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

Imports dplyr, magrittr, furrr, future, MASS, mvtnorm, survival

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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)
)
```

`getNe_Surv` *Number of events and power for survival endpoints*

Description

Calculating required number of events when given power or power when given number of events for survival endpoints.

Usage

```
getNe_Surv_Super(delta, alpha = 0.025, beta = NA, Ne = NA, r = 1)

getNe_Surv_Noninf(
  delta,
  cut,
  alpha = 0.025,
  beta = NA,
  Ne = NA,
  r = 1,
  direct = 1
```

```
)

getNe_Surv_Equi(
  delta,
  cut,
  alpha = 0.025,
  beta = NA,
  Ne = NA,
  r = 1,
  maxNe = 1e+06
)
```

Arguments

`delta`	A vector. log(HR) between treatment and control groups.
`alpha`	A vector. One-sided type I error rate. Default value is 0.025.
`beta`	A vector. Type II error rate. When `beta` is `NA` and `Ne` is not `NA`, the power will be returned.
`Ne`	A vector. Number of events. When `Ne` is `NA` and `beta` is not `NA`, the number of events will be returned.
`r`	A vector. Ratio of number of events of the treatment group to the control group. Default value is 1 which under H0 assumption.
`cut`	A vector. 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.
`maxNe`	Maximum possible number of events (`Ne`) in equivalence design. Default value is 1e+06.

Details

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

in superiority design:

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

in non-inferiority design:

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

in equivalence design:

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

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

Value

A data frame containing input parameters and returned number of events or power.

Examples

```
(v <- getNe_Surv_Super(
  delta = log(1.2),
  alpha = 0.025, beta = 0.2, Ne = NA, r = 1
))
getNe_Surv_Super(
  delta = log(1.2),
  alpha = 0.025, beta = NA, Ne = v$Ne, r = 1
)

(v <- getNe_Surv_Noninf(
  delta = log(1.1),
  cut = log(1.3),
  alpha = 0.025, beta = 0.2, Ne = NA, r = 1, direct = -1
))
getNe_Surv_Noninf(
  delta = log(1.1),
  cut = log(1.3),
  alpha = 0.025, beta = NA, Ne = v$Ne, r = 1, direct = -1
)
```

---

getNe_Surv_JM1 *Regional number of events allocation using Japan's Method 1 for survival endpoints*

Description

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

Usage

```
getNe_Surv_Super_JM1(
  delta_a,
  delta_j,
  pi = 0.5,
  alpha = NA,
  beta = NA,
  beta1 = 0.2,
  Ne = NA,
  r = 1,
  criterion = 1
)

getNe_Surv_Noninf_JM1(
  delta_a,
```

```
  delta_j,
  pi = 0.5,
  cut,
  alpha = NA,
  beta = NA,
  beta1 = 0.2,
  Ne = NA,
  r = 1,
  criterion = 1,
  direct = 1
)

getNe_Surv_Equi_JM1(
  delta_a,
  delta_j,
  pi = 0.5,
  cut,
  alpha = NA,
  beta = NA,
  beta1 = 0.2,
  Ne = NA,
  r = 1,
  criterion = 1,
  maxNe = 1e+06
)
```

Arguments

delta_a	A vector. log(HR) between treatment and control groups globally.
delta_j	A vector. log(HR) between treatment and control groups in target region.
pi	A vector. Proportion of global efficacy to retain. Default value is 0.5, which means retaining half of the efficacy.
alpha	A vector. One-sided type I error rate for global success, which is used to calculate global number of events only when Ne is NA. Default value is 0.025.
beta	A vector. Type II error rate for global success, which is used to calculate global number of events only when Ne is NA.
beta1	A vector. Type II error rate for efficacy consistency between target region and globally. Default value is 0.2.
Ne	A vector. Global number of events. When Ne is NA and alpha and beta are not NA, Ne will be calculated automatically.
r	A vector. Ratio of the number of events of the treatment group to the control group. Default value is 1.
criterion	A vector. 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 vector. 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.

maxNe — Maximum possible number of events (Ne) in equivalence design. Default value is 1e+06.

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 number of events allocated to the target region, and Nej is required number of events for the target region, calculated as Nej = Ne * 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, getNe_Surv_Super.

Examples

