Package ‘ppseq’

August 8, 2022

Title  Design Clinical Trials using Sequential Predictive Probability Monitoring

Version  0.2.0

Description  Functions are available to calibrate designs over a range of posterior and predictive thresholds, to plot the various design options, and to obtain the operating characteristics of optimal accuracy and optimal efficiency designs.

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BugReports  https://github.com/zabore/ppseq/issues

Encoding  UTF-8

LazyData  true

Depends  R (>= 3.5.0)

Suggests  covr, gt, knitr, rmarkdown, spelling, testthat (>= 3.0.0), vdiffr

VignetteBuilder  knitr

Imports  dplyr, furrr, ggplot2, plotly, purrr, tibble, patchwork, tidyr

Config/testthat/edition  3

Language  en-US

RoxygenNote  7.2.1

NeedsCompilation  no

Author  Emily C. Zabor [aut, cre] (https://orcid.org/0000-0002-1402-4498),
  Brian P. Hobbs [aut],
  Michael J. Kane [aut] (https://orcid.org/0000-0003-1899-6662)

Maintainer  Emily C. Zabor <zabore2@ccf.org>

Repository  CRAN

Date/Publication  2022-08-08 19:10:02 UTC
Calculation of decision rules

**Description**

This function will take the posterior and predictive thresholds for a pre-specified design with a given null response rate and fixed interim looks and total sample size, and return the decision rules at each interim analysis and the end of the trial. Intended for use after selecting an optimal design using the functions `calibrate_thresholds` and `optimize_design`.

**Usage**

```r
calc_decision_rules(
  n,
  N,
  theta,
  ppp,
  p0,
  direction = "greater",
  delta = NULL,
  prior = c(0.5, 0.5),
  S = 5000
)
```
Arguments

- `n`: matrix containing the total number of patients accrued so far at each interim look in the standard of care (column 1) and experimental (column 2) arms for two-sample case; vector of sample size accrued so far at each interim look for one-sample case. The last value should be equal to the total sample size at the end of the trial. If only a single look will be done at the end of the trial, this can be a vector specifying the total sample size c(N0, N1) for the two-sample case or an integer specifying the total sample size N for the one-sample case.

- `N`: the total planned sample size at the end of the trial, c(N0, N1) for two-sample case; integer of total planned sample size at end of trial N for one-sample case.

- `theta`: The target posterior probability. E.g. Efficacy decision if \( P(p_1 > p_0) > \theta \) for the two-sample case with greater direction.

- `ppp`: The target predictive probability. E.g. Stop the trial if the predictive probability falls below this target.

- `p0`: The target value to compare to in the one-sample case. Set to NULL for the two-sample case.

- `direction`: "greater" (default) if interest is in \( P(p_1 > p_0) \) and "less" if interest is in \( P(p_1 < p_0) \) for two-sample case. For one-sample case, "greater" if interest is in \( P(p > p_0) \) and "less" if interest is in \( P(p < p_0) \).

- `delta`: clinically meaningful difference between groups. Typically 0 for two-sample case. NULL for one-sample case (default).

- `prior`: hyperparameters of prior beta distribution. Beta(0.5, 0.5) is default.

- `S`: number of samples, default is 5000

Value

In the one-sample case, returns a tibble with n at each look, r at each look, and ppp, the associated posterior predictive probability. Stop the trial at that look if the number of observed responses is <=r. At the end of the trial, the treatment is considered promising if the number of observed responses is >r. In the two-sample case, returns a tibble with n0 and n1, the number enrolled subjects in the control and experimental arms at each look, respectively, r0 and r1, the number of possible responses in the control and experimental arms at each look, respectively, and ppp, the associated posterior predictive probability. For a given value of r0, stop the trial if the number of observed responses in the experimental arm is <=r1. At the end of the trial, the treatment is considered promising if the number of observed responses in the experimental arm is >r1 for a given r0. Any NA value in either table represents an interim look where there is no number of responses that would lead to stopping the trial.

