Package 'bfboin'

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Type Package

Title Operating Characteristics for the Bayesian Optimal Interval Design with Back Filling

Version 0.1.0

Description Calculate the operating characteristics of the Bayesian Optimal Interval with Back Filling Design for dose escalation in early-phase oncology trials.

License GPL (>= 3)

Encoding UTF-8

RoxygenNote 7.3.1

Imports BOIN, purrr

Suggests knitr, rmarkdown, testthat (>= 3.0.0), tidyr, dplyr

Config/testthat/edition 3

VignetteBuilder knitr

URL https://openpharma.github.io/bfboin/

NeedsCompilation no

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Repository CRAN

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Contents

get.oc.bf *Get Operating Characteristics for the BF-BOIN Design*

Description

Get Operating Characteristics for the BF-BOIN Design

Usage

```
get.oc.bf(
  ntrial = 1000,
  seed = 3262,
  target = 0.25,
  p.true = c(0.1, 0.3, 0.5),
  ncohort = 10,
  cohortsize = 3,
  n.earlystop = 100,
  startdose = 1,
  titration = FALSE,
  p.saf = 0.6 * target,
  p.tox = 1.4 * target,
  cutoff.eli = 0.95,
  extrasafe = FALSE,
  offset = 0.05,
  boundMTD = FALSE,
  n.cap = 12,
  end.backfill = TRUE,
  n.per.month = 3,
  dlt.window = 1,
  p.response.true = c(1, 1, 1),
  three.plus.three = FALSE,
  accrual = "uniform",
  backfill.assign = "highest"
)
```

Arguments

ntrial	the total number of trials to be simulated
seed	the random number seed for simulation
target	the target DLT rate
p.true	a vector containing the true toxicity probabilities of the investigational dose levels.
ncohort	the total number of cohorts
cohortsize	the cohort size

n.earlystop	the early stopping parameter. If the number of patients treated at the current dose reaches n.earlystop, stop the trial and select the MTD based on the observed data. The default value n.earlystop=100 essentially turns off this type of early stopping.
startdose	the starting dose level for the trial
titration	set titration=TRUE to perform dose escalation with cohort size = 1 to accelerate dose escalation at the begining of the trial.
p.saf	the highest toxicity probability that is deemed subtherapeutic (i.e. below the MTD) such that dose escalation should be undertaken. The default value is p.saf=0.6*target.
p.tox	the lowest toxicity probability that is deemed overly toxic such that deescalation is required. The default value is p.tox=1.4*target).
cutoff.eli	the cutoff to eliminate an overly toxic dose for safety. We recommend the default value of (cutoff.eli=0.95) for general use.
extrasafe	set extrasafe=TRUE to impose a more stringent stopping rule
offset	a small positive number (between 0 and 0.5) to control how strict the stopping rule is when extrasafe=TRUE. A larger value leads to a more strict stopping rule. The default value offset=0.05 generally works well.
boundMTD	set boundMTD=TRUE to impose the condition: the isotonic estimate of toxicity probability for the selected MTD must be less than de-escalation boundary.
n.cap	permanently close a dose for backfilling if the number of patients assigned to the dose reaches n.cap
end.backfill	when the dose escalation ends, the backfilling by definition also ends. Default is TRUE.
n.per.month	patient accrual rate per month
dlt.window	DLT assessment window (months)
p.response.true	a vector containing the true response probabilities of the investigational dose levels
three.plus.three	modify the decision from de-escalation to stay when observing 1 DLT out of 3 patients
accrual	"uniform" or "poisson", according to whether accrual distribution is uniform (consistent with Shiny App) or a Poisson process (consistent with publication)
backfill.assign	How to assign backfill dose given the open backfill doses. Options are "highest" (default), "lowest", or "random".

Value

get.oc.bf() returns the operating characteristics of the BOIN design as a list, including: (1) selection percentage at each dose level ($selpercent), (2) the average number of patients treated at each dose level ($npatients), (3) the percentage of patients treated at each dose level on average ($percentpatients), (4) the average number of toxicities observed at each dose level ($ntox), (5) the average number of toxicities in total ($totaltox), (6) the average number of patients in total($totaln), (7) the percentage of early stopping without selecting the MTD ($percentstop), (8) the average duration of the trial (duration).

