Package ‘dfcrm’

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Description Provides functions to run the CRM and TITE-CRM in phase I trials and calibration tools for trial planning purposes.
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cohere

Coherence of two-stage CRM

Description

Returns a message on the coherence status of a two-stage CRM design.

Usage

cohere(prior, target, x0, method = "bayes", model = "empiric",
       intcpt = 3, scale = sqrt(1.34), detail = TRUE)

Arguments

prior A vector of initial guesses of toxicity probabilities associated the doses.
target The target DLT rate.
x0 The initial design containing a non-decreasing sequence of dose levels. The length of the initial design is the sample size.
method A character string to specify the method for parameter estimation. The default method “bayes” estimates the model parameter by the posterior mean. Maximum likelihood estimation is specified by “mle”.
model A character string to specify the working model used in the method. The default model is “empiric”. A one-parameter logistic model is specified by “logistic”.
intcpt The intercept of the working logistic model. The default is 3. If model="empiric", this argument will be ignored.
scale Standard deviation of the normal prior of the model parameter. Default is sqrt(1.34).
detail If TRUE, details about incoherent escalations will be displayed.

Value

message A string character giving a message regarding the coherence status of a two-stage CRM design.

References


See Also

crm
Examples

```r
prior <- c(0.05, 0.10, 0.20, 0.35, 0.50, 0.70)
x0 <- c(rep(1,3), rep(2,3), rep(3,3), rep(4,3), rep(5,3), rep(6,9))

# The above design is coherent when target rate = 0.20
foo <- cohere(prior, target=0.2, x0)
foo

# The design is incoherent if a larger target DLT rate is used.
foo2 <- cohere(prior, target=0.3, x0)
```

CRM

Executing the CRM

Description

crm is used to compute a dose for the next patient in a phase I trial according to the CRM.

Usage

crm(prior, target, tox, level, n = length(level), dosename = NULL,
include = 1:n, pid = 1:n, conf.level = 0.9, method = "bayes",
model = "empiric", intcpt = 3, scale = sqrt(1.34), model.detail = TRUE,
patient.detail = TRUE, var.est = TRUE)

Arguments

- **prior**: A vector of initial guesses of toxicity probabilities associated the doses.
- **target**: The target DLT rate.
- **tox**: A vector of patient outcomes; 1 indicates a toxicity, 0 otherwise.
- **level**: A vector of dose levels assigned to patients. The length of level must be equal to that of tox.
- **n**: The number of patients enrolled.
- **dosename**: A vector containing the names of the regimens/doses used. The length of dosename must be equal to that of prior.
- **include**: A subset of patients included in the dose calculation.
- **pid**: Patient ID provided in the study. Its length must be equal to that of level.
- **conf.level**: Confidence level for the probability/confidence interval of the returned dose-toxicity curve.
- **method**: A character string to specify the method for parameter estimation. The default method "bayes" estimates the model parameter by the posterior mean. Maximum likelihood estimation is specified by "mle".
- **model**: A character string to specify the working model used in the method. The default model is "empiric". A one-parameter logistic model is specified by "logistic".
intcet  The intercept of the working logistic model. The default is 3. If model="empiric", this argument will be ignored.

scale  Standard deviation of the normal prior of the model parameter. Default is sqrt(1.34).

model.detail  If FALSE, the model content of an "mtd" object will not be displayed. Default is TRUE.

patient.detail  If FALSE, patient summary of an "mtd" object will not be displayed. Default is TRUE.

var. est  If TRUE, variance of the estimate of the model parameter and probability/confidence interval for the dose-toxicity curve will be computed

Details
For maximum likelihood estimation, the variance of the estimate of $\beta$ (post.var) is approximated by the posterior variance of $\beta$ with a dispersed normal prior.

The empiric model is specified as $F(d,\beta) = d^{\exp(\beta)}$. The logistic model is specified as $\text{logit}(F(d,\beta)) = \text{intcet} + \exp(\beta) \times d$. For method="bayes", the prior on $\beta$ is normal with mean 0. Exponentiation of $\beta$ ensures an increasing dose-toxicity function.

