda0_a will be calculated automatically.
lambda0_a	Baseline hazard of control group globally.
t	Average exposure time.
k	The over-dispersion parameter for negative binomial distribution, which is 0 for poisson distribution.
f	Proportion of sample size allocated to target region.
pi	Proportion of global efficacy to retain. The default value is 0.5, which means retaining half of the efficacy.

alpha	One-sided type I error rate for global success. The default value is 0.025.
beta	Type II error rate for global success, which is used to calculate global sample size only when N is NA.
N	Global sample size. When N is NA and beta is not NA, N will be calculated automatically.
r	Ratio of the sample sizes of the treatment group to the control group. The default value is 1.
sim	Logical value. When set to FALSE, theoretical calculation is performed. When set to TRUE, simulation is used, which is more time-consuming.
nsim	Number of simulations.
seed	Random seed for simulation.
numcore	Number of CPU cores to use during simulation.
cut	A positive value for non-inferiority or equivalence margin. For example, if the non-inferiority margin for RR is 0.6, then cut = -log(0.6). If the non-inferiority margin for RR is 1.3, then cut = log(1.3).
direct	direct = 1 indicates that a larger RR is preferable, while direct = -1 indicates that a smaller RR is preferable.

Details

Taking the larger RR is preferable as an example. The global success criterion and the efficacy consistency criterion between target region and globally

in superiority design:

$$Z_a = \frac{\hat{\delta}_a}{\sqrt{Var(\hat{\delta}_a)}} > \Phi^{-1}(1-\alpha)$$

$$\hat{\delta}_j - \pi\hat{\delta}_a > 0$$

in non-inferiority design:

$$Z_a = \frac{\hat{\delta}_a + \Delta}{\sqrt{Var(\hat{\delta}_a)}} > \Phi^{-1}(1-\alpha)$$

$$\hat{\delta}_j - \hat{\delta}_a + \pi\Delta > 0$$

in equivalence design:

$$Z_{a_u} = \frac{\hat{\delta}_a + \Delta}{\sqrt{Var(\hat{\delta}_a)}} > \Phi^{-1}(1-\alpha) \text{ and } Z_{a_l} = \frac{\hat{\delta}_a - \Delta}{\sqrt{Var(\hat{\delta}_a)}} < \Phi^{-1}(\alpha)$$

$$\hat{\delta}_j - \hat{\delta}_a + \pi\Delta > 0 \text{ and } \hat{\delta}_j - \hat{\delta}_a - \pi\Delta < 0$$

Where $\hat{\delta} = log(\hat{RR})$ between treatment and control groups, and Δ is the non-inferiority or equivalence margin (cut).

Value

A data frame containing input parameters and returned power.

`pwr1` The marginal probability of global success.

`pwr2` The marginal probability that the target region efficacy is consistent with the global efficacy.

`pwr3` The conditional probability that the target region efficacy is consistent with the global efficacy given global success.

`pwr4` The joint probability of global success and the target region efficacy being consistent with the global efficacy.

References

1. Quan H, Li M, Chen J, et al. Assessment of Consistency of Treatment Effects in Multiregional Clinical Trials. Drug Information J. 2010;44(5):617-632. doi:10.1177/009286151004400509

2. Liao JJZ, Yu Z, Li Y. Sample size allocation in multiregional equivalence studies. Pharm Stat. 2018;17(5):570-577. doi:10.1002/pst.1871

Examples

```
getPwr_Count_Super_JM1(
  delta_j = log(1.2),
  delta_a = log(1.3),
  lambda0_j = 0.1, lambda0_a = 0.1, t = 5, k = 0, f = seq(0.1, 0.9, 0.1),
  pi = 0.5, alpha = 0.025, beta = NA, N = 300, r = 1, sim = FALSE
)

# delta_a will be calculated based on delta_j and delta_nj,
# and lambda0_a will be calculated based on lambda0_j and lambda0_nj.
# Global sample size will be calculated based on beta.
getPwr_Count_Noninf_JM1(
  delta_j = log(1.1),
  delta_nj = log(1.0),
  lambda0_j = 0.1, lambda0_nj = 0.1, t = 5, k = 0, f = seq(0.1, 0.9, 0.1),
  pi = 0.5, cut = log(1.3),
  alpha = 0.025, beta = 0.2, N = NA, r = 1, direct = -1, sim = FALSE
)
```

---

getPwr_Count_JM2 *Power of mRCT using Japan's Method 2 for count endpoints*

Description

Based on Japan's Method 2, given the global and target region sample sizes, calculate and simulate the marginal probabilities, conditional probabilities, and joint probabilities of global success and efficacy consistency between target region and globally, in clinical trials using superiority, non-inferiority, and equivalence designs with count endpoints.