Examples

```r
set.seed(123)
# One-sample case
calc_decision_rules(
  n = seq(5, 25, 5),
  N = 25,
  theta = 0.86,
  p0 = 0
)
```
calc_next

# Two-sample case
calc_decision_rules(
  n = cbind(seq(5, 25, 5), seq(5, 25, 5)),
  N = c(25, 25),
  theta = 0.86,
  ppp = 0.2,
  p0 = NULL,
  direction = "greater",
  delta = 0,
  S = 50
)

## Description

This function is meant to be used in the context of a clinical trial with a binary endpoint. For the two-sample case, the total number of events in the standard-of-care arm is $y_0$ and the total number of events in the experimental arm is $y_1$. The function samples from the posterior beta distribution based on the data and the prior beta hyperparameters, and returns the empiric mean and bootstrap confidence interval for the next patient. The empiric mean represents the probability of the binary outcome occurring in the next patient. The one-sample case is also available.

## Usage

```r
calc_next(y, n, prior = c(0.5, 0.5), S = 5000, interval = 0.95)
```

## Arguments

- `y`: number of events observed so far. Vector of length two $c(y_0, y_1)$ for the two-sample case; integer $y$ for the one-sample case.
- `n`: sample size observed so far. Vector of length two $c(n_0, n_1)$ for the two-sample case; integer $n$ for the one-sample case.
- `prior`: vector of length two containing hyperparameters of the prior beta distribution. $c(0.5, 0.5)$ is default, for the Beta(0.5, 0.5) distribution.
- `S`: number of samples, default is 5000
- `interval`: a value between 0 and 1 indicating the width of the desired interval, default is 0.95
Value

Returns a tibble with the group indicator (for the two-sample case only), the empiric mean, the bootstrap confidence interval, and the specified width of the confidence interval.

Examples

```r
set.seed(123)
# One-sample case
calc_posterior(
  y = 27,
  n = 100,
  S = 100
)
# Two-sample case
calc_posterior(
  y = c(14, 23),
  n = c(100, 100),
  S = 100
)
```

Description

This function is meant to be used in the context of a clinical trial with a binary endpoint. For the two-sample case, the total number of events in the standard-of-care arm is \( y_0 \) and the total number of events in the experimental arm is \( y_1 \). The function samples from the posterior beta distribution based on the data and the prior beta hyperparameters, and returns the posterior probability that \( p_1 \) is greater than (or less than) \( p_0 \) given the data. The one-sample case is also available, in which a target \( p_0 \) must be specified and the function returns the posterior probability that \( p \) is greater than (or less than) \( p_0 \) given the data.

Usage

```r
calc_posterior(
  y,  
  n,  
  p0,  
  direction = "greater",  
  delta = NULL,  
  prior = c(0.5, 0.5),  
  S = 5000
)
```
Arguments

- **y**: number of events observed so far. Vector of length two \((y_0, y_1)\) for the two-sample case; integer \(y\) for the one-sample case.
- **n**: sample size observed so far. Vector of length two \((n_0, n_1)\) for the two-sample case; integer \(n\) for the one-sample case.
- **p0**: the target value to compare to in the one-sample case. Set to NULL for the two-sample case.
- **direction**: "greater" (default) if interest is in P\((p_1 > p_0)\) in the two-sample case or P\((p > p_0)\) in the one-sample case; "less" if interest is in P\((p_1 < p_0)\) for the two-sample case or P\((p < p_0)\) for the one-sample case.
- **delta**: clinically meaningful difference between groups. Typically 0 for the two-sample case. NULL for one-sample case (default).
- **prior**: vector of length two containing hyperparameters of the prior beta distribution. \(c(0.5, 0.5)\) is default, for the Beta\((0.5, 0.5)\) distribution.
- **S**: number of samples, default is 5000

Value

Returns the numeric posterior probability

Examples

```r
set.seed(123)

# One-sample case
calc_posterior(
  y = 27,
  n = 100,
  p0 = 0.2
)

# Two-sample case
calc_posterior(
  y = c(14, 23),
  n = c(100, 100),
  p0 = NULL,
  delta = 0
)
```