```
getNe_Surv_Super_JM1(
  delta_a = log(1.4),
  delta_j = log(1.3),
  pi = 0.5, beta1 = 0.2, Ne = 200, r = 1, criterion = 1
)

# Global number of events will be calculated based on alpha and beta.
getNe_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, Ne = NA, r = 1, criterion = 2,
  direct = -1
)
```

---

getN_Bin *Sample size and power for binary endpoints*

Description

Calculating required 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	A vector. Rate of treatment group.
p0	A vector. Rate of control group.
alpha	A vector. One-sided type I error rate. Default value is 0.025.
beta	A vector. Type II error rate. When beta is NA and N is not NA, the power will be returned.
N	A vector. Sample size. When N is NA and beta is not NA, the sample size will be returned.
r	A vector. Ratio of sample sizes of treatment group to control group. Default value is 1.
scale	A vector. Optional values are "RD" for rate difference, "RR" for relative risk, and "OR" for odds ratio. Default value is "RD".
cut	A vector. 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, and OR are preferable. If direct = -1, smaller values of RD, RR, and OR are preferable.
maxN	Maximum possible sample size (N) in equivalence design. Default value is 1e+06.

Details

Taking the larger RD, RR, and OR are 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 (`cut`).

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	A vector. Rate of treatment group globally.
p0_a	A vector. Rate of the control group globally.
p1_j	A vector. Rate of treatment group in target region.
p0_j	A vector. Rate of control group in target region.
pi	A vector. Proportion of global efficacy to retain. Default value is 0.5, which means retaining half of the efficacy.
alpha	A vector. One-sided type I error rate for global success, which is used to calculate global sample size only when N is NA. Default value is 0.025.
beta	A vector. Type II error rate for global success, which is used to calculate global sample size only when N is missing.
beta1	A vector. Type II error rate for efficacy consistency between target region and globally. Default value is 0.2.
N	A vector. Global sample size. When N is NA and alpha and beta are not NA, N will be calculated automatically.
r	A vector. Ratio of sample sizes of treatment group to control group. Default value is 1.
scale	A vector. Optional values are "RD" for rate difference, "RR" for relative risk, and "OR" for odds ratio. Default value is "RD".
cut	A vector. 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, and OR are preferable. If direct = -1, smaller values of RD, RR, and OR are preferable.
maxN	Maximum possible sample size (N) in equivalence design. Default value is 1e+06.

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"
)

# Global sample size will be calculated based on alpha and beta.
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 required 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	A vector. Mean difference between treatment and control groups.
sigma	A vector. Common standard deviation.
alpha	A vector. One-sided type I error rate. Default value is 0.025.
beta	A vector. Type II error rate. When beta is NA and N is not NA, the power will be returned.
N	A vector. Sample size. When N is NA and beta is not NA, the sample size will be returned.
r	A vector. Ratio of sample sizes of treatment group to control group. Default value is 1.
cut	A vector. 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 1e+06.

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 (cut).

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	A vector. Mean difference between treatment and control groups globally.
delta_j	A vector. Mean difference between treatment and control groups in target region.
sigma	A vector. Common standard deviation.
pi	A vector. Proportion of global efficacy to retain. Default value is 0.5, which means retaining half of the efficacy.
alpha	A vector. One-sided type I error rate for global success, which is used to calculate global sample size only when N is NA. Default value is 0.025.
beta	A vector. Type II error rate for global success, which is used to calculate global sample size only when N is NA.
beta1	A vector. Type II error rate for efficacy consistency between target region and globally. Default value is 0.2.
N	A vector. Global sample size. When N is NA and alpha and beta are not NA, N will be calculated automatically.
r	A vector. Ratio of sample sizes of treatment group to control group. Default value is 1.
cut	A vector. 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 1e+06.

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
)

# Global sample size will be calculated based on alpha and beta.
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 required 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	A vector. log(RR) between treatment and control groups.
lambda0	A vector. Baseline hazard of control group.
t	A vector. Average exposure time.
k	A vector. The over-dispersion parameter (k > 0) for negative binomial distribution, which is 0 for poisson distribution. Default value is 0.
alpha	A vector. One-sided type I error rate. Default value is 0.025.
beta	A vector. Type II error rate. When beta is NA and N is not NA, the power will be returned.
N	A vector. Sample size. When N is NA and beta is not NA, the sample size will be returned.
r	A vector. Ratio of sample sizes of treatment group to control group. Default value is 1.
cut	A vector. 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 1e+06.

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, $\hat{\sigma}_0^2 = \frac{1}{\hat{\lambda}_0 t} + \hat{k}, \sigma_1^2 = \frac{1}{e^{\delta}\hat{\lambda}_0 t} + \hat{k}$, 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_a,
  t_j,
  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_a,
  t_j,
  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_a,
  t_j,
  k = 0,
  pi = 0.5,
  cut,
  alpha = NA,
  beta = NA,
  beta1 = 0.2,
  N = NA,
  r = 1,
  maxN = 1e+06
)
```

