

Package ‘UBCRM’

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Title Simulate and Conduct Dose-Escalation Phase I Studies

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Description Two Phase I designs are implemented in the package: the classical 3+3 and the Continual Reassessment Method (<[doi:10.2307/2531628](https://doi.org/10.2307/2531628)>). Simulations tools are also available to estimate the operating characteristics of the methods with several user-dependent options.

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 UBCRM-package

UBCRM is a package containing functions to simulate and conduct dose escalation phase I studies

Description

Two designs are implemented in the package: the classical 3+3 and the Continual Reassessment Method. Simulations tools are also available to estimate the operating characteristics of the methods with several user-dependent options.

Author(s)

Benjamin Esterni, Baboukar Mane. Unite de Biostatistique et de Methodologie, Institut Paoli-Calmettes, Marseille, France.

References

- O'Quigley J., Pepe M., Fisher L. (1990). Continual Reassessment Method: a practical design for Phase I clinical trials in cancer. *Biometrics* 46, 33-48. <<https://doi.org/10.2307/2531628>>
- O'Quigley J., Shen LZ. (1996). Continual Reassessment Method: a likelihood approach. *Biometrics* 52, 673-684. <<https://doi.org/10.2307/2532905>>
- Paoletti X., Kramar A. (2009). A comparison of model choices for the Continual Reassessment Method in phase I cancer trials. *Statistics in Medicine* 28, 3012-3028. <<https://doi.org/10.1002/sim.3682>>
- Chamorey Emmanuel. (2009). *Methodologie des essais de phase precoce en cancerologie: evolution des schemas et apport de la pharmacologie*. These.
- Garret-Mayer Elizabeth. (2006). The Continual Reassessment Method for dose-finding studies: a tutorial. *Clinical Trials*: 57-71. <<https://doi.org/10.1191/1740774506cn134oa>>

Examples

```
data<- CreData(4)
prior<-c(.05,.1,.15,.2)

# One study simulation
simCrm(prior=prior, firstdose = 2, truerate = prior, cohortsize = 3, target = 1/3,
nptmax = 18, nmaxmtd = 6, nmaxdose = 18, sd = 1.34, approach = "bayes", model = "power",
method = "fpost", nextlevel = "ntarget", upskipping = TRUE, downskipping = FALSE,
lastdose = NA, graphic = FALSE, seed = 20130110)

# N simulations with CRM
# Power model, no up skipping, start at dose 2
res1<- ssimCrm(prior=prior, 100, firstdose = 2, truerate = prior, cohortsize = 3,
target = 1/3, nptmax = 18, nmaxmtd = 6, nmaxdose = 18, sd = 1.34, approach = "bayes",
method = "fpost", model = "power", nextlevel = "ntarget", upskipping = TRUE,
downskipping = FALSE, r = 2, seed=20130110)
res1
```

```
# Simulations with 3+3 design
res2<- ssim3p3(truerate=prior, 100, r = 2, seed=20130110)
res2
```

aip

*Functions to calculate the appropriate dose level singletons***Description**

Pool of functions to calculate dose level singletons values: aip, ail2 and ait2 calculate sgl in order that $E[\text{psy}] = \text{prior}$, ail1 and ait1 calculate sgl in order that $\text{psy}(\text{sgl}, 1) = \text{prior}$.

Usage

```
aip(p_prior, sd = 1.34)
ait1(p_prior, a=1)
ail1(p_prior, a=1)
ait2(p_prior)
ail2(p_prior)
```

Arguments

p_prior	Prior toxicity probability.
sd	Standard deviation in case of normal distribution for the parameter.
a	Rate in case of exponential distribution for the parameter.

Value

Numeric length(p-prior)-vector.

Author(s)

Benjamin Esterni, Baboukar Mane. Unite de Biostatistique et de Methodologie, Institut Paoli-Calmettes, Marseille, France.