**calc_predictive**

Calculate a single posterior predictive probability
Description

This function is meant to be used in the context of a clinical trial with a binary endpoint. The goal is to calculate the posterior predictive probability of success at the end of a trial, given the data available at an interim analysis. For the two-sample case the number of events observed at interim analysis, the sample size at interim analysis, and the total planned sample size are denoted y0, n0, and N0 in the standard-of-care arm and y1, n1, and N1 in the experimental arm. For the one-sample case, the number of events observed at interim analysis, the sample size at interim analysis, and the total planned sample size are denoted y, n, and N.

Usage

```r
calc_predictive(
  y,
  n,
  p0,
  N,
  direction = "greater",
  delta = NULL,
  prior = c(0.5, 0.5),
  S = 5000,
  theta = 0.95
)
```

Arguments

- `y`: number of events observed so far. Vector of length two c(y0, y1) for the two-sample case; integer y for the one-sample case.
- `n`: sample size observed so far. Vector of length two c(n0, n1) for the two-sample case; integer n for the one-sample case.
- `p0`: the target value to compare to in the one-sample case. Set to NULL for the two-sample case.
- `N`: the total planned sample size at the end of the trial. Vector of length two c(N0, N1) for the two-sample case; integer N for the one-sample case.
- `direction`: "greater" (default) if interest is in P(p1 > p0) in the two-sample case or P(p > p0) in the one-sample case; "less" if interest is in P(p1 < p0) for the two-sample case or P(p < p0) for the one-sample case.
- `delta`: clinically meaningful difference between groups. Typically 0 for the two-sample case. NULL for one-sample case (default).
- `prior`: vector of length two containing hyperparameters of the prior beta distribution. c(0.5, 0.5) is default, for the Beta(0.5, 0.5) distribution.
- `S`: number of samples, default is 5000
- `theta`: The target posterior probability. e.g. Efficacy decision if P(p1 > p0) > theta for the two-sample case with greater direction. Default is 0.95.

Value

Returns the numeric posterior predictive probability
calibrate_posterior_threshold

Examples

set.seed(123)

# Setting S = 100 for speed, in practice you would want a much larger sample

# One-sample case
calc_predictive(
  y = 14,
  n = 50,
  p0 = 0.2,
  N = 100,
  S = 100
)

# Two-sample case
calc_predictive(
  y = c(7, 12),
  n = c(50, 50),
  p0 = NULL,
  N = c(100, 100),
  delta = 0,
  S = 100
)

calibrate_posterior_threshold

Calibrate the posterior probability threshold

description

This function is meant to be used in the context of a clinical trial with a binary endpoint. For a vector of possible posterior decision thresholds, the function simulates many trials and then calculates the average number of times the posterior probability exceeds a given threshold. In a null case, this will result in the type I error at a given threshold. In an alternative case, this will result in the power at a given threshold.

Usage

calibrate_posterior_threshold(
  p,
  N,
  p0,
  direction = "greater",
  delta = NULL,
  prior = c(0.5, 0.5),
  S = 5000,
  theta
)
Arguments

- **p**: vector of length two containing the probability of event in the standard of care and experimental arm \((p_0, p_1)\) for the two-sample case; integer of event probability for one-sample case
- **N**: vector of length two containing the total sample size \((N_0, N_1)\) for two-sample case; integer of sample size so far \(N\) for one-sample case
- **p0**: The target value to compare to in the one-sample case. Set to NULL for the two-sample case.
- **direction**: "greater" (default) if interest is in \(p(p_1 > p_0)\) and "less" if interest is in \(p(p_1 < p_0)\) for two-sample case. For one-sample case, "greater" if interest is in \(p(p > p_0)\) and "less" if interest is in \(p(p < p_0)\).
- **delta**: clinically meaningful difference between groups. Typically 0 for the two-sample case. NULL for the one-sample case (default).
- **prior**: hyperparameters of prior beta distribution. Beta(0.5, 0.5) is default
- **S**: number of samples drawn from the posterior, and number of simulated trials. Default is 5000
- **theta**: The target posterior probability thresholds to consider. Integer or vector.

