Package 'TITEgBOIN'

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Type Package

Title Time-to-Event Dose-Finding Design for Multiple Toxicity Grades

Version 0.4.0

Description In some phase I trials, the design goal is to find the dose associated with a certain target toxicity rate or the dose with a certain weighted sum of rates of various toxicity grades. 'TITEgBOIN' provides the set up and calculations needed to run a dose-finding trial using bayesian optimal interval (BOIN) (Yuan et al. (2016) <doi:10.1158/1078-0432.CCR-16-0592>), generalized bayesian optimal interval (gBOIN) (Mu et al. (2019) <doi:10.1111/rssc.12263>), time-to-event bayesian optimal interval (TITEBOIN) (Lin et al. (2020) <doi:10.1093/biostatistics/kxz007>) and time-to-event generalized bayesian optimal interval (TITEgBOIN) (Takeda et al. (2022) <doi:10.1002/pst.2182>) designs. 'TITEgBOIN' can conduct tasks: run simulations and get operating characteristics; determine the dose for the next cohort; select maximum tolerated dose (MTD). These functions allow customization of design characteristics to vary sample size, cohort sizes, target dose limiting toxicity (DLT) rates or target normalized equivalent toxicity score (ETS) rates to account for discrete toxicity score, and incorporate safety and/or stopping rules.

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Contents

`get_oc_TITE_QuasiBOIN` *get_oc_TITE_QuasiBOIN*

Description

Obtain the operating characteristics of the model-assisted design for single agent trials by simulating trials using Bayesian optimal interval (BOIN) (Yuan et al. 2016)/ Generalized Bayesian optimal interval (gBOIN) (Mu et al. 2019)/Time-to-event Bayesian optimal interval (TITEBOIN) (Lin et al. 2020)/Time-to-event generalized Bayesian optimal interval (TITEgBOIN) designs(Takeda et al. 2022).

Usage

```
get_oc_TITE_QuasiBOIN(
  target,
  prob,
  score = c(0, 0.5, 1, 1.5),
  TITE = TRUE,
  ncohort,
  cohortsize,
  maxt = 1,
  accrual = 3,
  maxpen = 0.5,
  alpha1 = 0.5,
  alpha2 = 0.5,
  n.earlystop = 100,
  Neli = 3,
  startdose = 1,
  p.saf = 0.6 * target,
  p.tox = 1.4 * target,
  cutoff.eli = 0.95,
  extrasafe = FALSE,
  offset = 0.05,
  ntrial = 1000,
  seed = 100,
  titration = FALSE,
  cap.titration = 0
)
```

Arguments

`target`	The target toxicity probability (example: `target <- 0.30`) or the target normalized equivalent toxicity score (ETS) (example: `target <- 0.47 / 1.5`).
`prob`	A vector (Bayesian optimal interval (BOIN) or Time-to-event Bayesian optimal interval (TITEBOIN) design) /matrix (Generalized Bayesian optimal interval (gBOIN) or Time-to-event generalized Bayesian optimal interval (TITEgBOIN)

design) containing the true toxicity probabilities of the investigational dose levels.

`score` For Generalized Bayesian optimal interval (gBOIN)/Time-to-event generalized Bayesian optimal interval (TITEgBOIN), a vector containing the relative severity of different toxicity grades in terms of dose limiting toxicity (DLTs) in the dose-finding procedure. As default, toxicity grades of 0/1,2,3, and 4 are assigned values of 0,0.5,1,1.5. For Bayesian optimal interval (BOIN)/Time-to-event Bayesian optimal interval (TITEBOIN), "NA" should be assigned.

`TITE` For Time-to-event Bayesian optimal interval (TITEBOIN)/Time-to-event generalized Bayesian optimal interval (TITEgBOIN), "TRUE" should be assigned. For Bayesian optimal interval (BOIN)/Generalized Bayesian optimal interval (gBOIN), "FALSE" should be assigned.