Arguments

delta_a	A vector. log(RR) between treatment and control groups globally.
delta_j	A vector. log(RR) between treatment and control groups for target region.
lambda0_a	A vector. Baseline hazard of control group globally.
lambda0_j	A vector. Baseline hazard of control group for target region.
t_a	A vector. Average exposure time globally.
t_j	A vector. Average exposure time for target region..
k	A vector. The over-dispersion parameter (k > 0) for negative binomial distribution, which is 0 for poisson distribution. Default value is 0.
pi	A vector. Proportion of global efficacy to retain. Default value is 0.5, which means retaining half of the efficacy.
alpha	A vector. One-sided type I error rate for global success, which is used to calculate global sample size only when N is NA. Default value is 0.025.
beta	A vector. Type II error rate for global success, which is used to calculate global sample size only when N is NA.
beta1	A vector. Type II error rate for efficacy consistency between target region and globally. Default value is 0.2.
N	A vector. Global sample size. When N is NA and alpha and beta are not NA, N will be calculated automatically.
r	A vector. Ratio of sample sizes of treatment group to control group. Default value is 1.
cut	A vector. 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 1e+06.

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_a = 5, t_j = 5, k = 0, pi = 0.5, beta1 = 0.2,
  N = 300, r = 1
)

# Global sample size will be calculated based on alpha and beta.
getN_Count_Noninf_JM1(
  delta_a = log(1.0),
  delta_j = log(1.1),
  lambda0_a = 0.1, lambda0_j = 0.1, t_a = 5, t_j = 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
)
```

---

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 = 2
)

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 = 2
)

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 = 2,
  maxN = 1e+06
)
```

Arguments

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

pi	A vector. Proportion of global efficacy to retain. Default value is 0.5, which means retaining half of the efficacy.
alpha	A vector. One-sided type I error rate for global success. Default value is 0.025.
beta	A vector. Type II error rate for global success, which is used to calculate global sample size only when N is NA.
N	A vector. Global sample size. When N is NA and alpha and beta are not NA, N will be calculated automatically.
r	A vector. Ratio of sample sizes of treatment group to control group. Default value is 1.
scale	A vector. 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. Default value is 2.
cut	A vector. 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, and OR are preferable. If direct = -1, smaller values of RD, RR, and OR are preferable.
maxN	Maximum possible global sample size (N) in equivalence design. Default value is 1e+06.