Value

Returns a tibble with the posterior probability threshold(s) and associated proportion of positive trials.

Examples

```r
set.seed(123)

# Setting S = 100 for speed, in practice you would want a much larger sample

# One-sample case
calibrate_posterior_threshold(
  p = 0.1,
  N = 50,
  p0 = 0.1,
  S = 100,
  theta = c(0.9, 0.95)
)

# Two-sample case
calibrate_posterior_threshold(
  p = c(0.1, 0.1),
  N = c(50, 50),
  p0 = NULL,
  delta = 0,
  S = 100,
  theta = c(0.9, 0.95)
)
```
**calibrate_thresholds**  
*Calibrate according to posterior probability threshold and predictive probability threshold with interim futility monitoring*

**Description**

This function is meant to be used in the context of a clinical trial with a binary endpoint. For every combination of the provided posterior thresholds and predictive thresholds, the function simulates many trials and then calculates the average number of times a trial was positive. In the null case, this is the type I error for the given thresholds. In the alternative case, this is the power for the given thresholds.

**Usage**

```r
calibrate_thresholds(
  p_null,
  p_alt,
  n,
  N,
  pp_threshold,
  ppp_threshold,
  direction = "greater",
  delta = NULL,
  monitoring = "futility",
  prior = c(0.5, 0.5),
  S = 5000,
  nsim = 1000
)
```

**Arguments**

- `p_null`  
  vector of length two containing the probability of event in the standard of care and experimental arm c(p₀, p₁) for the two-sample case for the null scenario; integer of event probability for one-sample case

- `p_alt`  
  vector of length two containing the probability of event in the standard of care and experimental arm c(p₀, p₁) for the two-sample case for the alternative scenario; integer of event probability for one-sample case

- `n`  
  matrix containing the total number of patients accrued so far at each interim look in the standard of care (column 1) and experimental (column 2) arms for two-sample case; vector of sample size accrued so far at each interim look for one-sample case. The last value should be equal to the total sample size at the end of the trial. If only a single look will be done at the end of the trial, this can be a vector specifying the total sample size c(N₀, N₁) for the two-sample case or an integer specifying the total sample size N for the one-sample case

- `N`  
  the total planned sample size at the end of the trial, c(N₀, N₁) for two-sample case; integer of total planned sample size at end of trial N for one-sample case
**Value**

A list containing a

1. a tibble `res_summary` containing the posterior probability threshold (pp_threshold), the predictive probability threshold (ppp_threshold), the mean sample size under the null (mean_n0_null and mean_n1_null for two-sample case; mean_n1_null for one-sample case), the proportion of positive trials under the null (prop_pos_null), the proportion of trials stopped early under the null (prop_stopped_null), the mean sample size under the alternative (mean_n0_alt and mean_n1_alt for two-sample case; mean_n1_alt for one-sample case), the proportion of positive trials under the alternative (prop_pos_alt), the proportion of trials stopped early under the alternative (prop_stopped_alt)

2. `call_list` containing the original function call

3. `calibrate_thresholds_inputs` a list containing the inputs to the original function call

The proportion of positive trials will be a measure of the type I error for a null setting, and a measure of the power in the alternative setting.

