Package ‘gscounts’

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Type Package

Title Group Sequential Designs with Negative Binomial Outcomes

Version 0.1-1

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Description Design and analysis of group sequential designs with negative binomial outcomes, as described by T Muetze, E Glimm, H Schmidli, T Friede (2017) <arXiv:1707.04612>.

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Imports stats, Rcpp(>= 0.12.9)

Suggests testthat, MASS, knitr, rmarkdown, dplyr, gsDesign, mvtnorm

License GPL (>= 2)

NeedsCompilation yes

URL https://github.com/tobiasmuetze/gscounts

BugReports https://github.com/tobiasmuetze/gscounts/issues

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**Group sequential design with negative binomial outcomes**

**Description**

Design a group sequential trial with negative binomial outcomes

**Usage**

```r
design_gsnb(rate1, rate2, dispersion, ratio_H0 = 1, random_ratio = 1, power, sig_level, timing, esf = obrien, esf_futility = NULL, futility = NULL, t_recruit1 = NULL, t_recruit2 = NULL, study_period = NULL, accrual_period = NULL, followup_max = NULL, ...)
```

**Arguments**

- `rate1`: numeric; assumed rate of treatment group 1 in the alternative
- `rate2`: numeric; assumed rate of treatment group 2 in the alternative
- `dispersion`: numeric; dispersion (shape) parameter of negative binomial distribution
- `ratio_H0`: numeric; positive number denoting the rate ratio \( \text{rate}_1/\text{rate}_2 \) under the null hypothesis, i.e. the non-inferiority or superiority margin
- `random_ratio`: numeric; randomization ratio \( n_1/n_2 \)
- `power`: numeric; target power of group sequential design
- `sig_level`: numeric vector; \( 0 < \text{timing}[1] < \ldots < \text{timing}[K] = 1 \) with \( K \) the number of analyses, i.e. \( (K-1) \) interim analyses and final analysis
- `esf`: function; error spending function
- `esf_futility`: function; futility error spending function
- `futility`: character; either "binding", "nonbinding", or NULL for binding, nonbinding, or no futility boundaries
- `t_recruit1`: numeric vector; recruit (i.e. study entry) times in group 1
- `t_recruit2`: numeric vector; recruit (i.e. study entry) times in group 2
- `study_period`: numeric; study duration
- `accrual_period`: numeric; accrual period
- `followup_max`: numeric; maximum exposure time of a patient
- `...`: further arguments to be passed to the error spending function
**design_gsnb**

**Value**

A list with class "gsnb" containing the following components:

- `rate1` as input
- `rate2` as input
- `dispersion` as input
- `power` as input
- `timing` as input
- `ratio_H0` as input
- `ratio_H1` as input
- `sig_level` as input
- `random_ratio` as input
- `power_fix` as input
- `expected_info` list; expected information under `ratio_H0` and `ratio_H1`
- `efficacy` list; contains the elements `esf` (type I error spending function), `spend` (type I error spend at each look), and `critical` (critical value for efficacy testing)
- `futility` list; only part of the output if argument `futility` is defined in the input. Contains the elements `futility` (input argument `futility`), `esf` (type II error spending function), `spend` (type II error spend at each look), and `critical` (critical value for futility testing)
- `stop_prob` list; contains the element `efficacy` with the probabilities for stopping for efficacy and, if `futility` bounds are calculated, the element `futility` with the probabilities for stopping for futility

- `t_recruit1` as input
- `t_recruit2` as input
- `study_period` as input
- `followup_max` as input
- `max_info` maximum information
- `calendar` calendar times of data looks; only calculated when exposure times are not identical

**Examples**

```r
# Calculate the sample sizes for a given accrual period and study period (without futility)
out <- design_gsnb(rate1 = 0.0875, rate2 = 0.125, dispersion = 5,
                   power = 0.8, timing = c(0.5, 1), esf = obrien,
                   ratio_H0 = 1, sig_level = 0.025,
                   study_period = 3.5, accrual_period = 1.25, random_ratio = 1)
out

# Calculate the sample sizes for a given accrual period and study period with binding futility
out <- design_gsnb(rate1 = 0.0875, rate2 = 0.125, dispersion = 5,
                   power = 0.8, timing = c(0.5, 1), esf = obrien,
                   ratio_H0 = 1, sig_level = 0.025, study_period = 3.5,
```
design_nb

Clinical trials with negative binomial outcomes

Description
Design a clinical trial with negative binomial outcomes

Usage

```r
design_nb(rate1, rate2, dispersion, power, ratio_H0 = 1, sig_level, random_ratio = 1, t_recruit1 = NULL, t_recruit2 = NULL, study_period = NULL, accrual_period = NULL, followup_max = NULL)
```

Arguments

- `rate1` numeric; assumed rate of treatment group 1 in the alternative
- `rate2` numeric; assumed rate of treatment group 2 in the alternative
- `dispersion` numeric; dispersion (shape) parameter of negative binomial distribution
- `power` numeric; target power
- `ratio_H0` numeric; positive number denoting the rate ratio rate_1/rate_2 under the null hypothesis, i.e. the non-inferiority or superiority margin
- `sig_level` numeric; Type I error / significance level
- `random_ratio` numeric; randomization ratio n1/n2
- `t_recruit1` numeric vector; recruit (i.e. study entry) times in group 1
- `t_recruit2` numeric vector; recruit (i.e. study entry) times in group 2
- `study_period` numeric; study duration
- `accrual_period` numeric; accrual period
- `followup_max` numeric; maximum exposure time of a patient
**Value**

