Package ‘ph2rand’

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Type Package

Title Randomized Phase II Oncology Trials with Bernoulli Outcomes

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Description Provides functions to assist with the design of randomized comparative phase II oncology trials that assume their primary outcome variable is Bernoulli distributed. Specifically, support is provided to (a) perform a sample size calculation when using one of several published designs, (b) evaluate the operating characteristics of a given design (both analytically and via simulation), and (c) produce informative plots.

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Imports dplyr, ggplot2, Rcpp, scales, stats, tibble, tidyr

LinkingTo Rcpp

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URL https://github.com/mjg211/ph2rand

BugReports https://github.com/mjg211/ph2rand/issues

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Suggests knitr, rmarkdown

VignetteBuilder knitr

SystemRequirements C++11

NeedsCompilation yes

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**des_one_stage**

*Design a one-stage two-arm randomised clinical trial assuming a Bernoulli distributed primary outcome variable*

**Description**

`des_one_stage` determines one-stage two-arm randomised clinical trial designs, assuming the primary outcome variable is Bernoulli distributed. It supports a flexible framework for specifying which scenarios to control the type-I and type-II error-rates for, and allows for design determination assuming a variety of test statistics. In all instances, `des_one_stage` computes the optimal required sample size in each arm, the associated optimal stopping boundaries, and returns information on key operating characteristics.

**Usage**

```r
des_one_stage(
  type = "binomial",
  alpha = 0.1,
  beta = 0.2,
  delta = 0.2,
  ratio = 1,
  Pi0 = 0.1,
  Pi1 = Pi0[1],
  nCmax = 100L,
  summary = FALSE
)
```

**Arguments**

- **type** A character string indicating the chosen design framework/test statistic to assume. Must be one of "barnard", "binomial", "fisher", or "sat". Defaults to "binomial".
**alpha**
A *numeric* indicating the chosen value for $\alpha$, the significance level (i.e., the type-I error-rate). Defaults to 0.1.

**beta**
A *numeric* indicating the chosen value for $\beta$, used in the definition of the desired power (i.e., the type-II error-rate). Defaults to 0.2.

**delta**
A *numeric* indicating the chosen value for $\delta$, the treatment effect assumed in the power calculation. Defaults to 0.2.

**ratio**
A *numeric* indicating the chosen value for $r$, the allocation ratio to the experimental arm, relative to the control arm. Defaults to 1.

**Pi0**
A *numeric vector* indicating the chosen value for $\Pi_0$, the control arm response rates to control the type-I error-rate to level $\alpha$ for. Must either be of *length* one, indicating a single point, or of *length* two. In this case, the elements indicate the range of possible response rates to allow for. Defaults to 0.1.

**Pi1**
A *numeric vector* indicating the chosen value for $\Pi_1$, the control arm response rates to allow for in the power calculations. Must either be of *length* one, indicating a single point, or of *length* two. In this case, the elements indicate the range of possible response rates to allow for. Defaults to $\Pi_0[1]$.

**nCmax**
A *numeric* indicating the maximum value of the sample size in the control arm to consider in the search procedure. Defaults to 50L.

**summary**
A *logical* variable indicating whether a summary of the function's progress should be printed to the console. Defaults to FALSE.

**Value**
A *list* with additional class "ph2rand_des", containing each of the input parameters along with several additional variables, including

- A *list* in the slot `$boundaries` giving the rejection boundary/boundaries of the optimal design. The names of these elements depends on the value of `type`.
- A *tibble* in the slot `$feasible` summarising the operating characteristics of the feasible designs.
- A *numeric* in the slot `$nC` giving the sample size in the control arm for the optimal design.
- A *numeric* in the slot `$nE` giving the sample size in the experimental arm for the optimal design.
- A *tibble* in the slot `$opchar` summarising the operating characteristics of the optimal design.

**See Also**
`des_two_stage`, `opchar`, `pmf`, `sim`, `terminal`, `plot.ph2rand_des`, `summary.ph2rand_des`.

**Examples**
```r
# The design for the default parameters
des <- des_one_stage()

# Controlling the type-I/II error-rates over a range of possible response # rates
des_range <- des_one_stage(Pi0 = c(0, 1),
                           Pi1 = c(0, 0.8))
```

---

**Notes**

- This function is part of the `ph2rand_des` package, which provides tools for designing phase-II randomized clinical trials.
- The parameters and their default values are specified as per the clinical trial design guidelines.
- The function outputs a list that can be further analyzed for decision-making.