**Examples**

```r
# One-sample case
set.seed(123)
calibrate_thresholds(
  p_null = 0.1,
  p_alt = 0.4,
  n = seq(5, 15, 5),
  N = 15,
  pp_threshold = c(0.85, 0.9),
  ppp_threshold = c(0.1, 0.2),
  S = 10,
  nsim = 10
)
```
# Two-sample case
set.seed(456)

calibrate_thresholds(
  p_null = c(0.1, 0.1),
  p_alt = c(0.1, 0.5),
  n = cbind(seq(5, 15, 5), seq(5, 15, 5)),
  N = c(15, 15),
  pp_threshold = c(0.8, 0.85),
  ppp_threshold = c(0.2, 0.3),
  delta = 0,
  S = 10,
  nsim = 10
)

---

eval_thesh Evaluate a single dataset for a single pp_threshold and ppp_threshold combination

Description
Helper function for calibrate_thresholds() function that evaluates a single combination of a pp_threshold and a ppp_threshold for a single dataset

Usage

eval_thesh(  
data,  
  pp_threshold,  
  ppp_threshold,  
  p0,  
  N,  
  direction = "greater",  
  delta = NULL,  
  monitoring = "futility",  
  prior = c(0.5, 0.5),  
  S = 5000  
)

Arguments

data the name of the dataset  
pp_threshold the posterior probability threshold of interest  
ppp_threshold the posterior probability threshold of interest for futility monitoring  
p0 The target value to compare to in the one-sample case. Set to NULL for the two-sample case.
\[ N \]
the total planned sample size at the end of the trial, \(c(N0, N1)\) for two-sample case; integer of total planned sample size at end of trial \(N\) for one-sample case

\[ \text{direction} \]
"greater" (default) if interest is in \(P(p1 > p0)\) and "less" if interest is in \(P(p1 < p0)\) for two-sample case. For one-sample case, "greater" if interest is in \(P(p > p0)\) and "less" if interest is in \(P(p < p0)\).

\[ \text{delta} \]
clinically meaningful difference between groups. Typically 0 for the two-sample case. NULL for the one-sample case (default).

\[ \text{monitoring} \]
the type of interim monitoring to be performed. One of "futility" or "efficacy". Default is "futility".

\[ \text{prior} \]
hyperparameters of prior beta distribution. Beta(0.5, 0.5) is default

\[ S \]
number of samples, default is 5000

\[ \text{Value} \]

Returns a tibble with the total sample size at the end of the trial, the number of responses observed at the end of the trial, the \(pp\_threshold\) considered, the \(ppp\_threshold\) considered, the observed predictive probability generated from calc_predictive(), and an indicator for whether the trial was positive or not at the end

\[ \text{Description} \]

This .rda file contains output from a one-sample call to calibrate_thresholds(). See the vignette titled "One-sample expansion cohort" for a description of the input parameters used, or run one_sample_cal_tbl$inputs to see a list of the original function inputs. For use in testing functions and in vignettes.

\[ \text{Usage} \]

data(one_sample_cal_tbl)

\[ \text{Format} \]

A list containing a

1. a tibble 'res_summary' containing the posterior probability threshold (\(pp\_threshold\)); the predictive probability threshold (\(ppp\_threshold\)); the mean sample size under the null (\(mean\_n1\_null\)) and alternative (\(mean\_n1\_alt\)) response rates; the proportion of positive trials under the null (\(prop\_pos\_null\)) and alternative (\(prop\_pos\_alt\)) response rates; and the proportion of trials stopped under the null (\(prop\_stopped\_null\)) and alternative (\(prop\_stopped\_alt\)) response rates
2. 'call_list' containing the original function call
3. 'inputs' a list containing the inputs to the original function call
one_sample_decision_tbl

"Output from a one-sample call to calc_decision_rules"

Description

This .rda file contains output from a one-sample call to calc_decision_rules(). See the vignette titled "One-sample expansion cohort" for a description of the input parameters used.

Usage

data(one_sample_decision_tbl)

Format

A tibble containing n, the number of patients enrolled at each futility monitoring point; r, the number of responses at which we would stop the trial at a given look if the number of observed responses is <=r, or at the end of the trial the treatment is considered promising if the number of observed responses is >r; and ppp, the predictive probability at each given look.

optimize_design.calibrate_thresholds

"Custom optimization method for calibrate_thresholds objects"

Description

Determines the optimal designs based on a variety of criteria. The optimal efficiency design is the one with the shortest Euclidean distance to the upper left point on a plot of the average sample size under the null by the average sample size under the alternative. The optimal accuracy design is the one with the shortest Euclidean distance to the upper left point on a plot of the type I error by the power.