References

- O'Quigley J., Pepe M., Fisher L. (1990). Continual Reassessment Method: a practical design for Phase I clinical trials in cancer. *Biometrics* 46, 33-48. <<https://doi.org/10.2307/2531628>>
- O'Quigley J., Shen LZ. (1996). Continual Reassessment Method: a likelihood approach. *Biometrics* 52, 673-684. <<https://doi.org/10.2307/2532905>>
- Paoletti X., Kramar A. (2009). A comparison of model choices for the Continual Reassessment Method in phase I cancer trials. *Statistics in Medicine* 28, 3012-3028. <<https://doi.org/10.1002/sim.3682>>
- Chamorey Emmanuel. (2009). Methodologie des essais de phase precoce en cancerologie: evolution des schemas et apport de la pharmacologie. These.
- Garret-Mayer Elizabeth. (2006). The Continual Reassessment Method for dose-finding studies: a tutorial. *Clinical Trials*: 57-71. <<https://doi.org/10.1191/1740774506cn134oa>>

CreData	<i>Creates a CRM dataframe</i>
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Description

Creates a n-row summary dataframe indicating the number of treated patients and observed DLTs at each of the n dose-levels. This is the dataframe structure that will be needed in the different functions of the UBCRM package.

Usage

```
CreData(ndose = 3, dosenames = paste("dose", 1:ndose, sep = " "))
```

Arguments

ndose	Number of dose levels.
dosenames	A ndose-length character vector of labels for the dose levels.

Value

A ndose * 3 dataframe containing:

dose	Integer value 1..ndose ordering the doses.
npt	Integer count of the treated patients at dose i.
ndlt	Integer count of the observed DLT at dose i.

Author(s)

Benjamin Esterni, Baboukar Mane. Unite de Biostatistique et de Methodologie, Institut Paoli-Calmettes, Marseille, France.

References

- O'Quigley J., Pepe M., Fisher L. (1990). Continual Reassessment Method: a practical design for Phase I clinical trials in cancer. *Biometrics* 46, 33-48. <<https://doi.org/10.2307/2531628>>
- O'Quigley J., Shen LZ. (1996). Continual Reassessment Method: a likelihood approach. *Biometrics* 52, 673-684. <<https://doi.org/10.2307/2532905>>
- Paoletti X., Kramar A. (2009). A comparison of model choices for the Continual Reassessment Method in phase I cancer trials. *Statistics in Medicine* 28, 3012-3028. <<https://doi.org/10.1002/sim.3682>>
- Chamorey Emmanuel. (2009). Methodologie des essais de phase precoce en cancerologie: evolution des schemas et apport de la pharmacologie. These.
- Garret-Mayer Elizabeth. (2006). The Continual Reassessment Method for dose-finding studies: a tutorial. *Clinical Trials*: 57-71. <<https://doi.org/10.1191/1740774506cn134oa>>

See Also

[updata](#)

Examples

```
data<- CreData(5,c("5 mg/m2","7 mg/m2","10 mg/m2","15 mg/m2","20 mg/m2"))
data
```

Crm

*Dose-escalation with the Continual Reassessment Method***Description**

The function gives the next level to include patients following a model-based design. Needs an updated input dataframe with the CreData() structure.

Usage

```
Crm(Dk, prior, target = 1/3, nptmax = 24, nmaxmtd = 6, nmaxdose = nptmax, sd = 1.34,
approach = "bayes", model = "power", method = "fpost", nextlevel = "ntarget",
upskipping = F, downskipping = F, lastdose = NA)
```

Arguments

Dk	Study dataframe with CreData() structure.
prior	Numeric vector of prior DLTs probabilities.
target	Target used for the MTD determination.
nptmax	Maximum number of patients to include in the study.
nmaxmtd	Maximum number of patients to be treated at the designated MTD. Assign a high value (=nptmax) to avoid such a stopping rule.
nmaxdose	Maximum number of patients to be treated at the same dose. Assign a high value (=nptmax) to avoid such a stopping rule.
sd	Standard deviation used in case of a normal distribution assumption for the parameter.
approach	Character indicating the estimation method: "bayes" (default value) for CRM or "mle" for CRML.
model	Character indicating the dose-DLT relationship model: "power", "tangent" or "logistic". More informations in the details section.
method	Estimation method for the posterior probabilities. "fpost" (default) estimates the mean of the posterior distribution of the parameter alpha ($\hat{\alpha}=E[\alpha]$) and uses it in <code>psy(hat_alpha,...)</code> . "ppostp" and "pposts" directly estimate the mean of the posterior DLT probability. "ppostp" uses prior as singletons whereas "pposts" calculates appropriate singletons (see <code>ail</code> , <code>ait</code> or <code>aip</code> functions).
nextlevel	Character option used for determining the next dose level. "ntarget" (default) if the next level is chosen as the closest level to the desired target (may be higher than target). "utarget" if the next level is the closest level with the restriction to be lower than the target value.