Usage

```
getPwr_Count_Super_JM2(
  delta_i,
  lambda0_i,
  t,
  k = 0,
  fi,
  alpha = 0.025,
  beta = NA,
  N = NA,
  r = 1,
  sim = FALSE,
  nsim = 1000,
  seed = 0
)

getPwr_Count_Noninf_JM2(
  delta_i,
  lambda0_i,
  t,
  k = 0,
  fi,
  cut,
  alpha = 0.025,
  beta = NA,
  N = NA,
  r = 1,
  direct = 1,
  sim = FALSE,
  nsim = 1000,
  seed = 0
)

getPwr_Count_Equi_JM2(
  delta_i,
  lambda0_i,
  t,
  k = 0,
  fi,
  cut,
  alpha = 0.025,
  beta = NA,
  N = NA,
  r = 1,
  sim = FALSE,
  nsim = 1000,
  seed = 0
)
```

Arguments

delta_i	A vector. log(RR) between treatment and control groups for each region.

lambda0_i	A vector. Baseline hazard of control group for each region.
t	Average exposure time.
k	The over-dispersion parameter for negative binomial distribution, which is 0 for poisson distribution.
fi	A vector. Proportion of sample size allocated to each region.
alpha	One-sided type I error rate for global success. The default value is 0.025.
beta	Type II error rate for global success, which is used to calculate global sample size only when N is NA.
N	Global sample size. Global sample size. When N is NA and beta is not NA, N will be calculated automatically.
r	Ratio of the sample sizes of the treatment group to the control group. The default value is 1.
sim	Logical value. When set to FALSE, theoretical calculation is performed. When set to TRUE, simulation is used, which is more time-consuming.
nsim	Number of simulations.
seed	Random seed for simulation.
cut	A positive value for non-inferiority or equivalence margin. For example, if the non-inferiority margin for RR is 0.6, then cut = -log(0.6). If the non-inferiority margin for RR is 1.3, then cut = log(1.3).
direct	direct = 1 indicates that a larger RR is preferable, while direct = -1 indicates that a smaller RR is preferable.

Details

Taking the larger RR is preferable as an example. The global success criterion and the efficacy consistency criterion between target region and globally

in superiority design:

$$Z_a = \frac{\hat{\delta}_a}{\sqrt{Var(\hat{\delta}_a)}} > \Phi^{-1}(1-\alpha)$$

$$\hat{\delta}_i > 0 \text{ for i = 1, 2, .., m}$$

in non-inferiority design:

$$Z_a = \frac{\hat{\delta}_a + \Delta}{\sqrt{Var(\hat{\delta}_a)}} > \Phi^{-1}(1-\alpha)$$

$$\hat{\delta}_i + \Delta > 0 \text{ for i = 1, 2, .., m}$$

in equivalence design:

$$Z_{a_u} = \frac{\hat{\delta}_a + \Delta}{\sqrt{Var(\hat{\delta}_a)}} > \Phi^{-1}(1-\alpha) \text{ and } Z_{a_l} = \frac{\hat{\delta}_a - \Delta}{\sqrt{Var(\hat{\delta}_a)}} < \Phi^{-1}(\alpha)$$

$$\hat{\delta}_i + \Delta > 0 \text{ and } \hat{\delta}_i - \Delta < 0 \text{ for i = 1, 2, .., m}$$

Where $\hat{\delta} = log(\hat{RR})$ between treatment and control groups, and Δ is the non-inferiority or equivalence margin (cut).