Details

Taking the larger RD, RR, and OR are 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 alpha and 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,
  f_i,
  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,
  f_i,
  cut,
  cut_i = NA,
  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,
  f_i,
  cut,
  cut_i = NA,
  alpha = 0.025,
  beta = NA,
  N = NA,
  r = 1,
  scale = "RD",
  sim = FALSE,
  nsim = 1000,
  seed = 0,
  maxN = 1e+06
)
```

Arguments

p1_i	A vector with length equal to number of regions. Rate of treatment group in each region.
p0_i	A vector with length equal to number of regions. Rate of control group in each region.
f_i	A vector with length equal to number of regions. Proportion of sample size allocated to each region.
alpha	One-sided type I error rate for global success. 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 sample sizes of treatment group to control group. 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 in global trial, and this margin is also used in the ith region when the ith element of cut_i is NA. 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.
cut_i	A vector with length equal to number of regions. Positive value for non-inferiority or equivalence margin in each region. When cut_i = NA (default), globally margin will be used for each region.
direct	If direct = 1, larger values of RD, RR, and OR are preferable. If direct = -1, smaller values of RD, RR, and OR are preferable.
maxN	Maximum possible global sample size (N) in equivalence design. Default value is 1e+06.

Details

Taking the larger RD, RR, and OR are 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:

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

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

in equivalence design:

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

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

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 and Δ_i are the non-inferiority or equivalence margins in global trial (cut) and each region (cut_i), respectively.

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.
- cut_i The non-inferiority or equivalence margin in each region (cut_i).
- 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

```
getPwr_Bin_Super_JM2(
  p1_i = c(0.7, 0.75),
  p0_i = c(0.5, 0.5),
  f_i = c(0.5, 0.5),
  alpha = 0.025, beta = NA, N = 100, r = 1, scale = "RD", sim = FALSE
)

# Global rates of treatment and control groups will be calculated based on p1_i, p0_i, and f_i.
# Non-inferiority margin in global trial and each region is log(1.4).
# Global sample size will be calculated based on alpha and beta.
getPwr_Bin_Noninf_JM2(
  p1_i = c(0.6, 0.5),
  p0_i = c(0.5, 0.5),
  f_i = c(0.5, 0.5),
  cut = log(1.4),
  alpha = 0.025, beta = 0.2, N = NA, r = 1, scale = "RR", direct = -1, sim = FALSE
)
```

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 = 2
)

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 = 2
)

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 = 2,
  maxN = 1e+06
)
```

Arguments

delta_j	A vector. Mean difference between treatment and control groups in target region.
delta_nj	A vector. Mean difference between treatment and control groups in other regions. When delta_nj is not NA, delta_a will be calculated automatically.
delta_a	A vector. Mean difference between treatment and control groups globally.
sigma	A vector. Common standard deviation.
f	A vector. Proportion of sample size allocated to target region.
pi	A vector. Proportion of global efficacy to retain. Default value is 0.5, which means retaining half of the efficacy.
alpha	A vector. One-sided type I error rate for global success. Default value is 0.025.
beta	A vector. Type II error rate for global success, which is used to calculate global sample size only when N is NA.
N	A vector. Global sample size. When N is NA and beta is not NA, N will be calculated automatically.
r	A vector. Ratio of sample sizes of treatment group to control group. 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. Default value is 2.
cut	A vector. 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 global sample size (N) in equivalence design. Default value is 1e+06.