upskipping	Boolean option used for determining the next dose level. If TRUE no level skip in escalation will be allowed. If FALSE (default) the level skips will be permitted.
downskipping	Boolean option used for determining the next dose level. If TRUE no level skip in desescalation will be allowed. If FALSE (default) the level skips will be permitted.
lastdose	Integer representing the last experimented dose level.

Details

Details of the 3 dose-DLT relationship proposed models: "power" for the power model $\text{psy}(s,a)=s^{\exp(a)}$, "tangent" for the hyperbolic tangent model $\text{psy}(s,a)=((\tanh(s)+1)/2)**a$, "logistic" for the logistic model $\text{psy}(s,a) = \exp(3+a*s)/(1+\exp(3+a*s))$. Note: power and tangent models are equivalent after an appropriate transformation on the parameter.

Value

nextdose	An integer representing the next recommended dose to experiment.
mtd	If reached, an integer representing the MTD.
prob	Posterior DLTs probabilities.

Author(s)

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References

- O'Quigley J., Pepe M., Fisher L. (1990). Continual Reassessment Method: a practical design for Phase I clinical trials in cancer. *Biometrics* 46, 33-48. <<https://doi.org/10.2307/2531628>>
- O'Quigley J., Shen LZ. (1996). Continual Reassessment Method: a likelihood approach. *Biometrics* 52, 673-684. <<https://doi.org/10.2307/2532905>>
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- Chamorey Emmanuel. (2009). Methodologie des essais de phase precoce en cancerologie: evolution des schemas et apport de la pharmacologie. These.
- Garret-Mayer Elizabeth. (2006). The Continual Reassessment Method for dose-finding studies: a tutorial. *Clinical Trials*: 57-71. <<https://doi.org/10.1191/1740774506cn134oa>>

See Also

[simCrm](#), [ssimCrm](#)

Examples

```

data<- CreData(5)
data<- updata(data,1,3,0)
data<- updata(data,2,3,1)
data<- updata(data,2,3,1)
data
Crm(data,prior=c(0.1,0.15,0.25,0.35,0.45),target=0.3,nextlevel="ntarget",nptmax=24,nmaxmtd=6)
data<- updata(data,3,3,2)
data
Crm(data,prior=c(0.1,0.15,0.25,0.35,0.45),target=0.3,nextlevel="ntarget",nptmax=24,nmaxmtd=6)

```

fp

*Density functions***Description**

Density functions for the model parameter. $fp(a, sd)$ is the normal density: $1/(sd*\sqrt{2*\pi})*\exp(-(a^2)/(2*sd^2))$. ft and fl are the exponential density (with a fixed rate = 1): $\exp(-a)$.

Usage

```

fp(a, sd)
ft(a)
fl(a)

```

Arguments

a	Parameter.
sd	Standard deviation.

Value

Numeric value of the computed density.

Author(s)

Benjamin Esterni, Baboukar Mane. Unite de Biostatistique et de Methodologie, Institut Paoli-Calmettes, Marseille, France.

References

- O'Quigley J., Pepe M., Fisher L. (1990). Continual Reassessment Method: a practical design for Phase I clinical trials in cancer. *Biometrics* 46, 33-48. <<https://doi.org/10.2307/2531628>>
- O'Quigley J., Shen LZ. (1996). Continual Reassessment Method: a likelihood approach. *Biometrics* 52, 673-684. <<https://doi.org/10.2307/2532905>>
- Paoletti X., Kramar A. (2009). A comparison of model choices for the Continual Reassessment Method in phase I cancer trials. *Statistics in Medicine* 28, 3012-3028. <<https://doi.org/10.1002/sim.3682>>

Chamorey Emmanuel. (2009). Methodologie des essais de phase precoce en cancerologie: evolution des schemas et apport de la pharmacologie. These.