Value
An object of class "mtd" is returned, consisting of the summary of dose assignments thus far and the recommendation of dose for the next patient.

prior  Initial guesses of toxicity rates.

target  The target probability of toxicity at the MTD.

ptoxt  Updated estimates of toxicity rates.

ptoxtL  Lower confidence/probability limits of toxicity rates.

ptoxtU  Upper confidence/probability limits of toxicity rates.

mtd  The updated estimate of the MTD.

prior.var  The variance of the normal prior.

post.var  The posterior variance of the model parameter.

estimate  Estimate of the model parameter.

method  The method of estimation.

model  The working model.

dosescaled  The scaled doses obtained via backward substitution.

tox  Patients’ toxicity indications.

level  Dose levels assigned to patients.

References

**Examples**

```r
# Create a simple data set
prior <- c(0.05, 0.10, 0.20, 0.35, 0.50, 0.70)
target <- 0.2
level <- c(3, 4, 4, 3, 4, 3, 2, 2)
y <- c(0, 0, 1, 0, 0, 1, 1, 0, 0)
foo <- crm(prior, target, y, level)
ptox <- foo$ptox  # updated estimates of toxicity rates
```

---

**crmsens**  
_Model Sensitivity in the CRM_

**Description**

Evaluate the model sensitivity in the CRM by indifference intervals.

**Usage**

```r
crmsens(prior, target, model = "empiric", intcpt = 3, eps = 1e-06, 
        maxit = 100, detail = FALSE)
```

**Arguments**

- `prior`: A vector of initial guesses of toxicity probabilities associated the doses.
- `target`: The target DLT rate.
- `model`: A character string to specify the working model used in the method. The default model is “empiric”. A one-parameter logistic model is specified by “logistic”.
- `intcpt`: The intercept of the working logistic model. The default is 3. If `model="empiric``, this argument will be ignored.
- `eps`: Error tolerance in the computation of indifference intervals.
- `maxit`: Maximum number of iterations in the computation of indifference intervals.
- `detail`: If TRUE, the details of the “H sets” will be displayed. Default is FALSE.

**Value**

The function `crmsens` returns the model sensitivity for the model specifications given by the user.

- `Hset`: The “H sets” of the model parameter.
- `iint`: The indifference intervals of the dose-toxicity model associated with the test doses.
References


See Also

crm, getprior

Examples

prior <- c(0.05, 0.10, 0.20, 0.35, 0.50, 0.70)
target <- 0.2
foo <- crmsens(prior, target, model="logistic", intcpt=2, detail=TRUE)

---

crmsim

CRM Simulator

description

*crmsim* is used to generate simulation replicates of phase I trial using the (group) CRM under a specified dose-toxicity configuration.

Usage

```r

crmsim(pi, prior, target, n, x0, nsim = 1, mcohort = 1, restrict = TRUE, count = TRUE, method = "bayes", model = "empiric", intcpt = 3, scale = sqrt(1.34), seed = 1009)
```

Arguments

- **PI**: A vector of the true toxicity probabilities associated with the doses.
- **prior**: A vector of initial guesses of toxicity probabilities associated with the doses. Must be of same length as PI.
- **target**: The target DLT rate.
- **n**: Sample size of the trial.
- **x0**: The initial design. For one-stage TITE-CRM, it is a single numeric value indicating the starting dose. For two-stage TITE-CRM, it is a non-decreasing sequence of dose levels of length n.
- **nsim**: The number of simulations. Default is set at 1.
- **mcohort**: The number of patients enrolled before the next model-based update. Default is set at 1, i.e., a fully sequential update.
- **restrict**: If TRUE, restrictions apply during the trials to avoid (1) skipping doses in escalation and (2) escalation immediately after a toxic outcome (i.e., incoherent escalation). If FALSE, dose assignments are purely model-based.
count  If TRUE, the number of the current simulation replicate will be displayed.
method  A character string to specify the method for parameter estimation. The default method “bayes” estimates the model parameter by the posterior mean. Maximum likelihood estimation is specified by “mle”.
model  A character string to specify the working model used in the method. The default model is “empiric”. A one-parameter logistic model is specified by “logistic”.
intcpt  The intercept of the working logistic model. The default is 3. If model=“empiric”, this argument will be ignored.
scale  Standard deviation of the normal prior of the model parameter. Default is sqrt(1.34).
seed  Seed of the random number generator.