`ncohort` The total number of cohorts.

`cohortsize` The cohort size.

`maxt` For Time-to-event bayesian optimal interval (TITEBOIN)/Time-to-event generalized bayesian optimal interval (TITEgBOIN), the maximum follow-up time. for Bayesian optimal interval (BOIN)/ Generalized Bayesian optimal interval (gBOIN), if you don't need to get 1, the average trial duration needed for the trial, 2, the standard deviation of average trial duration needed for the trial. Then "NA" should be assigned; If you need to get 1,the average trial duration needed for the trial, 2, the standard deviation of average trial duration needed for the trial. Then please specify the accrual rate and the maximum follow-up time.

`accrual` For Time-to-event bayesian optimal interval (TITEBOIN)/Time-to-event generalized bayesian optimal interval (TITEgBOIN), the accrual rate, i.e., the number of patients accrued in 1 unit of time, for Bayesian optimal interval (BOIN)/ Generalized Bayesian optimal interval (gBOIN), if you don't need to get 1,the average trial duration needed for the trial, 2, the standard deviation of average trial duration needed for the trial. Then "NA" should be assigned; if you need to get 1,the average trial duration needed for the trial, 2, the standard deviation of average trial duration needed for the trial, Then please specify the accrual rate and the maximum follow-up time.

`maxpen` For Time-to-event bayesian optimal interval (TITEBOIN)/Time-to-event generalized bayesian optimal interval (TITEgBOIN), the upper limit of the ratio of pending patients. For Bayesian optimal interval (BOIN)/Generalized Bayesian optimal interval (gBOIN), "NA" should be assigned.

`alpha1` For Time-to-event bayesian optimal interval (TITEBOIN)/Time-to-event generalized bayesian optimal interval (TITEgBOIN), a number from (0,1) that assume toxicity outcomes occurred with probability alpha1 in the last fraction of alpha2 of the assessment window. The default is `alpha1=0.5`. For Bayesian optimal interval (BOIN)/Generalized Bayesian optimal interval (gBOIN), "NA" should be assigned.

`alpha2` For Time-to-event bayesian optimal interval (TITEBOIN)/Time-to-event generalized bayesian optimal interval (TITEgBOIN), a number from (0,1) that assume toxicity outcomes occurred with probability alpha1 in the last fraction of alpha2 of the assessment window. The default is `alpha2=0.5`. For Bayesian optimal interval (BOIN)/Generalized Bayesian optimal interval (gBOIN), "NA" should be assigned.

n.earlystop	The early stopping parameter and the decision is to stay. If the number of patients treated at the current dose reaches n.earlystop, stop the trial and select the maxinum tolerated dose (MTD) based on the observed data. The default value n.earlystop=100 essentially turns off this type of early stopping.
Neli	The sample size cutoff for elimination. The default is Neli=3.
startdose	The starting dose level for the trial.
p.saf	The lower bound. The default value is p.saf=0.6*target.
p.tox	The upper bound. 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.
ntrial	The total number of trials to be simulated.
seed	The seed, The default value is seed = 100
titration	set titration=TRUE to perform dose escalation with cohort size = 1 to accelerate dose escalation at the beginning of the trial. The default value titration=FALSE.
cap.titration	cap the titration up to dose level, set cap.titration=3 to cap the titration up to dose level 3 with cohort size = 1. The default value cap.titration=0.

Details

This function generates he operating characteristics of the Bayesian optimal interval (BOIN)/ Generalized Bayesian optimal interval (gBOIN)/Time-to-event Bayesian optimal interval (TITEBOIN)/ Time-to-event generalized Bayesian optimal interval (TITEgBOIN) designs for trials by simulating trials under the prespecified true toxicity probabilities of the investigational doses.

