

Package ‘HybridDesign’

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Type Package

Title Hybrid Design for Phase I Dose-Finding Studies

Version 1.0

Maintainer Heng Zhou <heng.zhou@merck.com>

Description The Hybrid design is a combination of model-assisted design (e.g., the modified Toxicity Probability Interval design) with dose-toxicity model-based design for phase I dose-finding studies. The hybrid design controls the overdosing toxicity well and leads to a recommended dose closer to the true maximum tolerated dose (MTD) due to its ability to calibrate for an intermediate dose. More details can be found in Liao et al. 2022 <[doi:10.1002/ijc.34203](https://doi.org/10.1002/ijc.34203)>.

Imports testit, ResourceSelection

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License GPL-3

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Author Heng Zhou [aut, cre],
Feng Zhou [aut],
Jason Liao [aut]

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get_boundary_mtpi *Generate modified mTPI Design Decision Boundary*

Description

Generate dose escalation and deescalation boundaries of modified Toxicity Probability Interval (mTPI) design with overdose control.

Usage

```
get_boundary_mtpi(
  target,
  ncohort,
  cohortsize,
  eps1 = 0.05,
  eps2 = 0.05,
  a = 1,
  b = 1,
  cutoff.eli = 0.95,
  tox.control = FALSE,
  cut.tox = 0.8,
  esc.control = FALSE,
  cut.esc = 0.5
)
```

Arguments

target	target toxicity rate
ncohort	the total number of cohorts
cohortsize	the cohort size
eps1	modified Toxicity Probability Interval (mTPI) design parameter epsilon1. Default: 0.05
eps2	modified Toxicity Probability Interval (mTPI) design parameter epsilon2. Default: 0.05
a	Beta prior shape parameter 1. Default: 1
b	Beta prior shape parameter 2. Default: 1
cutoff.eli	Posterior probability cutoff of eliminating dose due to unacceptable toxicity. Default: 0.95
tox.control	indicator of whether to perform toxicity control. If TRUE, change "stay" to "deescalation" if the posterior probability of DLT rate greater than target+eps2 is greater than the toxicity control cutoff cut.tox
cut.tox	toxicity control cutoff. Default: 0.8
esc.control	indicator of whether to perform escalation control. If TRUE, change decision of "escalation" to "stay" if the posterior probability of DLT rate less than target-eps1 is greater than the escalation control cutoff cut.esc
cut.esc	escalation control cutoff. Default: 0.5

Value

This function returns the table of escalation and deescalation boundaries.

Examples

```
get_boundary_mtpi(target=0.30, ncohort=10, cohortsize=3)
```

get_oc_hybrid	<i>Generate operating characteristics for single-agent dose-finding studies using the Hybrid design</i>
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Description

Obtain the operating characteristics of the Hybrid design for single-agent dose-finding studies by simulation.

Usage

```
get_oc_hybrid(trueMTD, trueDLTvec, dose, target, ncohort, cohortsize,
              eps1=0.05, eps2=0.05, a=1, b=1, cutoff.eli=0.95,
              tox.control=TRUE, cut.tox=0.8, esc.control=FALSE, cut.esc=0.5,
              ntrial, seednum=10000)
```

Arguments

trueMTD	the dosage of true maximum tolerated dose (MTD)
trueDLTvec	a vector of true dose-limiting toxicity (DLT) rates at each dose level
dose	a vector containing the numerical dosage of each dose level
target	target toxicity rate
ncohort	the total number of cohorts
cohortsize	the cohort size
eps1	mTPI design parameter epsilon1. Default: 0.05
eps2	mTPI design parameter epsilon2. Default: 0.05
a	Beta prior shape parameter 1. Default: 1
b	Beta prior shape parameter 2. Default: 1
cutoff.eli	Posterior probability cutoff of eliminating dose due to unacceptable toxicity. Default: 0.95
tox.control	indicator of whether to perform toxicity control. If TRUE, change "stay" to "deescalation" if the posterior probability of DLT rate greater than target+eps2 is greater than the toxicity control cutoff cut.tox
cut.tox	toxicity control cutoff. Default: 0.8

esc.control	indicator of whether to perform escalation control. If TRUE, change decision of "escalation" to "stay" if the posterior probability of DLT rate less than target-eps1 is greater than the escalation control cutoff cut.esc
cut.esc	escalation control cutoff. Default: 0.5
ntrial	the total number of trials to be simulated
seednum	the random seed for simulation

