

Package ‘CRM’

September 26, 2018

Title Continual Reassessment Method (CRM) for Phase I Clinical Trials

Version 1.2.4

Date 2018-9-25

Depends R (>= 2.10.0)

Author Qianxing Mo

Maintainer Qianxing Mo <qianxing.mo@moffitt.org>

Description Functions for phase I clinical trials using the continual reassessment method.

LazyData no

License GPL (>= 2)

NeedsCompilation yes

Repository CRAN

Date/Publication 2018-09-26 16:10:02 UTC

R topics documented:

crm	1
crmsim	3
Index	6

crm	<i>A function for the continued reassessment method (CRM) used in Phase I clinical trials</i>
-----	---

Description

Function `crm` implement the continued reassessment method (CRM) for dose finding in Phase I clinical trials.

Usage

```
crm(target, prior, ptdata, model=1, a0=1, b=3)
```

Arguments

target	Target probability of toxicity. The value must be in (0, 1).
prior	Prior probabilities of toxicity for each dose. The values must be in (0,1) and in an ascending order. For example, prior=c(0.05,0.1,0.2,0.3,0.5,0.7),which corresponds to dose levels 1, 2, 3, 4, 5 and 6,respectively.
ptdata	A n by 2 matrix in which the first column contains dose levels and the second column contains toxicity indicators. Dose levels must be integers (e.g., 1, 2, 3, ..., N). Toxicity indicators must be 0 and 1, where 0 indicates no toxicity and 1 indicates toxicity.
model	Dose-toxicity model. The value must be 1 (hyperbolic tangent model) or 2 (one-parameter logistic model). Default is 1. Hyperbolic tangent model: $p(y=1 x,a) = ((\tanh(x)+1)/2)^a$. One-parameter logistic model: $p(y=1 x,a,b) = \exp(b+ax)/(1+\exp(b+ax))$. For both models, y=1 indicates toxicity is observed; a is the parameter that can be updated based on the outcome of the trail; b is a fixed parameter. The prior for a is $\exp(-a)$.
a0	Initial value for parameter a. Default is 1.0.
b	A fixed parameter for the one-parameter logistic model. Default is 3.0.

Value

A list with the following two objects:

MTD	The dose level proposed as the maximum tolerated dose (MTD) based on the patient data
a	The updated value for parameter a

Author(s)

Qianxing Mo; <qianxing.mo@moffitt.org>

References

John O'Quigley, Margaret Pepe, and Lloyd Fisher. (1990). Continual Reassessment Method: A Practical Design for Phase 1 Clinical Trials in Cancer. *Biometrics*, 46, pp.33-48

See Also

[crmsim](#), [crmsiminc1](#), [crmsiminc2](#)

Examples

```
#The table 1 in O'Quigley et al.'s paper, page 40
#This example is used to illustrate how the program is used to find
#the MTD and the updated parameter

target <- 0.2
prior <- c(0.05,0.1,0.2,0.3,0.5,0.7)
```


true	True probabilities of toxicity. The values must be in (0,1) and in an ascending order. e.g. (0.1,0.2,0.3,0.4,0.5,0.8)
rate	Recruitment/accrual rate of subjects in a 30 window. For example,if 1 subject can be recruited per 30 days, then set rate = 1/30 = 0.033; if 2 patients per 30 day then rate = 2/30 = 0.0667.
cycle	The length of treatment cycle in days.
cohort	Cohort size of subjects entering into the trials. Default is 1. The value for cohort must be less than or equal to the value for nsubject.
nsubject	Total number of subjects in one simulation(or trial). Default is 24. nsubject should be equal to n*cohort,where n is positive integer.
nsim	Total number of simulations. Default is 1000.
model	Dose-toxicity model. The value must be 1 (hyperbolic tangent model) or 2 (one-parameter logistic model). Default is 1. Hyperbolic tangent model: $p(y=1 x,a) = ((\tanh(x)+1)/2)^a$. One-parameter logistic model: $p(y=1 x,a,b) = \exp(b+ax)/(1+\exp(b+ax))$. For both models, y=1 indicates toxicity is observed; a is the parameter that can be updated based on the outcome of the trail; b is a fixed parameter. The prior for a is $\exp(-a)$.
a0	Initial value for parameter a. Default is 1.0.
b	A fixed parameter for the one-parameter logistic model. Default is 3.0.
jump	jump=FALSE means NOT allowing that the proposed dose by the CRM program has an increase of more than one level than the previous level; jump=TRUE means allowing more-than-one-level increase of the proposed dose by the CRM program.
start.dose	Initial dose for each trial. Default is 1.
seed	Seed for the random number generator. Default is 777.