References

Zhao Y, Yuan Y, Korn EL, Freidlin B. Backfilling patients in phase I dose-escalation trials using Bayesian optimal interval design (BOIN). Clinical Cancer Research. 2024 Feb 16;30(4):673-9.

See Also

Shiny app: https://biostatistics.mdanderson.org/shinyapps/BF-BOIN/

Examples

```
get.oc.bf(ntrial = 1000,
          seed = 9,
          target = 0.25,
          p.true = c(0.1, 0.5),
          ncohort = 10,
          cohortsize = 3,
          n.earlystop = 9,
          startdose = 1,
          titration = FALSE,
          cutoff.eli = 0.95,
          extrasafe = TRUE,
          offset = 0.1,
          boundMTD=FALSE,
          n.cap = 12,
          end.backfill = TRUE,
          n.per.month = 1,
          dlt.window = 1,
          p.response.true = c(0.001, 0.001))
```

`sim.one.trial` *Simulate one BF-BOIN trial*

Description

Simulate one BF-BOIN trial

Usage

```
sim.one.trial(
  trial.id = 1,
  target = 0.25,
  p.true = c(0.1, 0.3, 0.5),
  ncohort = 10,
  cohortsize = 3,
  n.earlystop = 100,
```

```
  startdose = 1,
  titration = FALSE,
  p.saf = 0.6 * target,
  p.tox = 1.4 * target,
  cutoff.eli = 0.95,
  extrasafe = FALSE,
  offset = 0.05,
  boundMTD = FALSE,
  n.cap = 12,
  end.backfill = TRUE,
  n.per.month = 3,
  dlt.window = 1,
  p.response.true = c(1, 1, 1),
  three.plus.three = FALSE,
  accrual = "uniform",
  backfill.assign = "highest"
)
```

Arguments

`trial.id`	an ID for the trial
`target`	the target DLT rate
`p.true`	a vector containing the true toxicity probabilities of the investigational dose levels.
`ncohort`	the total number of cohorts
`cohortsize`	the cohort size
`n.earlystop`	the early stopping parameter. If the number of patients treated at the current dose reaches `n.earlystop`, stop the trial and select the MTD based on the observed data. The default value `n.earlystop=100` essentially turns off this type of early stopping.
`startdose`	the starting dose level for the trial
`titration`	set `titration=TRUE` to perform dose escalation with cohort size = 1 to accelerate dose escalation at the begining of the trial.
`p.saf`	the highest toxicity probability that is deemed subtherapeutic (i.e. below the MTD) such that dose escalation should be undertaken. The default value is `p.saf=0.6*target`.
`p.tox`	the lowest toxicity probability that is deemed overly toxic such that deescalation is required. The default value is `p.tox=1.4*target`).
`cutoff.eli`	the cutoff to eliminate an overly toxic dose for safety. We recommend the default value of (`cutoff.eli=0.95`) for general use.
`extrasafe`	set `extrasafe=TRUE` to impose a more stringent stopping rule
`offset`	a small positive number (between `0` and `0.5`) to control how strict the stopping rule is when `extrasafe=TRUE`. A larger value leads to a more strict stopping rule. The default value `offset=0.05` generally works well.

boundMTD	set boundMTD=TRUE to impose the condition: the isotonic estimate of toxicity probability for the selected MTD must be less than de-escalation boundary.
n.cap	permanently close a dose for backfilling if the number of patients assigned to the dose reaches n.cap
end.backfill	when the dose escalation ends, the backfilling by definition also ends. Default is TRUE.
n.per.month	patient accrual rate per month
dlt.window	DLT assessment window (months)
p.response.true	a vector containing the true response probabilities of the investigational dose levels
three.plus.three	modify the decision from de-escalation to stay when observing 1 DLT out of 3 patients
accrual	"uniform" or "poisson", according to whether accrual distribution is uniform (consistent with Shiny App) or a Poisson process (consistent with publication)
backfill.assign	How to assign backfill dose given the open backfill doses. Options are "highest" (default), "lowest", or "random".

Value

A data frame with the number of patients and number of DLTs at each dose level

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