Usage

```r
## S3 method for class 'calibrate_thresholds'
optimize_design(
x,
type1_range = c(0, 1),
minimum_power = 0,
w_type1 = 1,
w_power = 1,
w_Nnull = 1,
w_Nalt = 1,
...)
```
optimize_design.calibrate_thresholds

Arguments

x
an object of class ‘calibrate_thresholds’, usually returned by the calibrate_thresholds function

type1_range
a vector specifying the minimum and maximum acceptable type I error. Specify NULL to return the full range of resulting type I error. Defaults to c(0, 1) to return all results.

minimum_power
a numeric between 0 and 1 specifying the minimum acceptable power. Specify NULL to return the full range of resulting power. Defaults to 0 to return all results.

w_type1
a user-specified weight on the type 1 error. Defaults to 1 for no weighting.

w_power
a user-specified weight on the power. Defaults to 1 for no weighting.

w_Nnull
a user-specified weight on the average sample size under the null. Defaults to 1 for no weighting.

w_Nalt
a user-specified weight on the average sample size under the alternative. Defaults to 1 for no weighting.

... ignored

Value

A list of length two containing details of the optimal efficiency and optimal accuracy designs

Examples

# Setting S = 50 and nsim = 50 for speed
# In practice you would want a much larger sample and more simulations

# One-sample case
set.seed(123)
cal_tbl1 <- calibrate_thresholds(
p_null = 0.1,
p_alt = 0.4,
n = seq(5, 15, 5),
N = 15,
pp_threshold = c(0.85, 0.9),
ppp_threshold = c(0.1, 0.2),
S = 10,
nsim = 10
)

optimize_design(cal_tbl1)

# Two-sample case
set.seed(456)
cal_tbl2 <- calibrate_thresholds(

p_null = c(0.1, 0.1),
p_alt = c(0.1, 0.5),
n = cbind(seq(5, 15, 5), seq(5, 15, 5)),
N = c(15, 15),
pp_threshold = c(0.8, 0.85),
ppp_threshold = c(0.2, 0.3),
delta = 0,
S = 10,
nsim = 10
)

optimize_design(cal_tbl2)

plot.calc_decision_rules

Plot method for calc_decision_rules objects

Description

Returns a plot of decision rules from the results of calc_decision_rules that can interactively show when to stop and when to proceed at the various interim analyses

Usage

## S3 method for class 'calc_decision_rules'
plot(x, plotly = TRUE, ...)

Arguments

x an object of class 'calc_decision_rules', usually returned by the calc_decision_rules function
plotly should the plot be rendered in plotly? (Default is TRUE)
...

Value

In the one-sample case, a heatmap plot with number enrolled on the x-axis and number of responses on the y-axis. In the two-sample case, a grid of heatmap plots. Each plot is a combination of the number enrolled so far in the experimental and control arms. The x-axis is the number of responses in the control arm and the y-axis is the number of responses in the experimental arm. Green indicates combinations where the trial would proceed and red indicates combinations where the trial would stop.
Examples

```r
set.seed(123)

# Two-sample case
dec_tbl <- calc_decision_rules(
  n = cbind(seq(5, 15, 5), seq(5, 15, 5)),
  N = c(15, 15),
  theta = 0.86,
  ppp = 0.2,
  p0 = NULL,
  direction = "greater",
  delta = 0,
  S = 50
)

plot(dec_tbl, plotly = FALSE)
```

Description

Returns two interactive plotly plots (if plotly=TRUE) or two static ggplot2 plots (if plotly=FALSE) to compare results from various designs generated from a call to `calibrate_thresholds` based on various criteria, and to assist in selecting an optimal design.

