Package ‘EWOC2’

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Author Quanlin Li and Mourad Tighiouart
Maintainer Quanlin Li <choplum@gmail.com>
Description Implements escalation with overdose control (EWOC) trial designs using two drug combinations described by Tighiouart, Li and Rogatko (2017) <doi:10.1002/sim.6961>. It calculates the recommended dose for next cohorts and perform simulations to obtain operating characteristics.
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Description

Implements escalation with overdose control (EWOC) trial designs using two drug combinations described by Tighiouart, Li and Rogatko (2017) <doi:10.1002/sim.6961>. It calculates the recommended dose for next cohorts and perform simulations to obtain operating characteristics.

Author(s)

Quanlin Li and Mourad Tighiouart
Maintainer: Quanlin Li <choplum@gmail.com>

References


Usage

ewocR(dose.a, dose.b, resp, theta, alpha, min.dose.a, max.dose.a, min.dose.b, max.dose.b, a01, b01, a10, b10, a00, b00, a, b, delta1x, delta1y, burn, mm, delta1)

CC default S3 method:
ewocR(dose.a, dose.b, resp, theta, alpha, Min.Dose.A, Max.Dose.A, Min.Dose.B, Max.Dose.B, a01, b01, a10, b10, a00, b00, a, b, delta1x, delta1y, burn=T000, mm=R000, delta1=0.05)

Arguments

dose.a  a numeric vector of allowable doses for drug A
dose.b  a numeric vector of allowable doses for drug B
resp     a numeric vector of allowable responses, 0 or 1
theta   a numeric value defining the proportion of expected patients to experience a medically unacceptable, dose-limiting toxicity (DLT) if administered the MTD.
alpha a numerical value defining the probability that dose selected by EWOC is higher than the MTD.

Min.Dose.A a numeric value defining the lower bound of the support of the MTD for drug A
Max.Dose.A a numeric value defining the upper bound of the support of the MTD for drug A
Min.Dose.B a numeric value defining the lower bound of the support of the MTD for drug B
Max.Dose.B a numeric value defining the upper bound of the support of the MTD for drug B

a01 a numeric value for beta prior distribution associated with parameter rho01
b01 a numeric value for beta prior distribution associated with parameter rho01
a10 a numeric value for beta prior distribution associated with parameter rho10
b10 a numeric value for beta prior distribution associated with parameter rho10
a00 a numeric value for beta prior distribution associated with parameter rho00
b00 a numeric value for beta prior distribution associated with parameter rho00

a a numeric value for gamma prior distribution associated with parameter eta
b a numeric value for the gamma prior distribution associated with the parameter eta

delta1x Maximum dose escalation at each step for drug A, the default is 0.2*(Max.Dose.A-Min.Dose.A if not assigned)
delta1y Maximum dose escalation at each step for drug B, the default is 0.2*(Max.Dose.B-Min.Dose.B if not assigned)
burn Number of iterations for adaption, see n.adapt in jags.model for detail
mm Number of iterations to monitor, see n.iter in code.samples for detail
delta1 Threshold for toxicity

Value

data a data frame containing the current doses and responses set
parameters list of input parameters
priors list of prior parameters
nextdose.x the next recommended doses for drug A
nextdose.y the next recommended doses for drug B

References


Examples

test = ewoc2(dose.a=c(0,0),dose.b=c(0,0),resp=c(0,0),theta=0.33, alpha=0.25, Min.Dose.A=0, Max.Dose.A=1, Min.Dose.B=0, Max.Dose.B=1, a01=1, b01=1, a10=1, b10=1, a00=1, b00=1, a=0.8, b=0.0384)
print(test)
**Description**

Generic function for simulating EWOC trials for 2 drugs combination

**Usage**

```r
ewoc2simu(ntrials, nsamples, type, trho00, trho01, teta, nx, ny, tp, Min.Dose.A, Max.Dose.A, Min.Dose.B, Max.Dose.B, alpha, theta, vai, a01, b01, a10, b10, a00, b00, a, b, delta1x, delta1y, burn, mm, delta1, seed)
```

## Default S3 method:

```r
ewoc2simu(ntrials, nsamples, type, trho00, trho01, teta, nx, ny, tp, Min.Dose.A, Max.Dose.A, Min.Dose.B, Max.Dose.B, alpha, theta, vai, a01, b01, a10, b10, a00, b00, a, b, delta1x, delta1y, burn=4000, mm=2000, delta1=0.05, seed)
```