Value

get_oc_TITE_QuasiBOIN() returns the operating characteristics of the Bayesian optimal interval (BOIN)/ Generalized Bayesian optimal interval (gBOIN)/Time-to-event bayesian optimal interval (TITEBOIN)/Time-to-event generalized Bayesian optimal interval (TITEgBOIN) designs as a data frame, including: (1) the percentage of trials that the maximum tolerated dose (MTD) is correctly selected, (2) the percentage of patients that are correctly allocated to the maximum tolerated dose (MTD), (3) the percentage of overdosing selection, (4) the percentage of overdosing allocation, (5) selection percentage at each dose level, (6) the number of patients treated at each dose level, (7) the percentage of patients treated at each dose level, (8) the number of toxicities observed at each dose level, (9) the average number of toxicities, (10) the average number of patients, (11) the percentage of early stopping without selecting the maxinum tolerated dose (MTD), (12) the average trial duration needed for the trial, (13) the standard deviation of average trial duration needed for the trial, (14) simulation set up data frame, include the target toxicity probability/the normalized target equivalent toxicity score (ETS); the true target toxicity probability/ the true normalized equivalent toxicity score (ETS) at each dose level based on prob and score, and lambda_e denotes the lower Bayesian optimal boundary and lambda_d denotes the upper Bayesian optimal boundary.

Note

We should avoid setting the values of p.saf and p.tox very close to the target. This is because the small sample sizes of typical phase I trials prevent us from differentiating the target toxicity rate from the rates close to it. In addition, in most clinical applications, the target toxicity rate is often a rough guess, and finding a dose level with a toxicity rate reasonably close to the target rate will still be of interest to the investigator. In addition, we recommend setting the value of priortox relatively small, for example, priortox=target/2 to accelerate the escalation procedure.

References

1. Liu S. and Yuan, Y. (2015). Bayesian optimal interval designs for phase I clinical trials, Journal of the Royal Statistical Society: Series C , 64, 507-523. 2. Yuan, Y., Hess, K. R., Hilsenbeck, S. G., & Gilbert, M. R. (2016). Bayesian optimal interval design: a simple and well-performing design for phase I oncology trials. Clinical Cancer Research, 22(17), 4291-4301. 3. Zhou, H., Yuan, Y., & Nie, L. (2018). Accuracy, safety, and reliability of novel phase I trial designs. Clinical Cancer Research, 24(18), 4357-4364. 4. Zhou, Y., Lin, R., Kuo, Y. W., Lee, J. J., & Yuan, Y. (2021). BOIN Suite: A Software Platform to Design and Implement Novel Early-Phase Clinical Trials. JCO Clinical Cancer Informatics, 5, 91-101. 5. Takeda K, Xia Q, Liu S, Rong A. TITE-gBOIN: Time-to-event Bayesian optimal interval design to accelerate dose-finding accounting for toxicity grades. Pharm Stat. 2022 Mar;21(2):496-506. doi: 10.1002/pst.2182. Epub 2021 Dec 3. PMID: 34862715. 6. Yuan, Y., Lin, R., Li, D., Nie, L. and Warren, K.E. (2018). Time-to-event Bayesian Optimal Interval Design to Accelerate Phase I Trials. Clinical Cancer Research, 24(20): 4921-4930. 7. Rongji Mu, Ying Yuan, Jin Xu, Sumithra J. Mandrekar, Jun Yin, gBOIN: A Unified Model-Assisted Phase I Trial Design Accounting for Toxicity Grades, and Binary or Continuous End Points, Journal of the Royal Statistical Society Series C: Applied Statistics, Volume 68, Issue 2, February 2019, Pages 289–308, https://doi.org/10.1111/rssc.12263. 8. Lin R, Yuan Y. Time-to-event model-assisted designs for dose-finding trials with delayed toxicity. Biostatistics. 2020 Oct 1;21(4):807-824. doi: 10.1093/biostatistics/kxz007. PMID: 30984972; PMCID: PMC8559898. 9. Hsu C, Pan H, Mu R (2022). _UnifiedDoseFinding: Dose-Finding Methods for Non-Binary Outcomes_. R package version 0.1.9, <https://CRAN.R-project.org/package=UnifiedDoseFinding>.