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Lp

Likelihood functions

Description

Lp is the likelihood function for the power model $\text{psy}(s,a)=s^{\exp(a)}$. Lt is the likelihood function for the hyperbolic tangent model $\text{psy}(s,a)=((\tanh(s)+1)/2)^{**a}$. Ll is the likelihood function for the logistic model $\text{psy}(s,a) = \exp(3+a*s)/(1+\exp(3+a*s))$.

Usage

```
Lp(a, data, sgl)
Lt(a, data, sgl)
Ll(a, data, sgl)
```

Arguments

a	Parameter.
data	CRM dataframe with a CreData() structure.
sgl	Dose level singleton.

Value

Numeric value of the computed likelihood.

Author(s)

Benjamin Esterni, Baboukar Mane. Unite de Biostatistique et de Methodologie, Institut Paoli-Calmettes, Marseille, France.

References

O'Quigley J., Pepe M., Fisher L. (1990). Continual Reassessment Method: a practical design for Phase I clinical trials in cancer. *Biometrics* 46, 33-48. <<https://doi.org/10.2307/2531628>>

O'Quigley J., Shen LZ. (1996). Continual Reassessment Method: a likelihood approach. *Biometrics* 52, 673-684. <<https://doi.org/10.2307/2532905>>

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Chamorey Emmanuel. (2009). Methodologie des essais de phase precoce en cancerologie: evolution des schemas et apport de la pharmacologie. These.

Garret-Mayer Elizabeth. (2006). The Continual Reassessment Method for dose-finding studies: a tutorial. *Clinical Trials*: 57-71. <<https://doi.org/10.1191/1740774506cn134oa>>

 psip

Dose-Toxicity modelisation functions

Description

psip corresponds to the power model $\text{psy}(s,a)=s^{\exp(a)}$. psit corresponds to the hyperbolic tangent model $\text{psy}(s,a)=((\tanh(s)+1)/2)^{**a}$. psil corresponds to the logistic model $\text{psy}(s,a) = \exp(3+a*s)/(1+\exp(3+a*s))$.

Usage

```
psip(sgl, a)
psit(sgl, a)
psil(sgl, a)
```

Arguments

sgl	Dose level singleton.
a	Parameter.

Value

Numeric value of the computed function.

Author(s)

Benjamin Esterni, Baboukar Mane. Unite de Biostatistique et de Methodologie, Institut Paoli-Calmettes, Marseille, France.

References

- O'Quigley J., Pepe M., Fisher L. (1990). Continual Reassessment Method: a practical design for Phase I clinical trials in cancer. *Biometrics* 46, 33-48. <<https://doi.org/10.2307/2531628>>
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- Paoletti X., Kramar A. (2009). A comparison of model choices for the Continual Reassessment Method in phase I cancer trials. *Statistics in Medecine* 28, 3012-3028. <<https://doi.org/10.1002/sim.3682>>
- Chamorey Emmanuel. (2009). Methodologie des essais de phase precoce en cancerologie: evolution des schemas et apport de la pharmacologie. These.
- Garret-Mayer Elizabeth. (2006). The Continual Reassessment Method for dose-finding studies: a tutorial. *Clinical Trials*: 57-71. <<https://doi.org/10.1191/1740774506cn134oa>>

 sim3p3

Simulation of one dose-escalation study with the classical 3+3 design

Description

Given a true rates vector of DLT probabilities, the function simulate a 3+3 dose-escalation design.

Usage

```
sim3p3(truerate, seed = NULL)
```

Arguments

truerate	A nlevel-length vector of true rates for the DLTs.
seed	If not empty, the seed to use for random generation.

Value

data	Study data.
mtd	If reached, an integer representing the MTD level.
lastdose	An integer representing the last experimented dose.

Author(s)

Benjamin Esterni, Baboukar Mane. Unite de Biostatistique et de Methodologie, Institut Paoli-Calmettes, Marseille, France.