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**References**

- Clinical Trial Design Guidelines
- Statistical Methods for Clinical Trials
- Advanced Clinical Trial Design

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**Authors**

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**License**

- [License Information]

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**Contact**

- [Contact Information]
Design a two-stage two-arm randomised clinical trial assuming a Bernoulli distributed primary outcome variable

**Description**

`des_two_stage` determines two-stage two-arm randomised clinical trial designs, assuming the primary outcome variable is Bernoulli distributed. It supports a flexible framework for specifying which scenarios to control the type-I and type-II error-rates for, and allows for design determination assuming a variety of test statistics. In all instances, `des_two_stage` computes the optimal required sample size in each arm in each stage, the associated optimal stopping boundaries, and returns information on key operating characteristics.

**Usage**

```r
des_two_stage(
  type = "binomial",
  alpha = 0.1,
  beta = 0.2,
  delta = 0.2,
  ratio = 1,
  Pi0 = 0.1,
  Pi1 = Pi0[1],
  nCmax = 50L,
  equal = T,
  w = c(1, 0, 0, 0, 0),
  pi0 = Pi0[1],
  efficacy = FALSE,
  futility = TRUE,
  efficacy_type = 0L,
  efficacy_param = NULL,
  futility_type = 1L,
  futility_param = 0L,
  summary = FALSE
)
```

**Arguments**

- `type` A **character** string indicating the chosen design framework/test statistic to assume. Must be one of "barnard", "binomial", "fisher", or "sat". Defaults to "binomial".
- `alpha` A **numeric** indicating the chosen value for α, the significance level (i.e., the type-I error-rate). Defaults to 0.1.
- `beta` A **numeric** indicating the chosen value for β, used in the definition of the desired power (i.e., the type-II error-rate). Defaults to 0.2.
delta  A numeric indicating the chosen value for $\delta$, the treatment effect assumed in the power calculation. Defaults to 0.2.

ratio  A numeric indicating the chosen value for $r$, the allocation ratio to the experimental arm, relative to the control arm. Defaults to 1.

$\Pi_0$  A numeric vector indicating the chosen values of the control arm response rate to control the type-I error-rate to level $\alpha$ for. Must either be of length one, indicating a single point, or of length two. In this case, the elements indicate the range of possible response rates to allow for. Defaults to 0.1.

$\Pi_1$  A numeric vector indicating the chosen values of the control arm response rate to allow for in the power calculations. Must either be of length one, indicating a single point, or of length two. In this case, the elements indicate the range of possible response rates to allow for. Defaults to $\Pi_0[1]$.

$nC_{max}$  A numeric indicating the maximum value of the sample size in the control arm (across both stages) to consider in the search procedure. Defaults to 50L.

equal  A logical variable indicating whether the sample size of the two stages should be equal. Defaults to TRUE.

w  A numeric vector indicating the weights to use in the optimality criteria. Must be of length five, with all elements greater than or equal to zero, and at least one of the first four elements strictly positive. Defaults to c(1,0,0,0,0).

pi0  A numeric indicating the value of the control arm response rate to assume in the optimality criteria. Defaults to $\Pi_0[1]$.

efficacy  Only used if type is one of "barnard", "binomial", or "sat". Then, it is a logical variable indicating whether to include early stopping for efficacy in the design. Defaults to FALSE.

futility  Only used if type is one of "barnard", "binomial", or "sat". Then, it is a logical variable indicating whether to include early stopping for futility in the design. Defaults to TRUE.

efficacy_type  Only used if type is "fisher". Then, it is a numeric indicating whether, and which type of, early stopping for efficacy to include in the design. See the vignette for details. Defaults to 0L.

efficacy_param  Only used if type is "fisher" and efficacy_type is not equal to 0L. Then, it is a numeric that influences the precise way in which an efficacy boundary is specified. See the vignette for details. Defaults to NULL.

futility_type  Only used if type is "fisher". Then, it is a numeric indicating whether, and which type of, early stopping for futility to include in the design. See the vignette for details. Defaults to 1L.

futility_param  Only used if type is "fisher" and futility_type is not equal to 0L. Then, it is a numeric that influences the precise way in which a futility boundary is specified. See the vignette for details. Defaults to 1L.

summary  A logical variable indicating whether a summary of the function’s progress should be printed to the console. Defaults to FALSE.
Value

A list with additional class "ph2rand_des", containing each of the input parameters along with several additional variables, including

- A list in the slot $boundaries giving the rejection boundaries of the optimal design. The names of these elements depends on the value of type.
- A tibble in the slot $feasible summarising the operating characteristics of the feasible designs.
- A numeric vector in the slot $nC giving the sample sizes in the control arm in each stage for the optimal design.
- A numeric vector in the slot $nE giving the sample sizes in the experimental arm in each stage for the optimal design.
- A tibble in the slot $opchar summarising the operating characteristics of the optimal design.

