

Package ‘BRACE’

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Type Package

Title Bayesian Response Adaptive randomization design for Composite Endpoint (BRACE).

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Description Some clinical trials have a composite endpoint of both mortality and morbidity, e.g. the endpoint of organ support-free days (OSFD) for sepsis patients admitted to the intensive care units (ICU). The package proposes a Bayesian mixture model to model the composite endpoint of OSFD and implements three response adaptive randomization (RAR) adaptation rules for patient allocation based on the estimated posterior probability from the Bayesian model at the interim analysis.

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Depends MCMCpack, truncnorm

Imports MCMCpack, truncnorm

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mcmc_theta	<i>MCMC function to generate posterior of θ</i>
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Description

Run MCMC and generate posterior samples of the estimand (mean transformed OSFD θ)

Usage

```
mcmc_theta(d, tau, B = 2000, burnin = 500, thin = 10)
```

Arguments

d	Data input of transformed OSFD
tau	Data input of death indicator
B	Number of MCMC iterations
burnin	Number of burn-in iterations
thin	A value thin = k would result in keeping every kth value and discarding all other values of the MCMC chain.

Value

A vector of θ values of all kept MCMC samples.

Examples

```
## Not run:
theta_ctrl <- mcmc_theta(data_ctrl$d, data_ctrl$tau)

## End(Not run)
```

prop_best_arm	<i>Calculate the proportion of patients assigned to the best arm</i>
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Description

Calculate the proportion of patients assigned to the best arm in response-adaptive randomization (RAR) design.

Usage

```
prop_best_arm(data_all, data_best_arm)
```

Arguments

data_all	A list of dataframes from all arms
data_best_arm	A dataframe from the best arm

Value

The proportion of patients assigned to the best arm, ranging from 0 to 1.

Examples

```
## Not run:
prop_best_arm(data_all, data_best_arm)

## End(Not run)
```

RuleI	<i>BRACE RAR Rule I</i>
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Description

Calculate the number of patients allocated to each arm at the interim stage following BRACE RAR Rule I.

Usage

```
RuleI(nj, n0, pvec)
```

Arguments

nj	Total sample size at jth interim stage
n0	Sample size for the control arm
pvec	Vector of allocation probability for all treatment arms

Value

A vector of number of patients allocated to each arm (for 4 arms scenario only).

Examples

```
nj <- 200
ctrl_prop <- 1/4
pvec <- c(0.8,0.1,0.1)
n_assign <- RuleI(nj=nj,n0=nj*ctrl_prop,pvec=pvec)
```

RuleII	<i>BRACE RAR Rule II</i>
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Description

Calculate the number of patients allocated to each arm at the interim stage following BRACE RAR Rule II.

Usage

```
RuleII(nj, pvec)
```

Arguments

nj	Total sample size at jth interim stage
pvec	Vector of allocation probability for all treatment arms

Value

A vector of number of patients allocated to each arm.

Examples

```

nj <- 200
pvec <- c(0.8,0.1,0.1)
n_assign <- RuleII(nj=nj,pvec=pvec)

```

RuleIII*BRACE RAR Rule III***Description**

Calculate the number of patients allocated to each arm at the interim stage following BRACE RAR Rule III.

Usage

```
RuleIII(nj, pvec)
```

Arguments

nj	Total sample size at jth interim stage
pvec	Vector of allocation probability for all treatment arms

Value

A vector of number of patients allocated to each arm.

Examples

```

nj <- 200
pvec <- c(0.8,0.1,0.1)
n_assign <- RuleIII(nj=nj,pvec=pvec)

```

sim_osfd_data*Simulate organ support-free days (OSFD) data***Description**

Simulate organ support-free days (OSFD) data with given sample size and parameter values.

Usage

```
sim_osfd_data(n, mu, sigma2, omega, lambda)
```

Arguments

n	Sample size
mu	Mean of transformed OSFD among non-censored patients
sigma2	Variance of transformed OSFD among non-censored patients
omega	Censoring prportion of patients
lambda	Mortality rate

Value

Simulated data consisting of OSFD on original scale (y), death indicator (τ) and transformed OSFD (d).

Examples

```
n0 <- 50
mean_osfd <- 20
mu_ctrl_true <- -log(30-mean_osfd)
sigma2_true <- 0.8^2
omega_true <- 0.3
lambda_ctrl_true <- 0.2
data_ctrl <- sim_osfd_data(n=n0, mu=mu_ctrl_true, sigma2=sigma2_true,
omega=omega_true, lambda=lambda_ctrl_true)
```

success_prob	<i>Success probability of the trial</i>
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Description

Calculate the success probability of the trial, defined as the probability of difference in estimand (mean transformed OSFD θ) between the best treatment arm and control arm passing a clinically meaningful difference.

Usage

```
success_prob(theta_best, theta_ctrl, clin_diff)
```

Arguments

theta_best	The posterior samples of θ in the best treatment arm
theta_ctrl	The posterior samples of θ in the control arm
clin_diff	Clinically meaningful difference

Value

Success probability of the trial, ranging from 0 to 1.

Examples

```
## Not run:
clin_diff <- 0.0647669
success_prob(theta_best, theta_ctrl, clin_diff)

## End(Not run)
```

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