Value

A list where:

- overall
  - pwr1 The marginal probability of global success.
  - pwr2 The marginal probability that all region's efficacy is consistent with the global efficacy.
  - pwr3 The conditional probability that all region's efficacy is consistent with the global efficacy given global success.
  - pwr4 The joint probability of global success and all region's efficacy being consistent with the global efficacy.
- pwr_margin The marginal probability that the ith region efficacy is consistent with the global efficacy.
- pwr_condition The conditional probability that the ith region efficacy is consistent with the global efficacy given global success.
- pwr_joint The joint probability of global success and the ith region efficacy being consistent with the global efficacy.

References

1. Quan H, Li M, Chen J, et al. Assessment of Consistency of Treatment Effects in Multiregional Clinical Trials. Drug Information J. 2010;44(5):617-632. doi:10.1177/009286151004400509

2. Liao JJZ, Yu Z, Li Y. Sample size allocation in multiregional equivalence studies. Pharm Stat. 2018;17(5):570-577. doi:10.1002/pst.1871

Examples

```
f_set <- seq(0.1, 0.9, 0.1)
map_dfr(
  .x = 1:length(f_set),
  .f = function(i) {
    f <- f_set[i]
    res <- getPwr_Count_Super_JM2(
      delta_i = c(
        log(1.2),
        log(1.4)
      ),
      lambda0_i = c(0.1, 0.1),
      t = 5, k = 0, fi = c(f, 1 - f),
      alpha = 0.025, beta = NA, N = 300, r = 1, sim = FALSE
    )$overall
    res$f <- f
    res
  }
)

# Global log(RR) will be calculated based on delta_i and fi,
# and global lambda0 will be calculated based on lambda0_i and fi
# Global sample size will be calculated based on beta.
f_set <- seq(0.1, 0.9, 0.1)
map_dfr(
  .x = 1:length(f_set),
  .f = function(i) {
```

```
    f <- f_set[i]
    res <- getPwr_Count_Noninf_JM2(
      delta_i = c(
        log(1.1),
        log(1.0)
      ),
      lambda0_i = c(0.1, 0.1),
      t = 5, k = 0, fi = c(f, 1 - f),
      cut = log(1.3),
      alpha = 0.025, beta = 0.2, N = NA, r = 1, direct = -1, sim = FALSE
    )$overall
    res$f <- f
    res
  }
)
```

`getPwr_Surv_JM1` *Power of mRCT using Japan's Method 1 for survival endpoints*

Description

Based on Japan's Method 1, given the global and target region sample sizes, calculate and simulate the marginal probabilities, conditional probabilities, and joint probabilities of global success and efficacy consistency between target region and global, in clinical trials using superiority, non-inferiority, and equivalence designs with survival endpoints.

Usage

```
getPwr_Surv_Super_JM1(
  delta_j,
  delta_nj = NA,
  delta_a = NA,
  f,
  pi = 0.5,
  alpha = 0.025,
  beta = NA,
  N = NA,
  r = 1,
  criterion = 1,
  sim = FALSE,
  nsim = 1000,
  seed = 0,
  numcore = 4
)

getPwr_Surv_Noninf_JM1(
  delta_j,
  delta_nj = NA,
  delta_a = NA,
  f,
  pi = 0.5,
  cut,
```

```
  alpha = 0.025,
  beta = NA,
  N = NA,
  r = 1,
  criterion = 1,
  direct = 1,
  sim = FALSE,
  nsim = 1000,
  seed = 0,
  numcore = 4
)

getPwr_Surv_Equi_JM1(
  delta_j,
  delta_nj = NA,
  delta_a = NA,
  f,
  pi = 0.5,
  cut,
  alpha = 0.025,
  beta = NA,
  N = NA,
  r = 1,
  criterion = 1,
  sim = FALSE,
  nsim = 1000,
  seed = 0,
  numcore = 4
)
```

Arguments

delta_j	log(HR) between treatment and control groups in target region.
delta_nj	log(HR) between treatment and control groups in other regions. When delta_nj is not NA, delta_a will be calculated automatically.
delta_a	log(HR) between treatment and control groups globally.
f	Proportion of sample size allocated to target region.
pi	Proportion of global efficacy to retain. The default value is 0.5, which means retaining half of the efficacy.
alpha	One-sided type I error rate for global success. The default value is 0.025.
beta	Type II error rate for global success, which is used to calculate global sample size only when N is NA.
N	Global sample size. When N is NA and beta is not NA, N will be calculated automatically.
r	Ratio of the sample sizes of the treatment group to the control group. The default value is 1.
criterion	If criterion = 1, the consistency criterion defined on the log(HR) scale will be used. If criterion = 2, the consistency criterion defined on the HR scale will be used. See details for more information.