**Arguments**

- `ntrials`: a number indicating the number of trials to be simulated
- `nsamples`: a number indicating the number of patients enrolled for each clinical trial
- `type`: a character indicating the type of design, could be 'continuous' or 'discrete' or their initials
- `trho00`: a numeric value indicating the true value of the parameter rho00, the probability of DLT when the levels of drugs A and B are both 0
- `trho01`: a numeric value indicating the true value of the parameter rho01, the probability of DLT when the levels of drugs A and B are 0 and 1, respectively
- `trho10`: a numeric value indicating the true value of the parameter rho10, the probability of DLT when the levels of drugs A and B are 1 and 0, respectively
- `teta`: a numeric value indicating the true value of the eta, the interaction parameter
- `nx`: a numeric value indicating the number of dose levels for drug A. It's only necessary if type = 'discrete'
- `ny`: a numeric value indicating the number of dose levels for drug B. It's only necessary if type = 'discrete'
- `tp`: a numerical vector indicating the true probabilities of DLT at each dose combinations, the order is by Drug B first, only necessary if type = 'discrete'
- `Min.Dose.A`: a numeric value defining the lower bound of the support of the MTD for drug A
- `Max.Dose.A`: a numeric value defining the upper bound of the support of the MTD for drug A
- `Min.Dose.B`: a numeric value defining the lower bound of the support of the MTD for drug B
- `Max.Dose.B`: a numeric value defining the upper bound of the support of the MTD for drug B
- `alpha`: a numerical value defining the probability that dose selected by EWOC is higher than the MTD.
theta  a numeric value defining the proportion of expected patients to experience a medically unacceptable, dose-limiting toxicity (DLT) if administered the MTD.

vai  a numeric value indicating variable alpha increment for each new cohort

a01  a numeric value for beta prior distribution associated with parameter rho01

b01  a numeric value for beta prior distribution associated with parameter rho01

a10  a numeric value for beta prior distribution associated with parameter rho10

b10  a numeric value for beta prior distribution associated with parameter rho10

a00  a numeric value for beta prior distribution associated with parameter rho00

b00  a numeric value for beta prior distribution associated with parameter rho00

a  a numeric value for gamma prior distribution associated with parameter eta

b  a numeric value for gamma prior distribution associated with parameter eta

del1x  Maximum dose escalation at each step for drug A, the default is 0.2*(Max.Dose.A-Min.Dose.A if not assigned)

del1y  Maximum dose escalation at each step for drug B, the default is 0.2*(Max.Dose.B-Min.Dose.B if not assigned)

burn  Number of iterations for adaption, see n.adapt in jags.model for detail

mm  Number of iterations to monitor, see n.iter in code.samples for detail

del1  Threshold for toxicity

seed  a numeric value used in random number generation

Value

type  same as input parameter type

parameters  list of input parameters

priors  list of prior parameters

Dose.A  a matrix ntrials x nsamples containing the doses of drug A assigned for each patient in a trial and each trial in the simulation

Dose.B  a matrix ntrials x nsamples containing the doses of drug B assigned for each patient in a trial and each trial in the simulation

Resp  a matrix ntrials x nsamples containing ones and zeros indicating the occurrence of DLT (1) and the absence of DLT (0) for each patient in the trial and each trial in the simulation

rho00  a numeric vector ntrials x 1 containing the estimated rho00 parameter for each trial in the simulation

rho01  a numeric vector ntrials x 1 containing the estimated rho01 parameter for each trial in the simulation

rho10  a numeric vector ntrials x 1 containing the estimated rho10 parameter for each trial in the simulation

eta  a numeric vector ntrials x 1 containing the estimated eta parameter for each trial in the simulation
Generating MTD curve based on logistic model for two drugs

Description

Generating MTD curve based on logistic model for two drugs

Usage

mtdcurve(rho00, rho01, rho10, eta, theta)
Arguments

rho00  a numeric value indicating the true value of the parameter rho00, the probability of DLT when the levels of drugs A and B are both 0

rho01  a numeric value indicating the true value of the parameter rho01, the probability of DLT when the levels of drugs A and B are 0 and 1, respectively

rho10  a numeric value indicating the true value of the parameter rho10, the probability of DLT when the levels of drugs A and B are 1 and 0, respectively

eta    a numeric value indicating the true value of the eta, the interaction parameter

theta  a numerical value defining the proportion of expected patients to experience a medically unacceptable, dose-limiting toxicity (DLT) if administered the MTD

Value

none

Examples

mtdcurve(rho00=0.01, rho01=0.2, rho10=0.9, eta=20, theta=0.2)

Description

Generating probability of DLT based on the EWOC2 model

Usage

pdlt(rho00, rho01, rho10, eta, theta, x, y)

Arguments

rho00  a numeric value indicating the true value of the parameter rho00, the probability of DLT when the levels of drugs A and B are both 0

rho01  a numeric value indicating the true value of the parameter rho01, the probability of DLT when the levels of drugs A and B are 0 and 1, respectively

rho10  a numeric value indicating the true value of the parameter rho10, the probability of DLT when the levels of drugs A and B are 1 and 0, respectively

eta    a numeric value indicating the true value of the eta, the interaction parameter

theta  a numerical value defining the proportion of expected patients to experience a medically unacceptable, dose-limiting toxicity (DLT) if administered the MTD

x      a numeric value of dose level for drug A

y      a numeric value of dose level for drug B
plot.ewoc2simu

Value

a numeric value indicating the probability of DLT with doses from input based on the logistic model