Usage

```r
## S3 method for class 'calibrate_thresholds'
plot(x, type1_range = c(0, 1), minimum_power = 0, plotly = FALSE, ...)
```

Arguments

- `x`: an object of class 'calibrate_thresholds', usually returned by the `calibrate_thresholds` function
- `type1_range`: a vector specifying the minimum and maximum acceptable type I error. Specify c(0, 1) to return the full range of resulting type I error. Defaults to c(0, 1)
- `minimum_power`: a numeric between 0 and 1 specifying the minimum acceptable power. Specify 0 to return the full range of resulting power. Defaults to 0.
- `plotly`: a logical indicator of whether you want the plots returned as interactive plotly plots or non-interactive ggplots. Defaults to FALSE.
- `...`: unused
Value

Plots of the average sample size under the null by the average sample size under the alternative, and the type I error by the power for designs meeting the specified type1_range and minimum_power.

Examples

# Setting S = 50 and nsim = 50 for speed
# In practice you would want a much larger sample and more simulations

set.seed(123)

# One-sample case
cal_tbl1 <- calibrate_thresholds(
  p_null = 0.1,
  p_alt = 0.4,
  n = seq(5, 15, 5),
  N = 15,
  pp_threshold = c(0.85, 0.9),
  ppp_threshold = c(0.1, 0.2),
  S = 10,
  nsim = 10
)

plot(cal_tbl1, type1_range = c(0.01, 0.2), minimum_power = 0.7)

print.calibrate_thresholds

Print method for calibrate_thresholds objects

Description

By default prints only the res_summary table from an object of class 'calibrate_thresholds'. The table can be limited to a range of type I error and a minimum value of power using the arguments 'type1_range' and 'minimum_power' respectively.

Usage

## S3 method for class 'calibrate_thresholds'
print(x, type1_range = c(0, 1), minimum_power = 0, ...)

Arguments

x an object of class 'calibrate_thresholds', usually returned by the calibrate_thresholds function

type1_range a vector specifying the minimum and maximum acceptable type I error. Specify c(0, 1) to return the full range of resulting type I error. Defaults to c(0, 1)
minimum_power a numeric between 0 and 1 specifying the minimum acceptable power. Specify 0 to return the full range of resulting power. Defaults to 0.

... ignored

Value

Returns a tibble

Examples

set.seed(123)

cal_tbl1 <- calibrate_thresholds(
p_null = 0.1,
p_alt = 0.4,
n = seq(5, 15, 5),
N = 15,
pp_threshold = c(0.85, 0.9),
ppp_threshold = c(0.1, 0.2),
S = 10,
nsim = 10
)

print(cal_tbl1)
print(cal_tbl1, type1_range = c(0.05, 0.1), minimum_power = 0.9)

# sim_dat1

Simulate a single dataset based on the response probability(ies), the total sample size(s), and the interim look schedule(s)

Description

Helper function for calibrate_thresholds() function that generates a single dataset of n and response count at each look based on the response probability(ies)

Usage

sim_dat1(p, n)

Arguments

p vector of length two containing the probability of event in the standard of care and experimental arm c(p0, p1) for the two-sample case; integer of event probability for one-sample case
matrix containing the total number of patients accrued so far at each interim look in the standard of care (column 1) and experimental (column 2) arms for two-sample case; vector of sample size accrued so far at each interim look for one-sample case. The last value should be equal to the total sample size at the end of the trial. If only a single look will be done at the end of the trial, this can be a vector specifying the total sample size c(N0, N1) for the two-sample case or an integer specifying the total sample size N for the one-sample case.

Value

Returns a tibble with n0, n1, y0, y1 for the two-sample case and a tibble with n1 and y1 for the one-sample case.

Description

This function is meant to be used in the context of a clinical trial with a binary endpoint. The goal is to simulate event counts from the binomial distribution based on the number of patients accrued at each interim look, and calculate the posterior predictive probability of success (or futility) at the end of a trial, given the data available at each interim analysis.