References

- O'Quigley J., Pepe M., Fisher L. (1990). Continual Reassessment Method: a practical design for Phase I clinical trials in cancer. *Biometrics* 46, 33-48. <<https://doi.org/10.2307/2531628>>
- O'Quigley J., Shen LZ. (1996). Continual Reassessment Method: a likelihood approach. *Biometrics* 52, 673-684. <<https://doi.org/10.2307/2532905>>
- Paoletti X., Kramar A. (2009). A comparison of model choices for the Continual Reassessment Method in phase I cancer trials. *Statistics in Medecine* 28, 3012-3028. <<https://doi.org/10.1002/sim.3682>>
- Chamorey Emmanuel. (2009). Methodologie des essais de phase precoce en cancerologie: evolution des schemas et apport de la pharmacologie. These.
- Garret-Mayer Elizabeth. (2006). The Continual Reassessment Method for dose-finding studies: a tutorial. *Clinical Trials*: 57-71. <<https://doi.org/10.1191/1740774506cn134oa>>

See Also

[troisPtrois](#), [ssim3p3](#)

Examples

```
# A 3-dose study with 10%, 20% and 30% of true rates for toxicity
sim3p3(c(0.1,0.2,0.3))
```

simCrm	<i>Simulation of one dose-escalation study with the Continual Reassessment Method</i>
--------	---

Description

Given prior and true rates vectors of DLT probabilities, the function simulates a CRM dose-escalation design.

Usage

```
simCrm(prior, firstdose = NA, truerate = prior, cohortsize = 3, target = 1/3, nptmax = 24,
nmaxmtd = nptmax, nmaxdose = nptmax, sd = 1.34, approach = "bayes", model = "power",
method = "fpost", nextlevel = "ntarget", upskipping = F, downskipping = F, lastdose = NA,
graphic = F, seed = NULL)
```

Arguments

prior	Numeric vector of prior DLT probabilities.
firstdose	Integer representing the dose at which the first cohort will be treated.
truerate	A nlevel-length vector of true rates for the DLTs.
cohortsize	Size of the cohort. Default value = 3.
target	Target used for the MTD determination.
nptmax	Maximum number of patients to include in the study.
nmaxmtd	Maximum number of patients to be treated at the designated MTD. Assign a high value (=nptmax) to avoid such a stopping rule.
nmaxdose	Maximum number of patients to be treated at the same dose. Assign a high value (=nptmax) to avoid such a stopping rule.
sd	Standard deviation used in case of a normal distribution assumption for the parameter.
approach	Character indicating the estimation method: "bayes" (default value) for CRM or "mle" for CRML.
model	Character indicating the dose-DLT relationship model: "power", "tangent" or "logistic".
method	Estimation method for the posterior probabilities. "fpost" (default) estimates the mean of the posterior distribution of the parameter α ($\hat{\alpha} = E[\alpha]$) and uses it in $\text{psy}(\hat{\alpha}, \dots)$. "ppostp" and "pposts" directly estimate the mean of the posterior DLT probability. "ppostp" uses prior as singletons whereas "pposts" calculates appropriate singletons (see ail, ait or aip functions).

nextlevel	Character option used for determining the next dose level. "ntarget" (default) if the next level is chosen as the closest level to the desired target (may be higher than target). "utarget" if the next level is the closest level with the restriction to be lower than the target value.
upskipping	Boolean option used for determining the next dose level. If TRUE no level skip in escalation will be allowed. If FALSE (default) the level skips will be permitted.
downskipping	Boolean option used for determining the next dose level. If TRUE no level skip in desescalation will be allowed. If FALSE (default) the level skips will be permitted.
lastdose	Integer representing the last experimented dose level.
graphic	Boolean option for graphic generation.
seed	If not empty, the seed to use for random generation.

Value

data	Study data.
dose	Integer vector representing for each cohort the experimented dose levels.
nDLT	Integer vector representing for each cohort the number of observed DLTs.
mtd	If reached, an integer representing the MTD level.
lastdose	An integer representing the last experimented dose.
prob	Posterior DLT probabilities.

Author(s)

Benjamin Esterni, Baboukar Mane. Unite de Biostatistique et de Methodologie, Institut Paoli-Calmettes, Marseille, France.