Value

SimResult is a matrix that summarizes the operating characteristics of CRM. The column names are the dose levels. The row names are the operating characteristics.

% Selection	the percentage of selection of each dose as MTD
% Subjects Treated	the percentage of subjects treated at each dose
# Subjects Treated	the average number of subjects treated at each dose
Average Toxicities	the average toxicities per trial at each dose
True Probabilities	the true probability of toxicity of each dose

TrialDuration is a table that summarizes the time needed for the trial based on the simulation.

Author(s)

Qianxing Mo; <qianxing.mo@moffitt.org>

References

John O'Quigley, Margaret Pepe, and Lloyd Fisher. (1990). Continual Reassessment Method: A Practical Design for Phase 1 Clinical Trials in Cancer. *Biometrics*, 46, pp.33-48

Alexia Iasonos, Andrew S Wilton, Elyn R Riedel, Venkatraman E Seshan and David R Spriggs. A comprehensive comparison of the continual reassessment method to the standard 3+3 dose escalation scheme in Phase I dose-finding studies. *Clinical Trials*, 2008, nil:1-12

See Also

[crm](#)

Examples

```
prior1 <- c(0.05,0.1,0.2,0.3,0.5,0.7)
true1 <- c(0.1,0.15,0.2,0.4,0.5,0.8)

### simulations using model 1 (hyperbolic tangent model)

### uncomment the following code to run ###
#crmsim(target=0.2,prior=prior1,true=true1,rate=0.1,cycle=21,cohort=1,nsubject=24,nsim=1000,
#       model=1,a0=1,b=3,jump=FALSE,start.dose=1,seed=777)

#crmsiminc1(target=0.2,prior=prior1,true=true1,rate=0.1,cycle=21,nsubject=24,nsim=1000,
#           model=1,a0=1,b=3,jump=FALSE,start.dose=1,seed=777)

#crmsiminc2(target=0.2,prior=prior1,true=true1,rate=0.1,cycle=21,nsubject=24,nsim=1000,
#           model=1,a0=1,b=3,jump=FALSE,start.dose=1,seed=777)

# simulations using model 2 (one-parameter logistic model)
#crmsim(target=0.2,prior=prior1,true=true1,rate=0.1,cycle=21,cohort=1,nsubject=24,nsim=1000,
#       model=2,a0=1,b=3,jump=FALSE,start.dose=1,seed=777)

#crmsiminc1(target=0.2,prior=prior1,true=true1,rate=0.1,cycle=21,nsubject=24,nsim=1000,
#           model=2,a0=1,b=3,jump=FALSE,start.dose=1,seed=777)

#crmsiminc2(target=0.2,prior=prior1,true=true1,rate=0.1,cycle=21,nsubject=24,nsim=1000,
#           model=2,a0=1,b=3,jump=FALSE,start.dose=1,seed=777)
```

Index

*Topic **design**

crm, 1

crmsim, 3

crm, 1, 5

crmsim, 2, 3

crmsiminc1, 2

crmsiminc1 (crmsim), 3

crmsiminc2, 2

crmsiminc2 (crmsim), 3