

Package ‘dtpcrm’

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Type Package

Title Dose Transition Pathways for Continual Reassessment Method

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Description Provides the dose transition pathways (DTP) to project in advance the doses recommended by a model-based design for subsequent patients (stay, escalate, deescalate or stop early) using all the accumulated toxicity information; See Yap et al (2017) <[doi:10.1158/1078-0432.CCR-17-0582](https://doi.org/10.1158/1078-0432.CCR-17-0582)>. DTP can be used as a design and an operational tool and can be displayed as a table or flow diagram. The 'dtpcrm' package also provides the modified continual reassessment method (CRM) and time-to-event CRM (TITE-CRM) with added practical considerations to allow stopping early when there is sufficient evidence that the lowest dose is too toxic and/or there is a sufficient number of patients dosed at the maximum tolerated dose.

License GPL (>= 2)

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Suggests knitr, rmarkdown, testthat

VignetteBuilder knitr

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applied_crm	<i>Execute the CRM</i>
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Description

applied_crm is used to execute the continual reassessment method with specified design options to determine the dose for the next subject.

Usage

```
applied_crm(prior, target, tox, level, no_skip_esc = TRUE,
             no_skip_deesc = TRUE, global_coherent_esc = TRUE, stop_func = NULL,
             ...)
```

Arguments

prior	A vector of prior estimates of toxicity probabilities for the dose levels.
target	The target DLT rate.
tox	A vector of subject outcomes; 1 indicates toxicity, 0 otherwise.
level	A vector of dose levels assigned to subjects. The length of level must be equal to that of tox.
no_skip_esc	If FALSE, the method will not enforce no skipping of doses in escalation. Default is TRUE.
no_skip_deesc	If FALSE, the method will not enforce no skipping of doses in de-escalation. Default is TRUE.
global_coherent_esc	If FALSE, the method will not enforce global coherent escalation, that is, escalation if the overall rate of toxicity seen at the current dose level is above the target rate. Default is TRUE.

stop_func	An optional argument to provide a function which will be utilised alongside the CRM to determine if the trial should be stopped.
...	Any other arguments detailed in <code>dfcrm::crm</code> .

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 $\text{logit}(F(d, \beta)) = \text{intcpt} + \exp(\beta) * d$. For `method="bayes"`, the prior on beta is normal with mean 0. Exponentiation of beta ensures an increasing dose-toxicity function.

This function is largely a wrapper for the `dfcrm` function `crm`. It provides functionality for additional design choices for the CRM including global coherency and stopping for excess toxicity and stopping when sufficient number of subjects are dosed at MTD.

Value

An object of class "mtd" is returned as per package "dfcrm", additional information is provided if a stopping function is used.

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.
stop	A logical variable detailing if the trial should be stopped; TRUE to stop, FALSE otherwise
stop_reason	A detailed reason for why the trial should be stopped. Only provided if stop is TRUE

References

O'Quigley, J. O., Pepe, M., and Fisher, L. (1990). Continual reassessment method: A practical design for phase I clinical trials in cancer. *Biometrics* 46:33-48.

Cheung, Y. K. (2011). *Dose Finding by the Continual Reassessment Method*. New York: Chapman & Hall/CRC Press.

Examples

```
prior <- c(0.1, 0.3, 0.5)
target <- 0.2
tox <- c(0, 0, 1, 0, 1, 1)
level <- c(1, 1, 1, 2, 2, 2)
applied_crm(prior, target, tox, level, no_skip_esc = TRUE, no_skip_deesc = TRUE,
            global_coherent_esc = TRUE, stop_func = NULL)
```

applied_crm_sim

Simulate CRM trials using specified design options

Description

applied_crm_sim is used to simulate trials using the continual reassessment method with specified design options to determine the operating characteristics.

Usage

```
applied_crm_sim(true_tox, prior, target, max_sample_size, first_dose,
               num_sims, cohort_size = 1, dose_func = applied_crm, ...)
```

Arguments

true_tox	A vector of 'true' underlying rates of toxicity for each of the dose levels.
prior	A vector of prior estimates of toxicity probabilities for the dose levels.
target	The target DLT rate.
max_sample_size	The maximum number of subjects to be recruited in any simulation.
first_dose	The first dose level to tested.
num_sims	The total number of simulations to be run.
cohort_size	The size of the cohorts. Default is 1.
dose_func	The function to be employed in executing the CRM. Default is applied_crm.
...	Any other arguments detailed in dtpcrm::applied_crm.