Examples

```
#For Bayesian optimal interval (BOIN) design and Output trial duration as an operating
#characteristics
get_oc_TITE_QuasiBOIN(target=0.3, score=NA,prob=c(0.25,0.30,0.45,0.49,0.53), TITE=FALSE,
                      ncohort=10, cohortsize=3,startdose=1,maxt=28,accrual=10,
                      maxpen=NA,alpha1=NA,alpha2=NA,cutoff.eli=0.95, ntrial=10,seed=6)


#For Bayesian optimal interval (BOIN) design and not Output trial duration as an operating
#characteristics
get_oc_TITE_QuasiBOIN(target=0.3, score=NA,prob=c(0.25,0.30,0.45,0.49,0.53), TITE=FALSE,
                      ncohort=10, cohortsize=3,startdose=1,maxt=NA,accrual=NA,
                      maxpen=NA,alpha1=NA,alpha2=NA,cutoff.eli=0.95, ntrial=10,seed=6)


#For Generalized Bayesian optimal interval (gBOIN) design and Output trial duration as an
#operating characteristics
target<-0.47/1.5
```

```
prob <- matrix(c(0.83,0.75,0.62,0.51,0.34,0.19,
                 0.12,0.15,0.18,0.19,0.16,0.11,
                 0.04,0.07,0.11,0.14,0.15,0.11,
                 0.01,0.03,0.09,0.16,0.35,0.59), ncol = 6, byrow = TRUE)
get_oc_TITE_QuasiBOIN(target=target, score=c(0,0.5,1,1.5),prob=prob, TITE=FALSE,ncohort=10,
                      cohortsize=3,startdose=1,maxt=28,accrual=10, maxpen=NA,alpha1=NA,
                      alpha2=NA,cutoff.eli=0.95, ntrial=10,seed=6)


#For Generalized Bayesian optimal interval (gBOIN) design and not Output trial duration as
#an operating characteristics
target<-0.47/1.5
prob <- matrix(c(0.83,0.75,0.62,0.51,0.34,0.19,
                 0.12,0.15,0.18,0.19,0.16,0.11,
                 0.04,0.07,0.11,0.14,0.15,0.11,
                 0.01,0.03,0.09,0.16,0.35,0.59), ncol = 6, byrow = TRUE)
get_oc_TITE_QuasiBOIN(target=target, score=c(0,0.5,1,1.5),prob=prob, TITE=FALSE,ncohort=10,
                      cohortsize=3,startdose=1,maxt=NA,accrual=NA, maxpen=NA,alpha1=NA,
                      alpha2=NA,cutoff.eli=0.95, ntrial=10,seed=6)


#For Time-to-event bayesian optimal interval (TITEBOIN) design
get_oc_TITE_QuasiBOIN(target=0.3, score=NA,prob=c(0.25,0.30,0.45,0.49,0.53), TITE=TRUE,
                      ncohort=10, cohortsize=3,startdose=1,maxt=28,accrual=10,
                      maxpen=0.5,alpha1=0.5,alpha2=0.5,cutoff.eli=0.95,
                      ntrial=10,seed=6)


#For Time-to-event generalized bayesian optimal interval (TITEgBOIN) design
target<-0.47/1.5
prob <- matrix(c(0.83,0.75,0.62,0.51,0.34,0.19,
                 0.12,0.15,0.18,0.19,0.16,0.11,
                 0.04,0.07,0.11,0.14,0.15,0.11,
                 0.01,0.03,0.09,0.16,0.35,0.59), ncol = 6, byrow = TRUE)
get_oc_TITE_QuasiBOIN(target=target, score=c(0,0.5,1,1.5),prob=prob, TITE=TRUE,ncohort=10,
                      cohortsize=3,startdose=1,maxt=28,accrual=10, maxpen=0.5,alpha1=0.5,
                      alpha2=0.5,cutoff.eli=0.95, ntrial=10,seed=6)
```

