Package 'MinEDfind'

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Type Package

Title A Bayesian Design for Minimum Effective Dosing-Finding Trial

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Description The nonparametric two-stage Bayesian adaptive design is a novel phase II clinical trial design for finding the minimum effective dose (MinED). This design is motivated by the top priority and concern of clinicians when testing a new drug, which is to effectively treat patients and minimize the chance of exposing them to subtherapeutic or overly toxic doses. It is used to design single-agent trials.

License GPL-2

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LazyData true

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NeedsCompilation no

Repository CRAN

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Contents

`get.OC.MinED` *Generate operating characteristics for finding the minimum effective dose (MinED)*

Description

Obtain the operating characteristics of the nonparametric two-stage Bayesian adaptive design for minimum effective dose (MinED)-based dosing-finding trials

Usage

```
get.OC.MinED(ttox, teff, phi_t, phi_e, ct = 0.95, eps_t, eps_e, d0 = 1,
             cohortsize = 3, ncohort1, ncohort2, ntrial = 100, extrasafe = TRUE,
              cutoff.eli = 0.95, n.earlystop = 12)
```

Arguments

`ttox`	a vector containing the true toxicity rates of the investigational dose levels
`teff`	a vector containing the true response rates of the investigational dose levels
`phi_t`	the target DLT rate
`phi_e`	the target response rate
`ct`	the cutoff used to eliminate the dose for too toxicity. The default value is ct = 0.95
`eps_t`	a small value such that (phi_t - eps_t, phi_t + eps_t) is an indifference interval of phi_t. The default value is eps_t = 0.1 * phi_t
`eps_e`	a small value such that (phi_e - eps_e, phi_e + eps_e) is an indifference interval of phi_e. The default value is eps_e = 0.1 * phi_e
`d0`	the starting dose level. The default value is d0 = 1
`cohortsize`	the cohort size
`ncohort1`	the number of cohort used in stage I
`ncohort2`	the number of cohort used in stage II
`ntrial`	the number of simulated trial
`extrasafe`	extrasafe set extrasafe = TRUE to impose a more stringent stopping rule
`cutoff.eli`	the cutoff to eliminate an overly toxic dose for safety. The default value is cutoff.eli = 0.95
`n.earlystop`	the early stopping parameter. The default value is n.earlystop = 12

Value

`get.oc.MinED()` returns the operating characteristics of nonparametric two-stage Bayesian adaptive design as a matrix object, including: (1) true DLT rate at each dose level, (2) true efficacy rate at each dose level, (3) selection percentage at each dose level, (4) the average number of patients treated at each dose level, (5) the average number of patients responded to toxicity at each dose level, (6) the average number of patients responded to efficacy at each dose level

Author(s)

Chia-Wei Hsu, Fang Wang, Rongji Mu, Haitao Pan, Guoying Xu

References

Rongji Mu, Guoying Xu, Haitao Pan (2020). A nonparametric two-stage Bayesian adaptive design for minimum effective dose (MinED)-based dosing-finding trials, (under review)

Examples

```
ttox = c(0.05, 0.15, 0.3, 0.45, 0.6)
teff = c(0.05, 0.15, 0.3, 0.45, 0.6)
phi_t = 0.3
phi_e = 0.3
eps_t = 0.1 * phi_t
eps_e = 0.1 * phi_e

oc = get.OC.MinED(ttox = ttox, teff = teff, phi_t = phi_t, phi_e = phi_e,
                  eps_t = eps_t, eps_e = eps_e, cohortsize = 3, ncohort1 = 6,
                  ncohort2 = 14, ntrial = 100)
print(oc)
```

`next.MinED` *Determine the dose for the next cohort of new patients for single-agent trials that aim to find a minimum effective dose (MinED)*

Description

Determine the dose for the next cohort of new patients for single-agent trials that aim to find a MinED

Usage

```
next.MinED(n, y, z, d, phi_t, phi_e, eps_t, eps_e, ct = 0.95, N1 = 18)
```

Arguments

`n`	a vector of number of patients treated at each dose level
`y`	a vector of number of patients experiencing the toxicity at each dose level (with the same length as candidate doses)
`z`	a vector of number of patients showing response at each dose level (with the same length as candidate doses)
`d`	the starting dose level
`phi_t`	the target DLT rate
`phi_e`	the target response rate

eps_t	a small value such that (phi_t - eps_t, phi_t + eps_t) is an indifference interval of phi_t. The default value is eps_t = 0.1 * phi_t
eps_e	a small value such that (phi_e - eps_e, phi_e + eps_e) is an indifference interval of phi_e. The default value is eps_e = 0.1 * phi_e
ct	the cutoff used to eliminate the dose for too toxicity. The default value is ct = 0.95
N1	number of trials in the stage 1. The default value is N1 = 18

Value

next.MinED() returns recommended dose level for the next cohort as a list ($nextdose)

Author(s)