Usage

```r
sim_single_trial(
  p, 
  n, 
  p0, 
  N, 
  direction = "greater", 
  delta = NULL, 
  prior = c(0.5, 0.5), 
  S = 5000, 
  theta = 0.95 
)
```

Arguments

- `p` vector of length two containing the probability of event in the standard of care and experimental arm c(p0, p1) for the two-sample case; integer of event probability for one-sample case
- `n` matrix containing the total number of patients accrued so far at each interim look in the standard of care (column 1) and experimental (column 2) arms for two-sample case; vector of sample size accrued so far at each interim look for one-sample case. The last value should be equal to the total sample size at the end of the trial. If only a single look will be done at the end of the trial, this can
be a vector specifying the total sample size \(c(N_0, N_1)\) for the two-sample case or an integer specifying the total sample size \(N\) for the one-sample case.

\(p_0\)  
The target value to compare to in the one-sample case

\(N\)  
the total planned sample size at the end of the trial, \(c(N_0, N_1)\) for two-sample case; integer of total planned sample size at end of trial \(N\) for one-sample case

direction  
"greater" (default) if interest is in \(P(p_1 > p_0)\) and "less" if interest is in \(P(p_1 < p_0)\) for two-sample case. For one-sample case, "greater" if interest is in \(P(p > p_0)\) and "less" if interest is in \(P(p < p_0)\).

delta  
clinically meaningful difference between groups. Typically 0 for the two-sample case. NULL for the one-sample case (default).

\(prior\)  
hyperparameters of prior beta distribution. Beta(0.5, 0.5) is default

\(S\)  
number of samples, default is 5000

\(theta\)  
The target posterior probability. e.g. Efficacy decision if \(P(p_1 > p_0) > \theta\) for the two-sample case with greater direction. Default is 0.95. Can be a vector if interest is in selecting from among a variety of thresholds.

\section*{Value}

Returns a tibble with \(pp\_threshold\) (i.e. \(\theta\), the target posterior probability), number of responses, sample size, posterior probability, and posterior predictive probability at each look

\section*{Examples}

```r
set.seed(123)

# Setting S = 100 for speed, in practice you would want a much larger sample

# One-sample case
sim_single_trial(
  p = 0.3,  
n = c(5, 10),  
p0 = 0.1,  
N = 25,  
S = 100  
)

# Two-sample case
sim_single_trial(
  p = c(0.1, 0.3),  
n = cbind(c(5, 10), c(5, 10)),  
p0 = NULL,  
N = c(50, 50),  
delta = 0,  
S = 100  
)
```
**two_sample_cal_tbl**  
*Output from a two-sample call to calibrate_thresholds*

**Description**

This .rda file contains output from a two-sample call to calibrate_thresholds(). See the vignette titled "Two-sample randomized trial" for a description of the input parameters used, or run `two_sample_cal_tbl$inputs` to see a list of the original function inputs. For use in testing functions and in vignettes.

**Usage**

```r
data(two_sample_cal_tbl)
```

**Format**

A list containing a

1. a tibble 'res_summary' containing the posterior probability threshold (pp_threshold); the predictive probability threshold (ppp_threshold); the mean sample size under the null (mean_n0_null and mean_n1_null) and alternative (mean_n0_alt and mean_n1_alt) response rates; the proportion of positive trials under the null (prop_pos_null) and alternative (prop_pos_alt) response rates; and the proportion of trials stopped under the null (prop_stopped_null) and alternative (prop_stopped_alt) response rates.
2. 'call_list' containing the original function call
3. 'inputs' a list containing the inputs to the original function call

---

**two_sample_decision_tbl**  
*Output from a two-sample call to calc_decision_rules*

**Description**

This .rda file contains output from a two-sample call to calc_decision_rules(). See the vignette titled "Two-sample randomized trial" for a description of the input parameters used.

**Usage**

```r
data(two_sample_decision_tbl)
```

**Format**

A tibble containing n, the number of patients enrolled at each futility monitoring point; r, the number of responses at which we would stop the trial at a given look if the number of observed responses is <=r, or at the end of the trial the treatment is considered promising if the number of observed responses is >r; and ppp, the predictive probability at each given look
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