`next_TITE_QuasiBOIN` *next_TITE_QuasiBOIN*

Description

Determine the dose for the next cohort of new patients for single-agent trials using Bayesian optimal interval (BOIN)/ Generalized Bayesian optimal interval (gBOIN)/Time-to-event bayesian optimal interval (TITEBOIN)/Time-to-event generalized Bayesian optimal interval (TITEgBOIN) designs.

Usage

```
next_TITE_QuasiBOIN(
```

```
  target,
  n,
  npend,
  y,
  ft,
  d,
  maxt = 28,
  p.saf = 0.6 * target,
  p.tox = 1.4 * target,
  elimination = NA,
  cutoff.eli = 0.95,
  extrasafe = FALSE,
  offset = 0.05,
  n.earlystop = 100,
  maxpen = 0.5,
  Neli = 3,
  print_d = FALSE,
  gdesign = FALSE
)
```

Arguments

target	The target toxicity probability (example: `target <- 0.30`) or the target normalized equivalent toxicity score (ETS) (example: `target <- 0.47 / 1.5`).
n	Number of patients treated at each dose level.
npend	For Time-to-event Bayesian optimal interval (TITEBOIN)/Time-to-event generalized Bayesian optimal interval (TITEgBOIN), the number of pending patients at each dose level.For Bayesian optimal interval (BOIN)/Generalized Bayesian optimal interval (gBOIN), "NA" should be assigned.
y	Number of patients with dose limiting toxicity (DLT) or the sum of Normalized equivalent toxicity score (ETS).
ft	For Time-to-event Bayesian optimal interval (TITEBOIN)/Time-to-event generalized Bayesian optimal interval (TITEgBOIN), Total follow-up time for pending patients for toxicity at each dose level (days). For Bayesian optimal interval (BOIN)/ Generalized Bayesian optimal interval (gBOIN), "NA" should be assigned.
d	Current dose level.
maxt	For Time-to-event Bayesian optimal interval (TITEBOIN)/Time-to-event generalized Bayesian optimal interval (TITEgBOIN), length of assessment window for toxicity (days). For Bayesian optimal interval (BOIN)/Generalized Bayesian optimal interval (gBOIN), "NA" should be assigned.
p.saf	The lower bound. The default value is `p.saf=0.6*target`.
p.tox	The upper bound. The default value is `p.tox=1.4*target`.
elimination	Elimination of each dose (0,1 should be assigned, 0 means the dose is not eliminated, 1 means the dose is eliminated due to over toxic(`elimination=NA`, 0 is defaulted for each dose level)).

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.
n.earlystop	The early stopping parameter. The default value is n.earlystop=100.
maxpen	For Time-to-event Bayesian optimal interval (TITEBOIN)/Time-to-event generalized Bayesian optimal interval (TITEgBOIN), the upper limit of the ratio of pending patients. For Bayesian optimal interval (BOIN)/Generalized Bayesian optimal interval (gBOIN), "NA" should be assigned.
Neli	The sample size cutoff for elimination. The default is Neli=3.
print_d	Print the additional result or not. The default value is print_d=FALSE.
gdesign	For Bayesian optimal interval (BOIN) and Time-to-event bayesian optimal interval (TITEBOIN), "FALSE" should be assigned. For Generalized Bayesian optimal interval (gBOIN) and Time-to-event generalized bayesian optimal interval (TITEgBOIN), "TRUE" should be assigned . The default is gdesign=FALSE.