sim	Logical value. When set to FALSE, theoretical calculation is performed. When set to TRUE, simulation is used, which is more time-consuming.
nsim	Number of simulations.
seed	Random seed for simulation.
numcore	Number of CPU cores to use during simulation.
cut	A positive value for non-inferiority or equivalence margin. For example, if the non-inferiority margin for HR is 0.6, then cut = -log(0.6). If the non-inferiority margin for HR is 1.3, then cut = log(1.3).
direct	direct = 1 indicates that a larger HR is preferable, while direct = -1 indicates that a smaller HR is preferable.

Details

Taking the larger HR is preferable as an example. The global success criterion and the efficacy consistency criterion between target region and globally

criterion = 1 in superiority design:

$$Z_a = \frac{\hat{\delta}_a}{\sqrt{Var(\hat{\delta}_a)}} > \Phi^{-1}(1-\alpha)$$

$$\hat{\delta}_j - \pi\hat{\delta}_a > 0$$

criterion = 2 in superiority design:

$$\text{uper limit of 95\% CI for } (1 - e^{\hat{\delta}_a}) < 0$$

$$1 - e^{\hat{\delta}_j} - \pi(1 - e^{\hat{\delta}_a}) < 0$$

criterion = 1 in non-inferiority design:

$$Z_a = \frac{\hat{\delta}_a + \Delta}{\sqrt{Var(\hat{\delta}_a)}} > \Phi^{-1}(1-\alpha)$$

$$\hat{\delta}_j - \hat{\delta}_a + \pi\Delta > 0$$

criterion = 2 in non-inferiority design:

$$\text{uper limit of 95\% CI for } (\frac{1}{e^{\Delta}} - e^{\hat{\delta}_a}) < 0$$

$$\frac{1}{e^{\Delta}} - e^{\hat{\delta}_j} - \pi(\frac{1}{e^{\Delta}} - e^{\hat{\delta}_a}) < 0$$

criterion = 1 in equivalence design:

$$Z_{a_u} = \frac{\hat{\delta}_a + \Delta}{\sqrt{Var(\hat{\delta}_a)}} > \Phi^{-1}(1-\alpha) \text{ and } Z_{a_l} = \frac{\hat{\delta}_a - \Delta}{\sqrt{Var(\hat{\delta}_a)}} < \Phi^{-1}(\alpha)$$

$$\hat{\delta}_j - \hat{\delta}_a + \pi\Delta > 0 \text{ and } \hat{\delta}_j - \hat{\delta}_a - \pi\Delta < 0$$

criterion = 2 in equivalence design:

$$\text{uper limit of 95\% CI for } (\frac{1}{e^{\Delta}} - e^{\hat{\delta}_a}) < 0 \text{ and lower limit of 95\% CI for } e^{\Delta} - e^{\hat{\delta}_a} > 0$$

$$\Delta - e^{\hat{\delta}_j} - \pi(\Delta - e^{\hat{\delta}_a}) < 0 \text{ and } \frac{1}{\Delta} - e^{\hat{\delta}_j} - \pi(\frac{1}{\Delta} - e^{\hat{\delta}_a}) > 0$$

Where $\hat{\delta} = log(\hat{HR})$ between treatment and control groups, and Δ is the non-inferiority or equivalence margin (`cut`).

For `criterion = 2`, by delta method, $e^{\hat{\delta}}$ approximately follows a distribution of $N(e^{\delta}, (e^{\delta}\sqrt{\frac{1}{N/(r+1)} + \frac{1}{Nr/(r+1)}})^2)$, used in theoretical calculation (`sim=FALSE`).

Value

A data frame containing input parameters and returned power.

`pwr1` The marginal probability of global success.

`pwr2` The marginal probability that the target region efficacy is consistent with the global efficacy.

`pwr3` The conditional probability that the target region efficacy is consistent with the global efficacy given global success.

`pwr4` The joint probability of global success and the target region efficacy being consistent with the global efficacy.