References

- O'Quigley J., Pepe M., Fisher L. (1990). Continual Reassessment Method: a practical design for Phase I clinical trials in cancer. *Biometrics* 46, 33-48. <<https://doi.org/10.2307/2531628>>
- O'Quigley J., Shen LZ. (1996). Continual Reassessment Method: a likelihood approach. *Biometrics* 52, 673-684. <<https://doi.org/10.2307/2532905>>
- Paoletti X., Kramar A. (2009). A comparison of model choices for the Continual Reassessment Method in phase I cancer trials. *Statistics in Medecine* 28, 3012-3028. <<https://doi.org/10.1002/sim.3682>>
- Chamorey Emmanuel. (2009). Methodologie des essais de phase precoce en cancerologie: evolution des schemas et apport de la pharmacologie. These.
- Garret-Mayer Elizabeth. (2006). The Continual Reassessment Method for dose-finding studies: a tutorial. *Clinical Trials*: 57-71. <<https://doi.org/10.1191/1740774506cn134oa>>

See Also

[Crm](#), [ssimCrm](#)

Examples

```
simCrm(c(0.1,0.2,0.3,0.35,0.45),firstdose=1,target=0.33)
```

ssim3p3

Simulation of n dose-escalation study with the 3+3 design

Description

The ssim3p3 function simulates n dose-escalation study with the 3+3 design and provides summarized results.

Usage

```
ssim3p3(truerate, n, r = 2, seed = NULL)
```

Arguments

truerate	A nlevel-length vector of true rates for the DLTs.
n	Number of studies to simulate.
r	Integer, number of digits for percentages in output.
seed	If not empty, the seed to use for random generation.

Value

data	Summarized result in a "np1" view.
norecommendation	Percentage of studies with no recommendation for the MTD (in case of the first level is considered as toxic).
mean.npt	Mean number of enrolled patients.
mean.ndlt	Mean number of observed DLTs.
mean.lastdose	Mean last experimented dose level.

Author(s)

Benjamin Esterni, Baboukar Mane. Unite de Biostatistique et de Methodologie, Institut Paoli-Calmettes, Marseille, France.

References

O'Quigley J., Pepe M., Fisher L. (1990). Continual Reassessment Method: a practical design for Phase I clinical trials in cancer. *Biometrics* 46, 33-48. <<https://doi.org/10.2307/2531628>>

O'Quigley J., Shen LZ. (1996). Continual Reassessment Method: a likelihood approach. *Biometrics* 52, 673-684. <<https://doi.org/10.2307/2532905>>

Paoletti X., Kramar A. (2009). A comparison of model choices for the Continual Reassessment Method in phase I cancer trials. *Statistics in Medecine* 28, 3012-3028. <<https://doi.org/10.1002/sim.3682>>

Chamorey Emmanuel. (2009). Methodologie des essais de phase precoce en cancerologie: evolution des schemas et apport de la pharmacologie. These.

Garret-Mayer Elizabeth. (2006). The Continual Reassessment Method for dose-finding studies: a tutorial. Clinical Trials: 57-71. <<https://doi.org/10.1191/1740774506cn134oa>>

See Also

[troisPtrois](#), [sim3p3](#)

Examples

```
ssim3p3(c(0.1,0.2,0.25,0.35),100)
```

ssimCrm	<i>Simulation of n dose-escalation study with the Continual Reassessment Method</i>
---------	---

Description

The `ssimCrm` function simulates n dose-escalation study with the CRM and provides summarized results.

Usage

```
ssimCrm(prior, n, firstdose = NA, truerate = prior, cohortsize = 3, target = 1/3,
nptmax = 24, nmaxmtd = nptmax, nmaxdose = nptmax, sd = 1.34, approach = "bayes",
method = "fpost", model = "power", nextlevel = "ntarget", upskipping = F,
downskipping = F, r = 2, seed = NULL)
```

Arguments

<code>prior</code>	Numeric vector of prior DLT probabilities.
<code>n</code>	Number of studies to simulate.
<code>firstdose</code>	Integer representing the dose at which the first cohort will be treated.
<code>truerate</code>	A <code>nlevel</code> -length vector of true rates for the DLTs.
<code>cohortsize</code>	Size of the cohort. Default value = 3.
<code>target</code>	Target used for the MTD determination.
<code>nptmax</code>	Maximum number of patients to include in the study.
<code>nmaxmtd</code>	Maximum number of patients to be treated at the designated MTD. Assign a high value (=nptmax) to avoid such a stopping rule.
<code>nmaxdose</code>	Maximum number of patients to be treated at the same dose. Assign a high value (=nptmax) to avoid such a stopping rule.
<code>sd</code>	Standard deviation used in case of a normal distribution assumption for the parameter.