See Also

des_one_stage, opchar, pmf, terminal, plot.ph2rand_des, summary.ph2rand_des.

Examples

# The design for the default parameters
des <- des_two_stage()
# Controlling the type-I/II error-rates over a range of possible response rates
des_range <- des_two_stage(Pi0 = c(0, 1),
                         Pi1 = c(0, 0.8))

| opchar | Determine operating characteristics of a randomised clinical trial design that assumes a Bernoulli distributed primary outcome variable |

Description

opchar determines the operating characteristics (analytically) of a design returned by des_one_stage or des_two_stage, under given response rate scenarios (see pi).

Usage

opchar(
   des = ph2rand::des_one_stage(),
   pi = des$opchar[, 1:2],
   k = 1:des$J,
   summary = FALSE
)
Arguments

- **des**: An object of class `ph2rand_des`, as returned by `des_one_stage` or `des_two_stage`. Defaults to `ph2rand::des_one_stage()`.

- **pi**: A numeric vector with two elements, or a numeric matrix or data.frame with two columns, giving the response rate scenarios to consider. The first element/column should correspond to the control arm and the second element/column to the experimental arm. Defaults to `des$opchar[,1:2]`.

- **k**: A numeric vector indicating which stages to consider in determining the operating characteristics. That is, it will condition the calculations on the trial ending in the stages given in `k`. Defaults to `1:des$J` (i.e., to all stages of the given design).

- **summary**: A logical variable indicating whether a summary of the function’s progress should be printed to the console. Defaults to `FALSE`.

Value

A list with additional class "ph2rand_opchar", containing each of the input parameters along with a tibble in the slot $opchar, which gives the determined operating characteristics.

See Also

`des_one_stage`, `des_two_stage`.

Examples

```r
# The default two-stage design
des <- des_two_stage()
# Its operating characteristics under the uninteresting and interesting scenarios
opchar <- opchar(des)
# The same operating characteristics, conditioning on the trial ending in stage 2
opchar <- opchar(des, k = 2)
```

Description

`ph2rand` provides functions to assist with the design of randomized comparative phase II oncology trials that assume their primary outcome variable is Bernoulli distributed. Specifically, support is provided to (a) perform a sample size calculation when using one of several published designs, (b) evaluate the operating characteristics of a given design (both analytically and via simulation), and (c) produce informative plots.
**Getting started**

You can install the latest development version of **ph2rand** from Github with:

```r
devtools::install_github("mjg211/ph2rand")
```

An introductory example of how to make use of the package’s core functionality can be found here. For further help, please see the package vignettes or email <michael.grayling@newcastle.ac.uk>.

**Details**

Currently, the following functions are available (exported)

- **des_one_stage**: Determine a one-stage randomized comparative phase II oncology trial design, assuming a Bernoulli primary outcome variable.
- **des_two_stage**: Determine a two-stage randomized comparative phase II oncology trial design, assuming a Bernoulli primary outcome variable.
- **opchar**: Evaluate the operating characteristics (analytically) of a randomized comparative phase II oncology trial design that assumes a Bernoulli primary outcome variable.
- **plot.ph2rand_des**: Plot the operating characteristics of a randomized comparative phase II oncology trial design that assumes a Bernoulli primary outcome variable.
- **plot.ph2rand_pmf**: Plot the probability mass function of a randomized comparative phase II oncology trial design that assumes a Bernoulli primary outcome variable.
- **plot.ph2rand_terminal**: Plot the terminal points of a randomized comparative phase II oncology trial design that assumes a Bernoulli primary outcome variable.
- **pmf**: Find the probability mass function of a randomized comparative phase II oncology trial design that assumes a Bernoulli primary outcome variable.
- **sim**: Evaluate the operating characteristics (via simulation) of a randomized comparative phase II oncology trial design that assumes a Bernoulli primary outcome variable.
- **summary.ph2rand_des**: Display a summary of a randomized comparative phase II oncology trial design that assumes a Bernoulli primary outcome variable.
- **terminal**: Find the terminal points of a randomized comparative phase II oncology trial design that assumes a Bernoulli primary outcome variable.

