Package ‘gscounts’

October 13, 2022

Type Package
Title Group Sequential Designs with Negative Binomial Outcomes
Version 0.1-4
Maintainer Tobias Mütze <tobias.muetze@outlook.com>
Depends R (>= 3.0.0)
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
VignetteBuilder knitr
LazyData true
LinkingTo Rcpp
Encoding UTF-8
RoxygenNote 7.1.2
Author Tobias Mütze [aut, cre] (<https://orcid.org/0000-0002-4111-1941>)
Repository CRAN
Date/Publication 2021-11-02 08:10:04 UTC

R topics documented:

design_gsnb .................................................. 2
design_nb .................................................. 5
get_calendartime_gsnb ..................................... 7
get_info_gsnb .............................................. 8
design_gsnb

Group sequential design with negative binomial outcomes

Description

Design a group sequential trial with negative binomial outcomes

Usage


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,  
  accrual_speed = 1,  
  ...
)  

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 $\mu_1/\mu_2$ under the null hypothesis, i.e. the non-inferiority or superiority margin
random_ratio numeric; randomization ratio n1/n2
power numeric; target power of group sequential design
sig_level numeric; Type I error / significance level
timing numeric vector; 0 < timing[1] < ... < timing[K] = 1 with K the number of analyses, i.e. (K-1) interim analyses and final analysis. When the timing of efficacy and futility analyses differ, timing should not be defined. Instead, the arguments timing_eff and timing_fut have to be used to specify the timing of the efficacy and futility analyses, respectively.
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; to be set when follow-up times are not identical between subjects, NULL otherwise
accrual_period numeric; accrual period
followup_max numeric; maximum exposure time of a subject; to be set when follow-up times are to be equal for each subject, NULL otherwise
accrual_speed numeric; determines accrual speed; values larger than 1 result in accrual slower than linear; values between 0 and 1 result in accrual faster than linear.
... further arguments. Will be passed to the error spending function.

Details

Denote $\mu_1$ and $\mu_2$ the event rates in treatment groups 1 and 2. This function considers smaller event rates to be better. The statistical hypothesis testing problem of interest is

$$H_0 : \frac{\mu_1}{\mu_2} \geq \delta \text{ vs. } H_1 : \frac{\mu_1}{\mu_2} < \delta,$$

with $\delta = \text{ratio}_H_0$. Non-inferiority of treatment group 1 compared to treatment group 2 is tested for $\delta \in (1, \infty)$. Superiority of treatment group 1 over treatment group 2 is tested for $\delta \in (0, 1]$. The calculation of the efficacy and (non)-binding futility boundaries are performed under the hypothesis $H_0 : \frac{\mu_1}{\mu_2} = \delta$ and under the alternative $H_1 : \frac{\mu_1}{\mu_2} = \frac{\text{rate}_1}{\text{rate}_2}$.

The argument 'accrual_speed' is used to adjust the accrual speed. Number of subjects in the study at study time $t$ is given by $f(t) = a * t^b$ with $a = n/\text{accrual_period}$ and $b = \text{accrual_speed}$. For linear recruitment, $b = 1$. $b > 1$ results is slower than linear recruitment for $t < \text{accrual_period}$ and faster than linear recruitment for $t > \text{accrual_period}$. Vice verse for $b < 1$.

Value

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

rate1 as input
rate2 as input
dispersion as input
design_power as input
timing as input
ratio_H0 as input
ratio_H1 as input
ratio rate1/rate2
sig_level as input
random_ratio as input
power_fix power of fixed design
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

References


Examples

# 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,
                   accrual_period = 1.25, random_ratio = 1, futility = "binding",
                   futility = "binding",
                   study_period = 3.5, accrual_period = 1.25, random_ratio = 1)
```r
# Calculate study period for given recruitment times
expose <- seq(0, 1.25, length.out = 1042)
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, t_recruit1 = expose,
                   t_recruit2 = expose, random_ratio = 1)
out

# Calculate sample size for a fixed exposure time
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,
                   followup_max = 0.5, random_ratio = 1)

# Different timing for efficacy and futility analyses
out <- design_gsnb(rate1 = 1, rate2 = 2, dispersion = 5,
                   power = 0.8, esf = obrien,
                   ratio_H0 = 1, sig_level = 0.025, study_period = 3.5,
                   accrual_period = 1.25, random_ratio = 1, futility = "binding",
                   esf_futility = pocock,
                   timing_eff = c(0.8, 1),
                   timing_fut = c(0.2, 0.5, 1))
```

---

**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,
  esf_futility = obrien)
```

accrual_speed = 1
)

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
accrual_speed numeric; determines accrual speed; values larger than 1 result in accrual slower than linear; values between 0 and 1 result in accrual faster than linear.

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 ratio rate_1/rate_2
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

# Calculate sample size for given accrual period and study duration assuming uniformal accrual
out <- design_nb(rate1 = 0.0875, rate2 = 0.125, dispersion = 5, power = 0.8,
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,
followup_max = 0.5, random_ratio = 2)
out

# Calculate study period for given recruitment time
t_recruit1 <- seq(0, 1.25, length.out = 1200)
t_recruit2 <- seq(0, 1.25, length.out = 800)
out <- design_nb(rate1 = 0.0875, rate2 = 0.125, dispersion = 5, power = 0.8,
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
get_info_gsnb

- **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**

```r
# 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**

```r
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

```r
# 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))
```

---

gcounts

Description

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

Author(s)

Tobias Muetze <tobias.muetze@outlook.com>

---

hospitalizations

Description

A dataset containing the hospitalization times of 1980 patients:

Usage

```r
data(hospitalizations)
```

Format

A data frame with 2323 rows and 4 variables

Details

- treatment. Treatment identifier.
- pat. Patient identifier. Unique within treatment
- t_recruit. Recruitment time of patient into the clinical trial.
- eventtime. Event time of hospitalization. NA corresponds to no event.
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 Pocock's 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)

print.gsnb

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

print.nb

Description

print method for instance of class nb

Usage

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

Arguments

x an object of class nb
...
optional arguments to print or plot methods
Index

* datasets
  hospitalizations, 9

  design_gsnb, 2
  design_nb, 5

  get_calendartime_gsnb, 7
  get_info_gsnb, 8
  gscounts, 9

  hospitalizations, 9

  obrien, 10

  pocock, 10
  print_gsnb, 11
  print_nb, 11