Chia-Wei Hsu, Fang Wang, Rongji Mu, Haitao Pan, Guoying Xu

References

Rongji Mu, Guoying Xu, Haitao Pan (2020). A nonparametric two-stage Bayesian adaptive design for minimum effective dose (MinED)-based dosing-finding trials, (under review)

Examples

```
n = c(3, 6, 0, 0, 0)
y = c(0, 1, 0, 0, 0)
z = c(0, 1, 0, 0, 0)
d = 2
phi_t = 0.3
phi_e = 0.3
eps_t = 0.1 * phi_t
eps_e = 0.1 * phi_e
next.dose <- next.MinED(n = n, y = y, z = z, d = d, phi_t = phi_t,
                        phi_e = phi_e, eps_t = eps_t, eps_e = eps_e)
print(next.dose)
```

---

plot.MinED *Plot the simulation results for nonparametric two-stage Bayesian adaptive designs*

Description

Plot the objects returned by other functions, including (1) operating characteristics of the design, including selection percentage and the number of patients treated at each dose; (2) the estimates of toxicity and response probability for each dose in the admissable set and corresponding 95% credible interval

Usage

```
## S3 method for class 'MinED'
plot(x, name, ...)
```

Arguments

x	the object returned by other functions
name	the name in the object to be plotted
...	ignored arguments

Value

plot.MinED() returns a figure

Author(s)

Chia-Wei Hsu, Fang Wang, Rongji Mu, Haitao Pan, Guoying Xu

References

Rongji Mu, Guoying Xu, Haitao Pan (2020). A nonparametric two-stage Bayesian adaptive design for minimum effective dose (MinED)-based dosing-finding trials, (under review)

Examples

```
## select the MinED based on the trial data
n = c(3, 6, 0, 0, 0)
y = c(0, 1, 0, 0, 0)
z = c(0, 1, 0, 0, 0)
phi_t = 0.3
phi_e = 0.3
eps_t = 0.1 * phi_t
eps_e = 0.1 * phi_e
select.dose <- select.MinED(n, y, z, phi_t, phi_e, eps_t, eps_e, ct = 0.95)
plot.MinED(select.dose)

## get the operating characteristics for nonparametric two-stage Bayesian adaptive designs
ttox = c(0.05, 0.15, 0.3, 0.45, 0.6)
teff = c(0.05, 0.15, 0.3, 0.45, 0.6)
phi_t = 0.3
phi_e = 0.3
eps_t = 0.1 * phi_t
eps_e = 0.1 * phi_e

oc = get.OC.MinED(ttox = ttox, teff = teff, phi_t = phi_t, phi_e = phi_e,
                  eps_t = eps_t, eps_e = eps_e, cohortsize=3, ncohort1 = 6,
                  ncohort2 = 14, ntrial = 100)

plot.MinED(oc, "Sel%")
plot.MinED(oc, "#Pts.treated")
plot.MinED(oc, "#Pts.response.to.tox")
```

```
plot.MinED(oc, "#Pts.response.to.eff")
```

`select.MinED` *Select the minimum effective dose (MinED) for single agent trials*

Description

Select the minimum effective dose (MinED) when the trial is completed

Usage

```
select.MinED(n, y, z, phi_t, phi_e, eps_t, eps_e, ct = 0.95)
```

Arguments

`n`	a vector of number of patients treated at each dose level
`y`	a vector of number of patients experiencing the toxicity at each dose level (with the same length as candidate doses)
`z`	a vector of number of patients showing response at each dose level (with the same length as candidate doses)
`phi_t`	the target DLT rate
`phi_e`	the target response rate
`eps_t`	a small value such that (phi_t - eps_t, phi_t + eps_t) is an indifference interval of phi_t. The default value is eps_t = 0.1 * phi_t
`eps_e`	a small value such that (phi_e - eps_e, phi_e + eps_e) is an indifference interval of phi_e. The default value is eps_e = 0.1 * phi_e
`ct`	the cutoff used to eliminate the dose for too toxicity. The default value is ct = 0.95

Value

`select.MinED()` returns the selected dose with detailed information as a list, including: (1) selected dose level (`$Selected_Dose`), (2) target level for efficacy and toxicity rate (`$Target_Level`), (3) posterior estimate of efficacy and toxicity with its corresponding lower and upper bound etc. (`$Info`)

Author(s)

Chia-Wei Hsu, Fang Wang, Rongji Mu, Haitao Pan, Guoying Xu

References

Rongji Mu, Guoying Xu, Haitao Pan (2020). A nonparametric two-stage Bayesian adaptive design for minimum effective dose (MinED)-based dosing-finding trials, (under review)

Examples

```
n = c(3, 6, 0, 0, 0)
y = c(0, 1, 0, 0, 0)
z = c(0, 1, 0, 0, 0)
phi_t = 0.3
phi_e = 0.3
eps_t = 0.1 * phi_t
eps_e = 0.1 * phi_e
select.dose <- select.MinED(n, y, z, phi_t, phi_e, eps_t, eps_e)
print(select.dose)
```

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