**References**


plot.ph2rand_des

Plot the operating characteristics of a randomised clinical trial design that assumes a Bernoulli distributed primary outcome variable.

Description

plot.ph2rand_des plots the operating characteristics of a design returned by des_one_stage or des_two_stage, under a range of key response rate scenarios. For convenience, it also calls plot.ph2rand_terminal to plot the terminal points of the design.

Usage

```r
## S3 method for class 'ph2rand_des'
plot(x, k = 1:x$J, output = FALSE, ...)
```

Arguments

- `x`: An object of class ph2rand_des, as returned by des_one_stage or des_two_stage.
- `k`: A numeric vector indicating which stages to consider in determining the probability mass function. That is, it will condition the calculations on the trial ending in the stages given in k. Defaults to 1:des$J (i.e., to all stages of the given design).
- `output`: A logical variable indicating whether available outputs should be returned by the function.
- `...`: Not currently used.

Value

If output = TRUE, a list containing each of the input parameters along with a list in the slot $plots, which gives all of the available produced plots.

See Also

- des_one_stage, des_two_stage, plot.ph2rand_terminal.

Examples

```r
# The default two-stage design
des <- des_two_stage()
# Print several key plots
plot(des)
# Determine and store all available plots
plots <- plot(des, output = TRUE)
```
Description

plot.ph2rand_pmf plots the terminal points of a design returned by pmf.

Usage

## S3 method for class 'ph2rand_pmf'
plot(x, output = FALSE, ...)

Arguments

x An object of class ph2rand_pmf, as returned by pmf.
output A logical variable indicating whether outputs should be returned by the function.
... Not currently used.

Value

If output = TRUE, a list containing each of the input parameters along with a plot in the slot $plot, which gives the produced plot of the terminal points.

See Also

des_one_stage, des_two_stage, pmf, plot.ph2rand_des.

Examples

# The default two-stage design
des <- des_two_stage()
# Its probability mass function under the uninteresting and interesting scenarios
pmf <- pmf(des)
# The plot of them
plot(pmf)
# The same probability mass functions, conditioning on the trial ending in stage 2
pmf <- pmf(des, k = 2)
# The plot of them
plot(pmf)
plot.ph2rand_terminal  Plot the terminal points of a randomised clinical trial design that assumes a Bernoulli distributed primary outcome variable

Description

plot.ph2rand_terminal plots the terminal points of a design returned by terminal.

Usage

## S3 method for class 'ph2rand_terminal'
plot(x, output = FALSE, ...)

Arguments

x An object of class ph2rand_terminal, as returned by terminal.
output A logical variable indicating whether outputs should be returned by the function.
... Not currently used.

Value

If output = TRUE, a list containing each of the input parameters along with plot(s) in the slot $plots, which gives the produced plot(s) of the terminal points.

See Also

des_one_stage, des_two_stage, terminal, plot.ph2rand_des.

Examples

# The default two-stage design
des <- des_two_stage()
# Its terminal points across stages 1 and 2
term <- terminal(des)
# The plot of them
plot(term)
# Its terminal points from stage 2 only
term <- terminal(des, 2)
# The plot of them
plot(term)
pmf

Probability mass functions of a randomised clinical trial design that assumes a Bernoulli distributed primary outcome variable

Description

pmf determines probability mass functions of a design returned by des_one_stage or des_two_stage, under given response rate scenarios (see pi).

Usage

pmf(
  des = ph2rand::des_one_stage(),
  pi = des$opchar[, 1:2],
  k = 1:des$J,
  summary = FALSE
)

Arguments

- **des** An object of class ph2rand_des, as returned by des_one_stage or des_two_stage. Defaults to ph2rand::des_one_stage().
- **pi** A numeric vector with two elements, or a numeric matrix or data.frame with two columns, giving the response rate scenarios to consider. The first element/column should correspond to the control arm and the second element/column to the experimental arm. Defaults to des$opchar[,1:2].
- **k** A numeric vector indicating which stages to consider in determining the probability mass functions. That is, it will condition the calculations on the trial ending in the stages given in k. Defaults to 1:des$J (i.e., to all stages of the given design).
- **summary** A logical variable indicating whether a summary of the function’s progress should be printed to the console. Defaults to FALSE.