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 (`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_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 alpha and 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,
  f_i,
  alpha = 0.025,
  beta = NA,
  N = NA,
  r = 1,
  sim = FALSE,
  nsim = 1000,
  seed = 0
)

getPwr_Con_Noninf_JM2(
  delta_i,
  sigma,
  f_i,
  cut,
  cut_i = NA,
  alpha = 0.025,
  beta = NA,
  N = NA,
  r = 1,
  direct = 1,
  sim = FALSE,
```

```
  nsim = 1000,
  seed = 0
)

getPwr_Con_Equi_JM2(
  delta_i,
  sigma,
  f_i,
  cut,
  cut_i = NA,
  alpha = 0.025,
  beta = NA,
  N = NA,
  r = 1,
  sim = FALSE,
  nsim = 1000,
  seed = 0,
  maxN = 1e+06
)
```

Arguments

delta_i	A vector with length equal to number of regions. Mean difference between treatment and control groups in each region.
sigma	Common standard deviation.
f_i	A vector with length equal to number of regions. Proportion of sample size allocated to each region.
alpha	One-sided type I error rate for global success. 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 sample sizes of treatment group to control group. 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 in global trial, and this margin is also used in the ith region when the ith element of cut_i is NA.
cut_i	A vector with length equal to number of regions. Positive value for non-inferiority or equivalence margin in each region. When cut_i = NA (default), globally margin will be used for each region.
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 global sample size (N) in equivalence design. Default value is 1e+06.

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:

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

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

in equivalence design:

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

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

Where $\hat{\delta}$ is the mean difference between treatment and control groups, and Δ and Δ_i are the non-inferiority or equivalence margins in global trial (`cut`) and each region (`cut_i`), respectively.

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.
- `cut_i` The non-inferiority or equivalence margin in each region (`cut_i`).
- `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

```
getPwr_Con_Super_JM2(
  delta_i = c(1, 0.8),
  sigma = 4, f_i = c(0.5, 0.5),
  alpha = 0.025, beta = NA, N = 200, r = 1, sim = FALSE
)

# Global mean difference will be calculated based on delta_i and f_i.
# Non-inferiority margin in global trial and each region is 2.
# Global sample size will be calculated based on alpha and beta.
getPwr_Con_Noninf_JM2(
  delta_i = c(1, 0),
  sigma = 4, f_i = c(0.5, 0.5),
  cut = 2, alpha = 0.025, beta = 0.2, N = NA, r = 1, direct = -1, sim = FALSE
)
```

---

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_j,
  t_nj = NA,
  t_a = NA,
  k = 0,
  f,
  pi = 0.5,
  alpha = 0.025,
  beta = NA,
  N = NA,
  r = 1,
  sim = FALSE,
  nsim = 1000,
  seed = 0,
  numcore = 2
)

getPwr_Count_Noninf_JM1(
```

```
  delta_j,
  delta_nj = NA,
  delta_a = NA,
  lambda0_j,
  lambda0_nj = NA,
  lambda0_a = NA,
  t_j,
  t_nj = NA,
  t_a = NA,
  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 = 2
)

getPwr_Count_Equi_JM1(
  delta_j,
  delta_nj = NA,
  delta_a = NA,
  lambda0_j,
  lambda0_nj = NA,
  lambda0_a = NA,
  t_j,
  t_nj = NA,
  t_a = NA,
  k = 0,
  f,
  pi = 0.5,
  cut,
  alpha = 0.025,
  beta = NA,
  N = NA,
  r = 1,
  sim = FALSE,
  nsim = 1000,
  seed = 0,
  numcore = 2,
  maxN = 1e+06
)
```

Arguments

delta_j	A vector. log(RR) between treatment and control groups for target region.