Value
An object of class “sim” is returned, consisting of the operating characteristics of the design specified. The time component of the design is suppressed for the CRM simulator. All “sim” objects generated by crmsim contain at least the following components:

\begin{itemize}
  \item \texttt{PI}  True toxicity rates.
  \item \texttt{prior}  Initial guesses of toxicity rates.
  \item \texttt{target}  The target probability of toxicity at the MTD.
  \item \texttt{n}  Sample size.
  \item \texttt{x0}  The initial design.
  \item \texttt{MTD}  Distribution of the MTD estimates. If \texttt{nsim}=1, this is a single numeric value of the recommended MTD of in simulated trial.
  \item \texttt{level}  Average number of patients treated at the test doses. If \texttt{nsim}=1, this is a vector of length \texttt{n} indicating the doses assigned to the patients in the simulated trial.
  \item \texttt{tox}  Average number of toxicities seen at the test doses. If \texttt{nsim}=1, this is a vector of length \texttt{n} indicating the toxicity outcomes of the patients in the simulated trial.
  \item \texttt{beta.hat}  The estimates of the model parameter throughout the simulated trial(s). The dose assignment of the jth patient in each trial corresponds to the jth element in each row.
  \item \texttt{final.est}  The final estimates of the model parameter of the simulated trials.
\end{itemize}

References


See Also

\texttt{crm}, \texttt{titesim}.  

Examples

PI <- c(0.10, 0.20, 0.40, 0.50, 0.60, 0.65)
prior <- c(0.05, 0.10, 0.20, 0.35, 0.50, 0.70)
target <- 0.2
x0 <- c(rep(1,3), rep(2,3), rep(3,3), rep(4,3), rep(5,3), rep(6,9))

# Generate a single replicate of two-stage group CRM trial of group size 3
foo <- crmsim(PI, prior, target, 24, x0, mcohort=3)
## Not run: plot(foo,ask=T)  # summarize trial graphically

# Generate 10 replicates of CRM trial with 24 subjects
foo10 <- crmsim(PI, prior, target, 24, 3, nsim=10, mcohort=2)

getinit
     Calibrating an initial design

Description

Returns an initial design that is compatible with the specified CRM setup when used in a two-stage design.

Usage

getinit(prior, target, n, nk = round(n/3), method = "bayes",
model = "empiric", intcpt = 3, scale = sqrt(1.34), detail = FALSE)

Arguments

prior  A vector of initial guesses of toxicity probabilities associated the doses.
target The target DLT rate.
n     The sample size of the trial.
nK    The minimum number of subjects required at the highest test dose in case of no toxicity throughout the trial.
method A character string to specify the method for parameter estimation. The default method “bayes” estimates the model parameter by the posterior mean. Maximum likelihood estimation is specified by “mle”.
model A character string to specify the working model used in the method. The default model is “empiric”. A one-parameter logistic model is specified by “logistic”.
intcpt The intercept of the working logistic model. The default is 3. If model="empiric", this argument will be ignored.
scale Standard deviation of the normal prior of the model parameter. Default is sqrt(1.34).
detail If TRUE, intermediate designs will be displayed.
**Details**

An initial design will be incompatible to the CRM setup if the escalation pace is too conservative, i.e. slow. The algorithm in `getinit` starts the search of a compatible design with an aggressive initial design that starts a trial at the second highest dose. A more conservative design will be subsequently tested for compatibility if the current design is compatible. The sequence returned may be viewed as a conservative compatible initial design.

**Value**

A non-decreasing sequence of dose levels is returned.

**References**


**See Also**

`cohere`

**Examples**

```r
prior <- c(0.05, 0.10, 0.20, 0.35, 0.50, 0.70)
target <- 0.2

# Search stops because it requires at least 8 subjects at the highest dose
getinit(prior, target, 25, nK=8, method="mle", detail=TRUE)

# Search stops because an incompatible design is reached
getinit(prior, 0.3, 25, nK=8, method="mle", detail=TRUE)
```

---

**getn**

*Sample size calculator for CRM trials*

**Description**

Sample size calculator for a one-stage Bayesian CRM (see Details for design specification).

