Describe the CRM function used in Phase I clinical trials.

**Description**

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

**Usage**

```r
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 trial; 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

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References


See Also

- `crmsim`
- `crmsiminc1`
- `crmsiminc2`

Examples

```r
# The table 1 in O'Quingley 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)
```
```r
x <- c(3, 4, 4, 3, 3, 2, 1, 1, 1, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 1)
y <- c(0, 0, 1, 0, 1, 1, 0, 0, 0, 0, 0, 0, 1, 0, 0, 0, 0, 0, 1, 0, 0, 0, 1, 1, 1)
ptdata <- cbind(x, y)
for(i in 1:25){
  if(i == 1){
    cat(1, 1, 3, 0, "\n")
  }
  res <- crm(target, prior, ptdata[1:i,], model=1, a0=1)
  if(i < 25){
    cat(i+1, res$a, res$MTD, ptdata[i+1, 2], "\n")
  } else {
    cat(i+1, res$a, res$MTD, "\n")
  }
}
# the proposed MTD is res$MTD
```

---

**crmsim**  
**CRM Simulator**

**Description**

`crmsim`, `crmsiminc1` and `crmsiminc2` implement the continued reassessment method (CRM) for dose finding in Phase I clinical trials. The operating characteristics of CRM are summarized through simulations.

`crmsim` allows users to select a variety of cohort sizes. A cohort of subjects are treated at the same dose.

The cohort size is fixed to 1 in `crmsiminc1` and `crmsiminc2`. `crmsiminc1` implements an algorithm that allows a clinical trial to proceed to the next subject’s dose assignment before observing the last subject’s toxicity data. `crmsiminc2` allows a clinical trial to proceed to the next subject’s dose assignment before observing the last two subject’s toxicity data (see Iasonos et al. for details).

**Usage**

```r
crmsim(target, prior, true, rate, cycle, cohort=1, nsubject=24, nsim=1000, 
       model=1, a0=1, b=3, jump=FALSE, start.dose=1, seed=777)
```

```r
crmsiminc1(target, prior, true, rate, cycle, nsubject=24, nsim=1000, 
           model=1, a0=1, b=3, jump=FALSE, start.dose=1, seed=777)
```

```r
crmsiminc2(target, prior, true, rate, cycle, nsubject=24, nsim=1000, 
           model=1, a0=1, b=3, jump=FALSE, start.dose=1, seed=777)
```

**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.
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 trial; 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.

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**References**


**See Also**

*crm*

**Examples**

```r
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 ###

```
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