Value

This function returns the operating characteristics of the Hybrid design as a list, including: (1) Percentage of correct selection of the true MTD in all simulated trials, (2) Percentage of selecting a dose above MTD in all simulated trials, (3) Percentage of selecting a dose below MTD in all simulated trials, (4) Average number of patients treated at MTD in all simulated trials.

Examples

```
get_oc_hybrid(trueMTD=12, trueDLTvec=c(0.15,0.20,0.25,0.30,0.35), dose=c(3, 6, 12, 18, 24),
  target=0.25, ncohort=10, cohortsize=3, eps1=0.05, eps2=0.05, a=1, b=1,
  cutoff.eli=0.95, tox.control=TRUE, cut.tox=0.8, esc.control=FALSE, cut.esc=0.5,
  ntrial=100, seednum=10000)
```

hybrid	<i>Implement Hybrid design with real data</i>
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Description

Obtain decision for the next dose level to be tested given current trial data.

Usage

```
hybrid(dose, nDLT, npts, currdose, nextdose=0, target, ncohort, cohortsize,
  eps1=0.05, eps2=0.05, a=1, b=1, cutoff.eli=0.95, tox.control=TRUE,
  cut.tox=0.8, esc.control=FALSE, cut.esc=0.5, regrule)
```

Arguments

dose	a vector containing the numerical dosage of each dose level
nDLT	a vector containing the number of patients who experienced dose-limiting toxicity at each dose level
npts	a vector containing the number of patients at each dose level
currdose	the dosage at the current dose level
nextdose	the dosage of next higher dose level; could be an intermediate dose
target	the target toxicity rate

ncohort	the total number of cohorts
cohortsizes	the cohort size
eps1	modified Toxicity Probability Interval (mTPI) design parameter epsilon1. Default: 0.05
eps2	modified Toxicity Probability Interval (mTPI) design parameter epsilon2. Default: 0.05
a	Beta prior shape parameter 1. Default: 1
b	Beta prior shape parameter 2. Default: 1
cutoff.eli	Posterior probability cutoff of eliminating dose due to unacceptable toxicity. Default: 0.95
tox.control	indicator of whether to perform toxicity control. If TRUE, change "stay" to "deescalation" if the posterior probability of DLT rate greater than target+eps2 is greater than the toxicity control cutoff cut.tox
cut.tox	toxicity control cutoff. Default: 0.8
esc.control	indicator of whether to perform escalation control. If TRUE, change decision of "escalation" to "stay" if the posterior probability of DLT rate less than target-eps1 is greater than the escalation control cutoff cut.esc
cut.esc	escalation control cutoff. Default: 0.5
regrule	indicator of whether to apply additional overdose control rule

Value

This function returns the decision of implementing the Hybrid design with real trial data as a list, including: (1) dose transition boundaries of modified mTPI design, (2) decision table of modified mTPI design, (3) the decision given current data, (4) the summary table of tested dose levels

Examples

```
hybrid(dose=c(2,4,8,16,22,28,40), nDLT=c(0,0,0,0,1,0,2), npts=c(3,3,4,6,9,5,16), currdose=40,
nextdose=54, target=0.3, ncohort=10, cohortsizes=3, eps1=0.05, eps2=0.05, a=1, b=1,
cutoff.eli=0.95, tox.control=TRUE, cut.tox=0.8, regrule=TRUE)
```

hybrid_MTD_selection *Select the maximum tolerated dose (MTD) for single-agent dose-finding studies*

Description

Select the maximum tolerated dose (MTD) when the single-agent dose-finding study is completed

Usage

```
hybrid_MTD_selection(target, dose, npts, nDLT, elimdose)
```


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