**Usage**

```r
getn(apcs, target, nlevel, psi, correction = TRUE, detail = FALSE)
```
Arguments

apcs The desired average probability of correction selection (PCS) under the logistic calibration set.
target The target DLT rate.
nlevel The number of test doses.
psi Effect size, i.e., odds ratio of the logistic dose-toxicity curves.
correction Continuity correction is applied in the sample size calculation if TRUE (default). Otherwise if FALSE.
detail Print only essential results for trial planning if FALSE (default). Otherwise if TRUE.

details

The sample size calculation is based on empirical approximation for the CRM using the power (or empiric) dose-toxicity function, \( F(d, \beta) = d^{\exp(\beta)} \), where \( \beta \) has a normal prior with mean 0 and variance 1.34, and the starting dose is the median level. The “skeleton” is obtained by setting halfwidth at \( 0.25 \times \text{target} \), and \( \nu \) at the median level in the function \text{getprior}. The calculation is intended to serve as an initial sample size for the CRM calibration process depicted in Figure 7.1 in Cheung (2011).

Value

An object of class “crmsize” is returned, consisting of the following components:

n The calculated sample size.
astar The desired average PCS.
target The target DLT rate.
nlevel The number of test doses.
psi Odds ratio.
bstar An intermediate value used to calculate the sample size. Shown only if detail=TRUE.
efficiency Ratio of required sample sizes of the optimal benchmark and the CRM. Shown only if detail=TRUE.
correction Whether continuity correction is applied. Shown only if detail=TRUE.
na The CRM sample size before rounding up.
nb The sample size lower bound before rounding up.
messages String characters prompt warning messages and caveats regarding the sample size calculation.

References

getprior

See Also

getprior

Examples

apcs <- 0.6
target <- 0.25
nlevel <- 5
psi <- 1.8

# Sample size calculation with continuity correction
obj = getn(apcs, target, nlevel, psi, correction=TRUE)
obj

N = obj$n

description

Calibrating prior DLT rates

Description

Returns a vector of initial guesses of toxicity probabilities associated the doses for a given model sensitivity (set of indifference intervals).

Usage

getprior(halfwidth, target, nu, nlevel, model = "empiric", intcpt = 3)

Arguments

halfwidth The desired halfwidth of the indifference intervals.
target The target DLT rate.
nu The prior guess of MTD.
nlevel The number of test doses.
model A character string to specify the working model used in the method. The default model is “empiric”. A one-parameter logistic model is specified by “logistic”.
intcpt The intercept of the working logistic model. The default is 3. If model="empiric", this argument will be ignored.

Details

getprior is an “inverse” function of crmsens which gives the indifference intervals for a given set of initial guesses.

Value

A vector of length nlevel is returned.
References


See Also

crmsens

Examples

target <- 0.25
delta <- 0.10
mtd0 <- 3

# initial DLT rates with indifference intervals [0.15, 0.35].
prior <- getprior(delta, target, mtd0, nlevel=6, model="logistic")

# Executing the TITE-CRM

Description

titecrm is used to compute a dose for the next patient in a phase I trial according to the TITE-CRM.

Usage

titecrm(prior, target, tox, level, n = length(level), weights = NULL, followup = NULL, entry = NULL, exit = NULL, obswin = NULL, scheme = "linear", conf.level = 0.9, dosename = NULL, include = 1:n, pid = 1:n, method = "bayes", model = "empiric", var.est = TRUE, scale = sqrt(1.34), intcpt = 3, model.detail = TRUE, patient.detail = TRUE, tite = TRUE)

Arguments

prior A vector of initial guesses of toxicity probabilities associated the doses.
target The target DLT rate.
tox A vector of patient outcomes; 1 indicates a toxicity, 0 otherwise.
level A vector of dose levels assigned to patients. The length of level must be equal to that of tox.
n The number of patients enrolled.
weights  A vector of weights assigned to observations. A weight must be between 0 and 1. If given, the arguments followup, entry, exit, obswin, and scheme will be ignored. If not supplied, users must provide follow-up information via the argument followup or entry and exit, as well as the observation window obswin. The length of weights must be equal to that of tox.

followup  A vector of follow-up times of patients. If given, the arguments entry and exit will be ignored.

dose    A vector of entry times of the patients.

exit    A vector of exit times of the patients due to either end of follow-up or toxicity.

obswin  The observation window with respect to which the MTD is defined. If not supplied, users must provide weights.

scheme  A character string to specify the method for assigning weights. Default is “linear”. An adaptive weight function is specified by “adaptive”.

conf.level  Confidence level for the probability/confidence interval of the returned dose-toxicity curve.

dose    A vector containing the names of the regimens/doses used. The length of dosename must be equal to that of prior.