Value

next_TITE_QuasiBOIN() returns the toxicity probability and the recommended dose level for the next cohort including: (1) the lower Bayesian optimal boundary (lambda_e) (2) the upper Bayesian optimal boundary (lambda_d) (3) The number of patients or the effective sampe size (ESS) at each dose level (ESS) (4) The dose limiting toxicity (DLT) rate or mu (the estimated quasi-Bernoulli toxicity probability) at each dose level (mu) (5) the recommended dose level for the next cohort as a numeric value under (d)

References

1. Liu S. and Yuan, Y. (2015). Bayesian optimal interval designs for phase I clinical trials, Journal of the Royal Statistical Society: Series C , 64, 507-523. 2. Yuan, Y., Hess, K. R., Hilsenbeck, S. G., & Gilbert, M. R. (2016). Bayesian optimal interval design: a simple and well-performing design for phase I oncology trials. Clinical Cancer Research, 22(17), 4291-4301. 3. Zhou, H., Yuan, Y., & Nie, L. (2018). Accuracy, safety, and reliability of novel phase I trial designs. Clinical Cancer Research, 24(18), 4357-4364. 4. Zhou, Y., Lin, R., Kuo, Y. W., Lee, J. J., & Yuan, Y. (2021). BOIN Suite: A Software Platform to Design and Implement Novel Early-Phase Clinical Trials. JCO Clinical Cancer Informatics, 5, 91-101. 5. Takeda K, Xia Q, Liu S, Rong A. TITE-gBOIN: Time-to-event Bayesian optimal interval design to accelerate dose-finding accounting for toxicity grades. Pharm Stat. 2022 Mar;21(2):496-506. doi: 10.1002/pst.2182. Epub 2021 Dec 3. PMID: 34862715. 6. Yuan, Y., Lin, R., Li, D., Nie, L. and Warren, K.E. (2018). Time-to-event Bayesian Optimal Interval Design to Accelerate Phase I Trials. Clinical Cancer Research, 24(20): 4921-4930. 7. Rongji Mu, Ying Yuan, Jin Xu, Sumithra J. Mandrekar, Jun Yin, gBOIN: A Unified Model-Assisted Phase I Trial Design Accounting for Toxicity Grades, and Binary or Continuous End Points, Journal of the Royal Statistical Society Series C: Applied Statistics, Volume 68, Issue 2, February 2019, Pages 289–308, https://doi.org/10.1111/rssc.12263. 8. Lin R, Yuan Y. Time-to-event model-assisted designs for dose-finding trials with delayed toxicity. Biostatistics. 2020 Oct 1;21(4):807-824. doi: 10.1093/biostatistics/kxz007. PMID: 30984972; PMCID: PMC8559898. 9. Hsu C, Pan H, Mu

R (2022). _UnifiedDoseFinding: Dose-Finding Methods for Non-Binary Outcomes_. R package version 0.1.9, <https://CRAN.R-project.org/package=UnifiedDoseFinding>.