A list containing the following components:

- `rate1` as input
- `rate2` as input
- `dispersion` as input
- `power` as input
- `ratio_H0` as input
- `ratio_H1` = `rate1/rate2`
- `sig_level` as input
- `random_ratio` as input
- `t_recruit1` as input
- `t_recruit2` as input
- `study_period` as input
- `followup_max` as input
- `max_info` = maximum information

**Examples**

```r
# Calculate sample size for given accrual period and study duration assuming uniform accrual
out <- design_nb(rate1 = 0.0875, rate2 = 0.125, dispersion = 5, power = 0.8,
                 ratio_H0 = 1, sig_level = 0.025,
                 study_period = 4, accrual_period = 1, random_ratio = 2)
out

# Calculate sample size for a fixed exposure time of 0.5 years
out <- design_nb(rate1 = 4.2, rate2 = 8.4, dispersion = 3, power = 0.8,
                 ratio_H0 = 1, sig_level = 0.025,
                 followup_max = 0.5, random_ratio = 2)
out

# Calculate study period for given recruitment time
out <- design_nb(rate1 = 0.0875, rate2 = 0.125, dispersion = 5, power = 0.8,
                 ratio_H0 = 1, sig_level = 0.025,
                 t_recruit1 = t_recruit1, t_recruit2 = t_recruit2)
```
get_calendartime_gsnb  

Calendar time of data looks

Description

Calculate the calendar time of looks given the information time

Usage

get_calendartime_gsnb(rate1, rate2, dispersion, t_recruit1, t_recruit2, timing, 
followup1, followup2)

Arguments

rate1  numeric; rate in treatment group 1
rate2  numeric; rate in treatment group 2
dispersion numeric; dispersion (shape) parameter of negative binomial distribution
t_recruit1 numeric vector; recruit (i.e. study entry) times in group 1
t_recruit2 numeric vector; recruit (i.e. study entry) times in group 2
timing numeric vector with entries in (0,1]; information times of data looks
followup1 numeric vector; final individual follow-up times in treatment group 1
followup2 numeric vector; final individual follow-up times in treatment group 2

Value

numeric; vector with calendar time of data looks

Examples

# Calendar time at which 50%, 75%, and 100% of the maximum information is attained
# 100 subjects in each group are recruited uniformly over 1.5 years
# Study ends after two years, i.e. follow-up times vary between 2 and 0.5 years
get_calendartime_gsnb(rate1 = 0.1, 
rate2 = 0.125, 
dispersion = 5, 
t_recruit1 = seq(0, 1.5, length.out = 100),
t_recruit2 = seq(0, 1.5, length.out = 100),
timing = c(0.5, 0.75, 1),
followup1 = seq(2, 0.5, length.out = 100),
followup2 = seq(2, 0.5, length.out = 100))
get_info_gsnb

Information level for log rate ratio

Description
Calculates the information level for the log rate ratio of the negative binomial model.

Usage
get_info_gsnb(rate1, rate2, dispersion, followup1, followup2)

Arguments
- rate1: numeric; rate in treatment group 1
- rate2: numeric; rate in treatment group 2
- dispersion: numeric; dispersion (shape) parameter of negative binomial distribution
- followup1: numeric vector; individual follow-up times in treatment group 1
- followup2: numeric vector; individual follow-up times in treatment group 2

Value
numeric; information level

Examples
# Calculates information level for case of 10 subjects per group
# Follow-up times of subjects in each group range from 1 to 3
get_info_gsnb(rate1 = 0.1,
              rate2 = 0.125,
              dispersion = 4,
              followup1 = seq(1, 3, length.out = 10),
              followup2 = seq(1, 3, length.out = 10))

gscounts

gscounts

Description
Design and monitoring of group sequential designs with negative binomial data.

Author(s)
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### hospitalizations

**Description**

A dataset containing the hospitalization times of 1980 patients:

**Usage**

`data(hospitalizations)`

**Format**

A data frame with 2323 rows and 4 variables

**Details**

- `treatment`. Treatment identifier.
- `t_recruit`. Recruitment time of patient into the clinical trial.
- `eventtime`. Event time of hospitalization. NA corresponds to no event.

---

### obrien

**Description**

Error spending function mimicking O'Brien & Fleming critical values

**Usage**

`obrien(t, sig_level, ...)`

**Arguments**

- `t` numeric; Non-negative information ratio
- `sig_level` numeric; significance level
- `...` optional arguments

**Value**

numeric

**Examples**

# O'Brien-Fleming-type error spending function
`obrien(t = c(0.5, 1), sig_level = 0.025)"
Description

Error spending function mimicking Pococks critical values

Usage

pocock(t, sig_level, ...)

Arguments

t numeric; Non-negative information ratio
sig_level numeric; significance level
... optional arguments

Value

numeric

Examples

# Pocock-type error spending function
pocock(t = c(0.5, 1), sig_level = 0.025)

Description

print method for instance of class gsnb

Usage

## S3 method for class 'gsnb'
print(x, ...)

Arguments

x an object of class gsnb
... optional arguments to print or plot methods
Description

print method for instance of class nb

Usage

```r
## S3 method for class 'nb'
print(x, ...)
```

Arguments

- `x`: an object of class nb
- `...`: optional arguments to print or plot methods
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