delta_nj	A vector. log(RR) between treatment and control groups for other regions. When delta_nj is not NA, delta_a will be calculated automatically.
delta_a	A vector. log(RR) between treatment and control groups globally.
lambda0_j	A vector. Baseline hazard of control group for target region.
lambda0_nj	A vector. Baseline hazard of control group for other regions. When lambda0_nj is not NA, lambda0_a will be calculated automatically.
lambda0_a	A vector. Baseline hazard of control group globally.
t_j	A vector. Average exposure time for target region.
t_nj	A vector. Average exposure time for other regions.
t_a	A vector. Average exposure time globally.
k	A vector. The over-dispersion parameter (k > 0) for negative binomial distribution, which is 0 for poisson distribution.
f	A vector. Proportion of sample size allocated to target region.
pi	A vector. Proportion of global efficacy to retain. Default value is 0.5, which means retaining half of the efficacy.
alpha	A vector. One-sided type I error rate for global success. Default value is 0.025.
beta	A vector. Type II error rate for global success, which is used to calculate global sample size only when N is NA.
N	A vector. Global sample size. When N is NA and beta is not NA, N will be calculated automatically.
r	A vector. Ratio of sample sizes of treatment group to control group. 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. Default value is 2.
cut	A vector. 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 global sample size (N) in equivalence design. Default value is 1e+06.

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_j = 5, t_a = 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_j = 5, t_nj = 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_i,
  k = 0,
  f_i,
  alpha = 0.025,
  beta = NA,
  N = NA,
  r = 1,
  sim = FALSE,
  nsim = 1000,
  seed = 0
)

getPwr_Count_Noninf_JM2(
  delta_i,
  lambda0_i,
  t_i,
  k = 0,
  f_i,
  cut,
  cut_i = NA,
  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_i,
  k = 0,
  f_i,
```

```
  cut,
  cut_i = NA,
  alpha = 0.025,
  beta = NA,
  N = NA,
  r = 1,
  sim = FALSE,
  nsim = 1000,
  seed = 0,
  maxN = 1e+06
)
```

Arguments

delta_i	A vector with length equal to number of regions. log(RR) between treatment and control groups for each region.
lambda0_i	A vector with length equal to number of regions. Baseline hazard of control group for each region.
t_i	Average exposure time for each region.
k	The over-dispersion parameter (k > 0) for negative binomial distribution, which is 0 for poisson distribution.
f_i	A vector with length equal to number of regions. Proportion of sample size allocated to each region.
alpha	One-sided type I error rate for global success. 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 sample sizes of treatment group to control group. 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 in global trial, and this margin is also used in the ith region when the ith element of cut_i is NA. 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).
cut_i	A vector with length equal to number of regions. Positive value for non-inferiority or equivalence margin in each region. When cut_i = NA (default), globally margin will be used for each region.
direct	direct = 1 indicates that a larger RR is preferable, while direct = -1 indicates that a smaller RR is preferable.
maxN	Maximum possible global sample size (N) in equivalence design. Default value is 1e+06.

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:

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

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

in equivalence design:

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

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

Where $\hat{\delta} = log(\hat{RR})$ between treatment and control groups, and Δ and Δ_i are the non-inferiority or equivalence margins in global trial (`cut`) and each region (`cut_i`), respectively.

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.
- `cut_i` The non-inferiority or equivalence margin in each region (`cut_i`).
- `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

```
getPwr_Count_Super_JM2(
  delta_i = c(log(1.2), log(1.4)),
  lambda0_i = c(0.1, 0.1),
  t_i = c(5, 5), k = 0, f_i = c(0.5, 0.5),
  alpha = 0.025, beta = NA, N = 300, r = 1, sim = FALSE
)

# Global log(RR) will be calculated based on delta_i and f_i,
# and global lambda0 will be calculated based on lambda0_i and f_i
# Non-inferiority margin in global trial and each region is log(1.3).
# Global sample size will be calculated based on beta.
getPwr_Count_Noninf_JM2(
  delta_i = c(log(1.1), log(1.0)),
  lambda0_i = c(0.1, 0.1),
  t_i = c(5, 5), k = 0, f_i = c(0.5, 1 - 0.5),
  cut = log(1.3),
  alpha = 0.025, beta = 0.2, N = NA, r = 1, direct = -1, sim = FALSE
)
```

---

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 number of events, 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,
  Ne = NA,
  r = 1,
  criterion = 1,
  sim = FALSE,
  nsim = 1000,
  seed = 0,
  numcore = 2
)

getPwr_Surv_Noninf_JM1(
  delta_j,
  delta_nj = NA,
```

```
  delta_a = NA,
  f,
  pi = 0.5,
  cut,
  alpha = 0.025,
  beta = NA,
  Ne = NA,
  r = 1,
  criterion = 1,
  direct = 1,
  sim = FALSE,
  nsim = 1000,
  seed = 0,
  numcore = 2
)

getPwr_Surv_Equi_JM1(
  delta_j,
  delta_nj = NA,
  delta_a = NA,
  f,
  pi = 0.5,
  cut,
  alpha = 0.025,
  beta = NA,
  Ne = NA,
  r = 1,
  criterion = 1,
  sim = FALSE,
  nsim = 1000,
  seed = 0,
  numcore = 2,
  maxNe = 1e+06
)
```