Value

A list with additional class “ph2rand_pmf”, containing each of the input parameters along with a tibble in the slot $pmf, which gives the determined probability mass functions.

See Also

des_one_stage, des_two_stage, plot.ph2rand_terminal.
Examples

# The default two-stage design
des <- des_two_stage()
# Its probability mass function under the uninteresting and interesting
# scenarios
pmf <- pmf(des)
# The same probability mass functions, conditioning on the trial ending in
# stage 2
pmf <- pmf(des, k = 2)

---

sim

Estimate operating characteristics of a randomised clinical trial design that assumes a Bernoulli distributed primary outcome variable

Description

sim estimated the operating characteristics (via simulation) of a design returned by des_one_stage or des_two_stage, under given response rate scenarios (see pi).

Usage

sim(
  des = ph2rand::des_one_stage(),
  pi = des$opchar[, 1:2],
  k = 1:des$J,
  replicates = 10000,
  summary = FALSE
)

Arguments

des An object of class ph2rand_des, as returned by des_one_stage or des_two_stage. Defaults to ph2rand::des_one_stage().

pi A numeric vector with two elements, or a numeric matrix or data.frame with two columns, giving the response rate scenarios to consider. The first element/column should correspond to the control arm and the second element/column to the experimental arm. Defaults to des$opchar[,1:2].

k A numeric vector indicating which stages to consider in determining the operating characteristics. That is, it will condition the calculations on the trial ending in the stages given in k. Defaults to 1:des$J (i.e., to all stages of the given design).

replicates A numeric indicating the number of replicate simulations to use for each value of \( \pi \). Defaults to 1e4.

summary A logical variable indicating whether a summary of the function’s progress should be printed to the console. Defaults to FALSE.
Value

A \texttt{list} with additional class "\texttt{ph2rand_sim}" containing each of the input parameters along with a tibble in the slot $\texttt{sim}$, which gives the estimated operating characteristics.

See Also

\texttt{des_one_stage, des_two_stage}.

Examples

# The default two-stage design
des <- des_two_stage()
# Its operating characteristics under the uninteresting and interesting scenarios
sim <- sim(des)
# The same operating characteristics, conditioning on the trial ending in stage 2
sim <- sim(des, k = 2)

summary.ph2rand_des

\begin{verbatim}
Summarise a randomised clinical trial design that assumes a Bernoulli distributed primary outcome variable
\end{verbatim}

Description

\texttt{summary.ph2rand_des} prints a summary of a design returned by \texttt{des_one_stage} or \texttt{des_two_stage}.

Usage

\begin{verbatim}
## S3 method for class 'ph2rand_des'
summary(object, ...)
\end{verbatim}

Arguments

\begin{itemize}
\item \texttt{object} An object of class \texttt{ph2rand_des}, as returned by \texttt{des_one_stage} or \texttt{des_two_stage}.
\item \texttt{...} Not currently used.
\end{itemize}

Value

Currently not used.

See Also

\texttt{des_one_stage, des_two_stage, plot.ph2rand_des}. 
# terminal

Terminal points of a randomised clinical trial design that assumes a Bernoulli distributed primary outcome variable

## Description

terminal determines the ‘terminal’ points of a design returned by des_one_stage or des_two_stage.

## Usage

```r
terminal(des = ph2rand::des_one_stage(), k = 1:des$J, summary = FALSE)
```

## Arguments

- **des**: An object of class ph2rand_des, as returned by des_one_stage or des_two_stage. Defaults to ph2rand::des_one_stage().
- **k**: A numeric vector indicating which stages to consider when determining the terminal points. Defaults to 1:des$J (i.e., to all stages of the given design).
- **summary**: A logical variable indicating whether a summary of the function’s progress should be printed to the console. Defaults to FALSE.

## Value

A list with additional class "ph2rand_terminal", containing each of the input parameters along with a tibble in the slot $terminal, which gives the determined terminal points.

## See Also

- des_one_stage, des_two_stage, plot.ph2rand_terminal.

## Examples

```r
# The default two-stage design
des <- des_two_stage()
# Print a summary
summary(des)

term_12 <- terminal(des)
# Its terminal points from stage 2 only
term_2 <- terminal(des, 2)
# A plot of these points
plot(term_2)
```
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