include  A subset of patients included in the dose calculation.

dose    Patient ID provided in the study. Its length must be equal to that of level.

method  A character string to specify the method for parameter estimation. The default method “bayes” estimates the model parameter by the posterior mean. Maximum likelihood estimation is specified by “mle”.

model  A character string to specify the working model used in the method. The default model is “empiric”. A one-parameter logistic model is specified by “logistic”.

var.est  If TRUE, variance of the estimate of the model parameter and probability/confidence interval for the dose-toxicity curve will be computed.

scale  Standard deviation of the normal prior of the model parameter. Default is sqrt(1.34).

intcpt  The intercept of the working logistic model. The default is 3. If model=“empiric”, this argument will be ignored.

model.detail  If FALSE, the model content of an “mtd” object will not be displayed. Default is TRUE.

patient.detail  If FALSE, patient summary of an “mtd” object will not be displayed. Default is TRUE.

tite  If FALSE, the time components in patient summary of an “mtd” object will be omitted. Default in TRUE.

Details

The adaptive weighting scheme is given in Cheung and Chappell (2000) given in the reference list.
Value

An object of class “mtd” is returned, consisting of the summary of dose assignments thus far and the recommendation of dose for the next patient.

- **prior**: Initial guesses of toxicity rates.
- **target**: The target probability of toxicity at the MTD.
- **ptox**: Updated estimates of toxicity rates.
- **ptoxL**: Lower confidence/probability limits of toxicity rates.
- **ptoxU**: Upper confidence/probability limits of toxicity rates.
- **mtd**: The updated estimate of the MTD.
- **prior.var**: The variance of the normal prior.
- **post.var**: The posterior variance of the model parameter.
- **estimate**: Estimate of the model parameter.
- **method**: The method of estimation.
- **model**: The working model.
- **dosescaled**: The scaled doses obtained via backward substitution.
- **tox**: Patients’ toxicity indications.
- **level**: Dose levels assigned to patients.
- **followup**: Follow-up times of patients.
- **obswin**: Observation window with respect to which the MTD is defined.
- **weights**: Weights assigned to patients.
- **entry**: Entry times of patients.
- **exit**: Exit times of patients.
- **scheme**: Weighting scheme.

References


See Also

- **crm**
Examples

# Create a simple data set
prior <- c(0.05, 0.10, 0.20, 0.35, 0.50, 0.70)
target <- 0.2
level <- c(3, 3, 4, 4, 3, 2, 2, 3)
y <- c(0, 0, 1, 1, 0, 0, 0, 0)
u <- c(178, 181, 168, 181, 24, 181, 179, 102, 42, 3)
tau <- 180

foo <- titecrm(prior, target, y, level, followup=u, obswin=tau)
rec <- foo$mtd # recommend a dose level for next patient

# An example with adaptive weight
foo2 <- titecrm(prior, target, y, level, followup=u, obswin=tau, scheme="adaptive")
wts <- foo2$weights

# The 'weights' argument makes 'followup' and 'obswin' obsolete
foo3 <- titecrm(prior, target, y, level, weights=wts, followup=u, obswin=tau)
## Not run: plot(foo3, ask=T)

## Patient time information via 'entry' and 'exit' arguments
# entry time (days since study begins)
entry <- c(7, 29, 49, 76, 92, 133, 241, 303, 363, 402)
# exit time (days since study begins)
exit <- c(185, 216, 217, 257, 116, 314, 420, 405, 405, 405)

foo4 <- titecrm(prior, target, y, level, exit=exit, entry=entry, obswin=tau)
## Not run: plot(foo4, ask=T)

---

**TITE-CRM Simulator**

Description

`titesim` is used to generate simulation replicates of phase I trial using the TITE-CRM under a specified dose-toxicity configuration.