Arguments

delta_j	A vector. log(HR) between treatment and control groups in target region.
delta_nj	A vector. log(HR) between treatment and control groups in other regions. When delta_nj is not NA, delta_a will be calculated automatically.
delta_a	A vector. log(HR) between treatment and control groups globally.
f	A vector. Proportion of number of events allocated to target region.
pi	A vector. Proportion of global efficacy to retain. Default value is 0.5, which means retaining half of the efficacy.
alpha	A vector. One-sided type I error rate for global success. Default value is 0.025.
beta	A vector. Type II error rate for global success, which is used to calculate global number of events only when Ne is NA.
Ne	A vector. Global number of events. When Ne is NA and beta is not NA, Ne will be calculated automatically.
r	A vector. Ratio of the number of events of the treatment group to the control group. Default value is 1.

criterion	A vector. 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. Default value is 2.
cut	A vector. 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.
maxNe	Maximum possible global number of events (Ne) in equivalence design. Default value is 1e+06.

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, $1-e^{\hat{\delta}}$ approximately follows a distribution of $N(1-e^{\delta}, (e^{\delta}\sqrt{\frac{1}{N_e/(r+1)} + \frac{1}{N_e r/(r+1)}}$ 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, Ne = 200, r = 1, criterion = 1,
  sim = FALSE
)

# Delta_a will be calculated based on delta_j and delta_nj.
# Global number of events will be calculated based on alpha and 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, Ne = 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 number of events, 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,
  f_i,
  alpha = 0.025,
  beta = NA,
  Ne = NA,
  r = 1,
  sim = FALSE,
  nsim = 1000,
  seed = 0
)

getPwr_Surv_Noninf_JM2(
  delta_i,
  f_i,
  cut,
  cut_i = NA,
  alpha = 0.025,
  beta = NA,
  Ne = NA,
  r = 1,
  direct = 1,
  sim = FALSE,
  nsim = 1000,
  seed = 0
)

getPwr_Surv_Equi_JM2(
  delta_i,
  f_i,
  cut,
  cut_i = NA,
  alpha = 0.025,
  beta = NA,
  Ne = NA,
  r = 1,
  sim = FALSE,
  nsim = 1000,
  seed = 0,
```

```
  maxNe = 1e+06
)
```

Arguments

delta_i	A vector with length equal to number of regions. log(HR) between treatment and control groups for each region.
f_i	A vector with length equal to number of regions. Proportion of number of events allocated to each region.
alpha	One-sided type I error rate for global success. Default value is 0.025.
beta	Type II error rate for global success, which is used to calculate global number of events only when Ne is NA.
Ne	Global number of events. When Ne is NA and beta is not NA, Ne will be calculated automatically.
r	Ratio of the number of events of the treatment group to the control group. 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 in global trial, and this margin is also used in the ith region when the ith element of cut_i is NA. 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).
cut_i	A vector with length equal to number of regions. Positive value for non-inferiority or equivalence margin in each region. When cut_i = NA (default), globally margin will be used for each region.
direct	direct = 1 indicates that a larger HR is preferable, while direct = -1 indicates that a smaller HR is preferable.
maxNe	Maximum possible global number of events (Ne) in equivalence design. Default value is 1e+06.

Details

Taking the larger HR 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:

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

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

in equivalence design:

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

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

Where $\hat{\delta} = log(\hat{HR})$ between treatment and control groups, and Δ and Δ_i are the non-inferiority or equivalence margins in global trial (`cut`) and each region (`cut_i`), respectively.

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.
- `cut_i` The non-inferiority or equivalence margin in each region (`cut_i`).
- `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