References

1. Quan H, Li M, Chen J, et al. Assessment of Consistency of Treatment Effects in Multiregional Clinical Trials. Drug Information J. 2010;44(5):617-632. doi:10.1177/009286151004400509

2. Liao JJZ, Yu Z, Li Y. Sample size allocation in multiregional equivalence studies. Pharm Stat. 2018;17(5):570-577. doi:10.1002/pst.1871

Examples

```
getPwr_Surv_Super_JM1(
  delta_j = log(1.3),
  delta_a = log(1.4),
  f = seq(0.1, 0.9, 0.1),
  pi = 0.5, alpha = 0.025, beta = NA, N = 200, r = 1, criterion = 1,
  sim = FALSE
)

# delta_a will be calculated based on delta_j and delta_nj.
# Global sample size will be calculated based on beta.
getPwr_Surv_Noninf_JM1(
  delta_j = log(1.1),
  delta_nj = log(1.0),
  f = seq(0.1, 0.9, 0.1),
  cut = log(1.3),
  pi = 0.5, alpha = 0.025, beta = 0.2, N = NA, r = 1, criterion = 2,
  direct = -1, sim = FALSE
)
```

getPwr_Surv_JM2 *Power of mRCT using Japan's Method 2 for survival endpoints*

Description

Based on Japan's Method 2, given the global and target region sample sizes, calculate and simulate the marginal probabilities, conditional probabilities, and joint probabilities of global success and efficacy consistency between target region and globally, in clinical trials using superiority, non-inferiority, and equivalence designs with survival endpoints.

Usage

```
getPwr_Surv_Super_JM2(
  delta_i,
  fi,
  alpha = 0.025,
  beta = NA,
  N = NA,
  r = 1,
  criterion = 1,
  sim = FALSE,
  nsim = 1000,
  seed = 0
)

getPwr_Surv_Noninf_JM2(
  delta_i,
  fi,
  cut,
  alpha = 0.025,
  beta = NA,
  N = NA,
  r = 1,
  criterion = 1,
  direct = 1,
  sim = FALSE,
  nsim = 1000,
  seed = 0
)

getPwr_Surv_Equi_JM2(
  delta_i,
  fi,
  cut,
  alpha = 0.025,
  beta = NA,
  N = NA,
  r = 1,
  criterion = 1,
  sim = FALSE,
  nsim = 1000,
```

```
  seed = 0
)
```

Arguments

delta_i	A vector. log(HR) between treatment and control groups for each region.
fi	A vector. Proportion of sample size allocated to each region.
alpha	One-sided type I error rate for global success. The default value is 0.025.
beta	Type II error rate for global success, which is used to calculate global sample size only when N is NA.
N	Global sample size. Global sample size. When N is NA and beta is not NA, N will be calculated automatically.
r	Ratio of the sample sizes of the treatment group to the control group. The default value is 1.
criterion	If criterion = 1, the consistency criterion defined on the log(HR) scale will be used. If criterion = 2, the consistency criterion defined on the HR scale will be used. See details for more information.
sim	Logical value. When set to FALSE, theoretical calculation is performed. When set to TRUE, simulation is used, which is more time-consuming.
nsim	Number of simulations.
seed	Random seed for simulation.
cut	A positive value for non-inferiority or equivalence margin. For example, if the non-inferiority margin for HR is 0.6, then cut = -log(0.6). If the non-inferiority margin for HR is 1.3, then cut = log(1.3).
direct	direct = 1 indicates that a larger HR is preferable, while direct = -1 indicates that a smaller HR is preferable.

Details

Taking the larger HR is preferable as an example.The global success criterion and the efficacy consistency criterion between target region and globally

criterion = 1 in superiority design:

$$Z_a = \frac{\hat{\delta}_a}{\sqrt{Var(\hat{\delta}_a)}} > \Phi^{-1}(1-\alpha)$$

$$\hat{\delta}_i > 0 \text{ for i = 1, 2, .., m}$$

criterion = 2 in superiority design:

$$\text{uper limit of 95\% CI for } (1 - e^{\hat{\delta}_a}) < 0$$

$$1 - e^{\hat{\delta}_i} < 0 \text{ for i = 1, 2, .., m}$$

criterion = 1 in non-inferiority design:

$$Z_a = \frac{\hat{\delta}_a + \Delta}{\sqrt{Var(\hat{\delta}_a)}} > \Phi^{-1}(1-\alpha)$$

$$\hat{\delta}_i + \Delta > 0 \text{ for i = 1, 2, .., m}$$

`criterion` = 2 in non-inferiority design:

$$\text{uper limit of 95\% CI for } (\frac{1}{e^{\Delta}} - e^{\hat{\delta}_a}) < 0$$

$$\frac{1}{e^{\Delta}} - e^{\hat{\delta}_i} < 0 \text{ for i = 1, 2, .., m}$$

`criterion` = 1 in equivalence design:

$$Z_{a_u} = \frac{\hat{\delta}_a + \Delta}{\sqrt{Var(\hat{\delta}_a)}} > \Phi^{-1}(1-\alpha) \text{ and } Z_{a_l} = \frac{\hat{\delta}_a - \Delta}{\sqrt{Var(\hat{\delta}_a)}} < \Phi^{-1}(\alpha)$$

$$\hat{\delta}_i + \Delta > 0 \text{ and } \hat{\delta}_i - \Delta < 0 \text{ for i = 1, 2, .., m}$$

`criterion` = 2 in equivalence design:

$$\text{uper limit of 95\% CI for } (\frac{1}{e^{\Delta}} - e^{\hat{\delta}_a}) < 0 \text{ and lower limit of 95\% CI for } e^{\Delta} - e^{\hat{\delta}_a} > 0$$

$$\frac{1}{e^{\Delta}} - e^{\hat{\delta}_i} < 0 \text{ and } e^{\Delta} - e^{\hat{\delta}_i} > 0 \text{ for i = 1, 2, .., m}$$

Where $\hat{\delta} = log(\hat{HR})$ between treatment and control groups, and Δ is the non-inferiority or equivalence margin (`cut`).

For `criterion` = 2, by delta method, $e^{\hat{\delta}}$ approximately follows a distribution of $N(e^{\delta}, (e^{\delta}\sqrt{\frac{1}{N/(r+1)} + \frac{1}{Nr/(r+1)}})^2)$, used in theoretical calculation (`sim=FALSE`).

Value

A list where:

- overall
  - `pwr1` The marginal probability of global success.
  - `pwr2` The marginal probability that all region's efficacy is consistent with the global efficacy.
  - `pwr3` The conditional probability that all region's efficacy is consistent with the global efficacy given global success.
  - `pwr4` The joint probability of global success and all region's efficacy being consistent with the global efficacy.
- `pwr_margin` The marginal probability that the ith region efficacy is consistent with the global efficacy.
- `pwr_condition` The conditional probability that the ith region efficacy is consistent with the global efficacy given global success.
- `pwr_joint` The joint probability of global success and the ith region efficacy being consistent with the global efficacy.

References

1. Quan H, Li M, Chen J, et al. Assessment of Consistency of Treatment Effects in Multiregional Clinical Trials. Drug Information J. 2010;44(5):617-632. doi:10.1177/009286151004400509

2. Liao JJZ, Yu Z, Li Y. Sample size allocation in multiregional equivalence studies. Pharm Stat. 2018;17(5):570-577. doi:10.1002/pst.1871

Examples

```
f_set <- seq(0.1, 0.9, 0.1)
map_dfr(
  .x = 1:length(f_set),
  .f = function(i) {
    f <- f_set[i]
    res <- getPwr_Surv_Super_JM2(
      delta_i = c(
        log(1.2),
        log(1.4)
      ),
      fi = c(f, 1 - f),
      alpha = 0.025, beta = NA, N = 300, r = 1, criterion = 1, sim = FALSE
    )$overall
    res$f <- f
    res
  }
)

f_set <- seq(0.1, 0.9, 0.1)
map_dfr(
  .x = 1:length(f_set),
  .f = function(i) {
    f <- f_set[i]
    res <- getPwr_Surv_Noninf_JM2(
      delta_i = c(
        log(1.1),
        log(1)
      ),
      fi = c(f, 1 - f),
      cut = log(1.3),
      alpha = 0.025, beta = 0.2, N = NA, r = 1, criterion = 2, direct = -1,
      sim = FALSE
    )$overall
    res$f <- f
    res
  }
)
```

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