Usage

`titesim(PI, prior, target, n, x0, nsim = 1, restrict = TRUE, obswin = 1, tgrp = obswin, rate = 1, accrual = "fixed", surv = "uniform", scheme = "linear", count = TRUE, method = "bayes", model = "empiric", intcpt = 3, scale = sqrt(1.34), seed = 1009)``

Arguments

- **PI**: A vector of the true toxicity probabilities associated with the doses.
- **prior**: A vector of initial guesses of toxicity probabilities associated with the doses.
  Must be of same length as PI.
target

The target DLT rate.

n

Sample size of the trial.

x0

The initial design. For one-stage TITE-CRM, it is a single numeric value indicating the starting dose. For two-stage TITE-CRM, it is a non-decreasing sequence of dose levels of length n.

nsim

The number of simulations. Default is set at 1.

restrict

If TRUE, restrictions apply during the trials to avoid (1) skipping doses in escalation and (2) escalation immediately after a toxic outcome (i.e., incoherent escalation). If FALSE, dose assignments are purely model-based.

obswin

The observation window with respect to which the MTD is defined.

tgrp

The minimum waiting time between two dose cohorts at the initial stage. Default is set as obswin, i.e., complete follow-up in all current patients is required before escalation to the next dose group. This argument is used only in two-stage TITE-CRM.

rate

Patient arrival rate: Expected number of arrivals per observation window. Example: obswin=6 and rate=3 means expecting 3 patients arrive in 6 time units.

accrual

Patient accrual scheme. Default is “fixed” whereby inter-patient arrival is fixed. Alternatively, use “poisson” to simulate patient arrivals by the Poisson process.

surv

Distribution for time-to-toxicity. Default is “uniform” where toxicity, if occurs, occurs uniformly on the interval [0, obswin]. Other survival distributions including exponential and Weibull are to be made available.

scheme

A character string to specify the method for assigning weights. Default is “linear”. An adaptive weight is specified by “adaptive”.

count

If TRUE, the number of the current simulation replicate will be displayed.

method

A character string to specify the method for parameter estimation. The default method “bayes” estimates the model parameter by the posterior mean. Maximum likelihood estimation is specified by “mle”.

model

A character string to specify the working model used in the method. The default model is “empiric”. A one-parameter logistic model is specified by “logistic”.

intcpt

The intercept of the working logistic model. The default is 3. If model="empiric", this argument will be ignored.

scale

Standard deviation of the normal prior of the model parameter. Default is sqrt(1.34).

seed

Seed of the random number generator.

Value

An object of class “sim” is returned, consisting of the operating characteristics of the design specified.

For a “sim” object with nsim=1, the time component of individual subjects in the simulated trial is available via the values arrival, toxicity.time, and toxicity.study.time which respectively contain patients’ arrival times, times-to-toxicity, and the times-to-toxicity per study time.

For a “sim” object with nsim>1, the time component of the design is summarized via the value duration, which is the duration of the simulated trials, computed by adding the arrival time of the last patient and obswin.

All “sim” objects contain at least the following components:
**PI**  True toxicity rates.
**prior**  Initial guesses of toxicity rates.
**target**  The target probability of toxicity at the MTD.
**n**  Sample size.
**x0**  The initial design.
**MTD**  Distribution of the MTD estimates. If \( n_{\text{sim}}=1 \), this is a single numeric value of the recommended MTD of in simulated trial.
**level**  Average number of patients treated at the test doses. If \( n_{\text{sim}}=1 \), this is a vector of length \( n \) indicating the doses assigned to the patients in the simulated trial.
**tox**  Average number of toxicities seen at the test doses. If \( n_{\text{sim}}=1 \), this is a vector of length \( n \) indicating the toxicity outcomes of the patients in the simulated trial.
**beta.hat**  The estimates of the model parameter throughout the simulated trial(s). The dose assignment of the jth patient in each trial corresponds to the jth element in each row.
**final.est**  The final estimates of the model parameter of the simulated trials.

**References**


**See Also**

`crmsim`, `titecrm`.

**Examples**

```r
PI <- c(0.10, 0.20, 0.40, 0.50, 0.60, 0.65)
prior <- c(0.05, 0.10, 0.20, 0.35, 0.50, 0.70)
target <- 0.2
x0 <- c(rep(1,3), rep(2,3), rep(3,3), rep(4,3), rep(5,3), rep(6,9))

# Generate a single replicate of two-stage TITE-CRM trial of size 24
foo <- titesim(PI, prior, target, 24, x0, obswin=6, rate=4, accrual="poisson")
# Not run: plot(foo, ask=T)  # summarize trial graphically

# Generate 10 replicates of TITE-CRM trial of size 24
foo10 <- titesim(PI, prior, target, 24, 3, nsim=10, obswin=6, rate=4, accrual="poisson")
foo10
```

foo10
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