Examples

pdlt(rho00=0.01, rho01=0.2, rho10=0.9, eta=20, theta=0.2, x=0.2, y=0.3)

plot.ewoc2simu

EWOC for 2 drugs combination trial design characteristics

Description

Function to plot the trial design characteristics from EWOC 2 drugs combination simulation results

Usage

## S3 method for class 'ewoc2simu'
pplot(x, type = "MTD", conf.reg=0.9, plot.figure="Y",...)

Arguments

x
an object of class "ewoc2simu", usually a result of a call to ewoc2simu

type
a character indicating the type of plots a user requests, could be "MTD", "bias", or "percent". For discrete simulations, "bias" is not available

conf.reg
confidence level that controls the region of the doses from the last trial in the MTD plot

plot.figure
a character indicating whether user wants the plot, 'Y' would be yes, otherwise would be no. It’s mainly for internal uses

...
arguments passed to or from methods

References


Examples

# continous
test1 = ewoc2simu(ntrials=10, nsamples=40, type="c", trho00=0.01, trho01=0.2, trho10=0.9, teta=20, Min.Dose.A=0, Max.Dose.A=1, Min.Dose.B=0, Max.Dose.B=1, alpha=0.25, theta=0.20, a01=1,b01=1, a10=1,b10=1, a00=1,b00=1,a=0.8,b=0.0384)

print(test1)
plot(test1, type="MTD")
plot(test1, type="bias")
print.ewoc2

```r
plot(test1, type="percent")

# discrete
tp = c(0.03, 0.05, 0.08, 0.05, 0.08, 0.13, 0.08, 0.13, 0.2, 0.13, 0.2, 0.29, 0.2, 0.29, 0.4, 0.29, 0.4, 0.53)
test2 = ewoc2simu(ntrials=10, nsamples=40, type="d", nx=6, ny=3, tp=tp,
Min.Dose.A=0, Max.Dose.A=1, Min.Dose.B=0, Max.Dose.B=1, alpha=0.25, theta=0.20,
a01=1,b01=1,a10=1,b10=1,a00=1,b00=1,a=0.8,b=0.0384)

print(test2)
plot(test2, type="MTD")
plot(test2, type="percent")
```

---

**print.ewoc2**  
*Summarizing EWOC2 next doses results*

---

**Description**

Summarizing EWOC2 next doses result

**Usage**

```r
## S3 method for class 'ewoc2'
print(x, ...)
```

**Arguments**

- `x` an object of class "ewoc2", usually, a result of a call to ewoc2
- `...` arguments passed to or from methods

**Value**

a data.frame of 2 x 4 with columns for cohort, patients, recommended dose of drug A and recommended dose of drug B for next cohort or 2 patients

**References**


**Examples**

```r
test = ewoc2(dose.a=c(0,0), dose.b=c(0,0), resp=c(0,0), theta=0.33, alpha=0.25, Min.Dose.A=0,
Max.Dose.A=1, Min.Dose.B=0, Max.Dose.B=1, a01=1,b01=1,a10=1,b10=1,a00=1,b00=1,a=0.8,b=0.0384)
print(test)
```
Summarizing EWOC2 simulation results

Usage

```r
## S3 method for class 'ewoc2simu'
print(x, ...)
```

Arguments

- `x`: an object of class "ewoc2simu", usually, a result of a call to `ewoc2simu`
- `...`: arguments passed to or from methods

Value

A data.frame of 7 x 1 with row representing Accuracy square discrepancy (sq), Accuracy absolute discrepancy (abs), Accuracy overdose (od), percent Selection, Average percent DLT, percent Trials with DLT rate > theta+0.05, percent Trials with LDT rate > theta+0.1.

References


Examples

```r
# continuous
test1 = ewoc2simu(ntrials=10, nsamples=40, type="c", trho00=0.01, trho01=0.2, trho10=0.9, teta=20, Min.Dose.A=0, Max.Dose.A=1, Min.Dose.B=0, Max.Dose.B=1, alpha=0.25, theta=0.20, a01=1, b01=1, a10=1, b10=1, a00=1, b00=1, a=0.8, b=0.0384)
print(test1)
plot(test1, type="MTD")
plot(test1, type="bias")
plot(test1, type="percent")

# discrete
tp = c(0.03, 0.05, 0.08, 0.05, 0.08, 0.13, 0.08, 0.13, 0.13, 0.2, 0.13, 0.2, 0.29, 0.29, 0.29, 0.29, 0.4, 0.29, 0.4, 0.53)
test2 = ewoc2simu(ntrials=10, nsamples=40, type="d", nx=6, ny=3, tp=tp, Min.Dose.A=0, Max.Dose.A=1, Min.Dose.B=0, Max.Dose.B=1, alpha=0.25, theta=0.20, a01=1, b01=1, a10=1, b10=1, a00=1, b00=1, a=0.8, b=0.0384)
print(test2)
```
plot(test2, type="MTD")
plot(test2, type="percent")
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