approach	Character indicating the estimation method: "bayes" (default value) for CRM or "mle" for CRML.
model	Character indicating the dose-DLT relationship model: "power", "tangent" or "logistic".
method	Estimation method for the posterior probabilities. "fpost" (default) estimates the mean of the posterior distribution of the parameter α ($\hat{\alpha}=E[\alpha]$) and uses it in <code>psy(hat_alpha,...)</code> . "ppostp" and "pposts" directly estimate the mean of the posterior DLT probability. "ppostp" uses prior as singletons whereas "pposts" calculates appropriate singletons (see <code>ail</code> , <code>ait</code> or <code>aip</code> functions).
nextlevel	Character option used for determining the next dose level. "ntarget" (default) if the next level is chosen as the closest level to the desired target (may be higher than target). "utarget" if the next level is the closest level with the restriction to be lower than the target value.
upskipping	Boolean option used for determining the next dose level. If TRUE no level skip in escalation will be allowed. If FALSE (default) the level skips will be permitted.
downskipping	Boolean option used for determining the next dose level. If TRUE no level skip in desescalation will be allowed. If FALSE (default) the level skips will be permitted.
r	Integer, number of digits for percentages in output.
seed	If not empty, the seed to use for random generation.

Value

data	Summarized result in a "np1" view.
norecommendation	Percentage of studies with no recommendation for the MTD (in case of the first level is considered as toxic).
mean.npt	Mean number of enrolled patients.
mean.ndlt	Mean number of observed DLTs.
mean.lastdose	Mean last experimented dose level.
mean.prob	Mean of posterior DLT probabilities.

Author(s)

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References

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See Also

[Crm](#), [simCrm](#)

Examples

```
ssimCrm(c(0.1,0.2,0.3,0.35,0.45),firstdose=1,target=0.33,n=100)
```

troisPtrois

Dose escalation with the 3+3 design

Description

The function gives the next level to include patients following a 3+3 design. Needs an updated input dataframe with the `CreData()` structure.

Usage

```
troisPtrois(data = data, lastdose)
```

Arguments

<code>data</code>	Study dataframe with <code>CreData()</code> structure.
<code>lastdose</code>	Integer representing the last experimented dose level.

Value

<code>nextdose</code>	An integer representing the next recommended dose to experiment.
<code>mtd</code>	If reached, an integer representing the MTD.

Author(s)

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References

- O'Quigley J., Pepe M., Fisher L. (1990). Continual Reassessment Method: a practical design for Phase I clinical trials in cancer. *Biometrics* 46, 33-48. <<https://doi.org/10.2307/2531628>>
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- Garret-Mayer Elizabeth. (2006). The Continual Reassessment Method for dose-finding studies: a tutorial. *Clinical Trials*: 57-71. <<https://doi.org/10.1191/1740774506cn134oa>>

See Also

[sim3p3](#), [ssim3p3](#)

Examples

```
# Study initialization
data<- CreData(5,c("5 mg/m2", "7 mg/m2", "10 mg/m2", "15 mg/m2", "20 mg/m2"))
data

# Three patients are treated at the dose 1, without any observed DLT:
data<- update(data,lastdose=1,npt=3,ndlt=0)
data

# 3+3 design
troisPtrois(data,lastdose=1)
```

update

Update the CRM dataframe after new patients' collected data

Description

This function updates the CRM dataframe (result of the CreData routine) with new treated patients or observed DLTs.

Usage

```
update(data = data, lastdose, npt, ndlt)
```

Arguments

data	Dataframe to be updated.
lastdose	Integer representing the dose to be updated.
npt	Number of new treated patients.
ndlt	Number of DLTs among the npt patients.

Value

Updated dataframe.

Author(s)

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References

- O'Quigley J., Pepe M., Fisher L. (1990). Continual Reassessment Method: a practical design for Phase I clinical trials in cancer. *Biometrics* 46, 33-48. <<https://doi.org/10.2307/2531628>>
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See Also

[CreData](#)

Examples

```
# Study initialization
data<- CreData(5,c("5 mg/m2","7 mg/m2","10 mg/m2","15 mg/m2","20 mg/m2"))
data

# Three patients are treated at the dose 1, without any observed DLT:
data<- updata(data,lastdose=1,npt=3,ndlt=0)
data
```

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