Examples

```
#For Bayesian optimal interval (BOIN) design
target<-0.3
next_TITE_QuasiBOIN(target=target,n=c(3,3,4,4,4,0),npend=NA, y=c(0,0,1,1,1,0), ft=NA,
                    d=5, maxt=NA,p.saf= 0.6 * target, p.tox = 1.4 * target,elimination=NA,
                     cutoff.eli = 0.95,extrasafe = FALSE, n.earlystop = 10,
                     maxpen=NA,print_d = TRUE,gdesign=FALSE)


#For Generalized Bayesian optimal interval (gBOIN) design
target=0.47/1.5
next_TITE_QuasiBOIN(target=target,n=c(3,3,4,4,4,0),npend=NA,
                     y=c(0, 0, 0.5/1.5, 1.0/1.5, 1.5/1.5, 0),ft=NA, d=5, maxt=NA,
                     p.saf= 0.6 * target, p.tox = 1.4 * target,elimination=NA,
                     cutoff.eli = 0.95,extrasafe = FALSE, n.earlystop = 10,
                     maxpen=NA,print_d = TRUE,gdesign=TRUE)


#For Time-to-event bayesian optimal interval (TITEBOIN) design
target=0.3
next_TITE_QuasiBOIN(target=target,n=c(3,3,4,4,4,0),npend=c(0,0,0,1,2,0), y=c(0,0,1,1,1,0),
                    ft=c(0, 0, 0, 14, 28, 0),d=5, maxt=28,p.saf= 0.6 * target,
                     p.tox = 1.4 * target,elimination=NA,cutoff.eli = 0.95,
                     extrasafe = FALSE, n.earlystop = 10,maxpen=0.5,print_d = TRUE,
                     gdesign=FALSE)


#For Time-to-event generalized bayesian optimal interval (TITEgBOIN) design
target=0.47/1.5
next_TITE_QuasiBOIN(target=target,n=c(3,3,4,4,4,0),npend=c(0,0,0,1,2,0),
                     y=c(0, 0, 0.5/1.5, 1.0/1.5, 1.5/1.5, 0),ft=c(0, 0, 0, 14, 28, 0),
                     d=5, maxt=28,p.saf= 0.6 * target, p.tox = 1.4 * target,
                     elimination=NA,cutoff.eli = 0.95,extrasafe = FALSE,
                     n.earlystop = 10,maxpen=0.5,print_d = TRUE,gdesign=TRUE)
```

`select_mtd_TITE_QuasiBOIN`

select_mtd_TITE_QuasiBOIN

Description

Obtain the maximum tolerated dose (MTD) of Bayesian optimal interval (BOIN) (Yuan et al. 2016)/ Generalized Bayesian optimal interval (gBOIN) (Mu et al. 2019)/Time-to-event Bayesian optimal interval (TITEBOIN) (Lin et al. 2020)/ Time-to-event generalized Bayesian optimal interval (TITEgBOIN) (Takeda et al. 2022) designs.

Usage

```
select_mtd_TITE_QuasiBOIN(
  target,
  ntox,
  npts,
  Neli = 3,
  cutoff.eli = 0.95,
  extrasafe = FALSE,
  offset = 0.05,
  print = FALSE,
  gdesign = FALSE
)
```

Arguments

target	The target toxicity probability (example: `target <- 0.30`) or the target normalized equivalent toxicity score (ETS) (example: `target <- 0.47 / 1.5`).
ntox	Number of patients with dose limiting toxicity (DLT) or the sum of normalized equivalent toxicity score (ETS).
npts	The number of patients enrolled at each dose level.
Neli	The sample size cutoff for elimination. The default is `Neli=3`.
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.
print	Print the additional result or not. The default value is `print=FALSE`.
gdesign	For Bayesian optimal interval (BOIN) and Time-to-event Bayesian optimal interval (TITEBOIN), "FALSE" should be assigned. For Generalized Bayesian optimal interval (gBOIN) and Time-to-event generalized Bayesian optimal interval (TITEgBOIN), "TRUE" should be assigned . The default is `gdesign=FALSE`.

Value

`select_mtd_TITE_QuasiBOIN()` returns the selected dose.

References

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Examples

```
#For Bayesian optimal interval (BOIN) design/Time-to-event bayesian optimal interval (TITEBOIN)
#design
target<-0.3
y<-c(0,0,1,2,3,0)
n<-c(3,3,6,9,9,0)
select_mtd_TITE_QuasiBOIN(target=target,ntox=y,npts=n,print=TRUE,gdesign=FALSE)


#For Generalized Bayesian optimal interval (gBOIN) design/Time-to-event generalized bayesian
#optimal interval (TITEgBOIN) design
target<-0.47/1.5
y<-c(0,0,2/1.5,3.5/1.5,5.5/1.5,0)
n<-c(3,3,6,9,9,0)
select_mtd_TITE_QuasiBOIN(target=target,ntox=y,npts=n,print=TRUE,gdesign=TRUE)
```

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