```
getPwr_Surv_Super_JM2(
  delta_i = c(log(1.2), log(1.4)),
  f_i = c(0.5, 0.5),
  alpha = 0.025, beta = NA, Ne = 300, r = 1, sim = FALSE
)

# Global delta will be calculated based on delta_i and f_i.
# Non-inferiority margin in global trial and each region is log(1.3).
# Global number of events will be calculated based on alpha and beta.
getPwr_Surv_Noninf_JM2(
  delta_i = c(log(1.1), log(1.0)),
  f_i = c(0.5, 0.5),
  cut = log(1.3),
  alpha = 0.025, beta = 0.2, Ne = NA, r = 1, direct = -1, sim = FALSE
)
```

Ne_to_N *Transform number of events to sample size*

Description

Calculate required sample size according to required number of events, given hazard of event and follow-up parameters in survival analysis. Assuming uniform enrollment of subject and the event time and dropout time follow an exponential distribution.

Usage

```
Ne_to_N(
  Ne = NA,
  r = 1,
  lambda0,
  lambda1,
  dropoutRate,
  dropoutTime = 1,
  a = NA,
  f = NA,
  l = NA,
  follow_up = "until_end"
)
```

Arguments

Ne	A vector. Number of events
r	A vector. Ratio of sample sizes of treatment group to control group. Default value is 1.
lambda0	A vector. Hazard of control group.
lambda1	A vector. Hazard of treatment group.
dropoutRate	A vector. Dropout rate within the time interval specified by dropoutTime parameter.
dropoutTime	A vector. Time interval for dropout rate.
a	A vector. Accrual time for trial, which is only used when follow_up = 'until_end'.
f	A vector. Follow up time for trial, which is only used when follow_up = 'until_end'.
l	A vector. Fixed follow up period for each subject, which is only used when follow_up = 'fixed_period'.
follow_up	A vector. If follow_up = 'until_end', subjects will be followed up until the end of trial. If follow_up = 'fixed_period', each subject will be followed up a fixed period.

Value

A data frame containing input parameters and returned event rate and required sample size.

- eventRate0 Event rate for control group.

- `eventRate1` Event rate for treatment group.
- `eventRate` Event rate for trial.
- `N0` Required sample size for control group.
- `N1` Required sample size for treatment group.
- `N` Required sample size for trial.

References

1. Quan H, Zhao PL, Zhang J, Roessner M, Aizawa K. Sample size considerations for Japanese patients in a multi-regional trial based on MHLW guidance. Pharm Stat. 2010;9(2):100-112. doi:10.1002/pst.380

Examples

```
# Median survival time in control group is 20 months, HR = 0.75, and annual dropout rate is 5%.
# Accrual time is 18 months, and follow-up time is 18 months.
# Each subject is followed up until the end of trial.
Ne_to_N(
  Ne = 100, r = 1, lambda0 = log(2) / 20, lambda1 = log(2) / 20 * 0.75,
  dropoutRate = 0.05, dropoutTime = 12,
  a = 18, f = 18, follow_up = "until_end"
)

# Each subject is followed for 18 months after enrollment.
Ne_to_N(
  Ne = 100, r = 1, lambda0 = log(2) / 20, lambda1 = log(2) / 20 * 0.75,
  dropoutRate = 0.05, dropoutTime = 12,
  l = 18, follow_up = "fixed_period"
)
```

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