Value

A list containing two further lists. The first of these lists contains the operating characteristics of the design, the second contains the underlying data for each of the simulation iterations.

References

O'Quigley, J. O., Pepe, M., and Fisher, L. (1990). Continual reassessment method: A practical design for phase I clinical trials in cancer. *Biometrics* 46:33-48.

Cheung, Y. K. (2011). *Dose Finding by the Continual Reassessment Method*. New York: Chapman & Hall/CRC Press.

Examples

```
# It may take quite long for large num_sims
prior <- c(0.1, 0.3, 0.5)
target <- 0.2
true_tox <- c(0.15, 0.25, 0.45)
first_dose <- 1
num_sims <- 5 # recommend doing 5000 simulations for the final design

applied_crm_sim(true_tox, prior, target, max_sample_size = 30, first_dose,
                num_sims, cohort_size = 1, dose_func = applied_crm)
```

applied_titecrm	<i>Execute the TITE-CRM</i>
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Description

applied_titecrm is used to execute the time-to-event continual reassessment method with specified design options to determine the dose for the next subject.

Usage

```
applied_titecrm(prior, target, tox, level, followup, obswin,
               no_skip_esc = TRUE, no_skip_deesc = TRUE, global_coherent_esc = TRUE,
               stop_func = NULL, ...)
```

Arguments

prior	A vector of prior estimates of toxicity probabilities for the dose levels.
target	The target DLT rate.
tox	A vector of subject outcomes; 1 indicates toxicity, 0 otherwise.
level	A vector of dose levels assigned to subjects. The length of level must be equal to that of tox.
followup	A vector of follow up times of subjects. The length must be equal to that of tox.
obswin	The observation period with respect to which DLT is assessed.
no_skip_esc	If FALSE, the method will not enforce no skipping of doses in escalation. Default is TRUE.
no_skip_deesc	If FALSE, the method will not enforce no skipping of doses in de-escalation. Default is TRUE.
global_coherent_esc	If FALSE, the method will not enforce global coherent escalation, that is, escalation if the overall rate of toxicity seen at the current dose level is above the target rate. Default is TRUE.
stop_func	An optional argument to provide a function which will be utilised alongside the TITE-CRM to determine if the trial should be stopped.
...	Any other arguments detailed in drcrm::titecrm.

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 as per package "dfcrm", additional information is provided if a stopping function is used.

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	subjects' toxicity indications.
level	Dose levels assigned to subjects.
followup	Follow-up times of subjects.
obswin	Observation window with respect to which DLT is assessed.
weights	Weights assigned to subjects.
entry	Entry times of subjects.
exit	Exit times of subjects.
scheme	Weighting scheme.
stop	A logical variable detailing if the trial should be stopped; TRUE to stop, FALSE otherwise
stop_reason	A detailed reason for why the trial should be stopped. Only provided if stop is TRUE

References

- O'Quigley, J. O., Pepe, M., and Fisher, L. (1990). Continual reassessment method: A practical design for phase I clinical trials in cancer. *Biometrics* 46:33-48.
- Cheung, Y. K. (2011). *Dose Finding by the Continual Reassessment Method*. New York: Chapman & Hall/CRC Press.
- Cheung, Y. K. and Chappell, R. (2000). Sequential designs for phase I clinical trials with late-onset toxicities. *Biometrics* 56:1177-1182.

Examples

```
prior    <- c(0.1, 0.3, 0.5)
target   <- 0.2
tox       <- c(0, 0, 1, 0, 1, 1)
level     <- c(1, 1, 1, 2, 2, 2)
followup <- c(96, 82, 77, 60, 51, 44)
obswin    <- 80

applied_titecrm(prior = prior, target = target, tox = tox, level = level,
                followup = followup, obswin = obswin)
```

`applied_titecrmts_sim` *Simulate TITE-CRM trials using specified design options*

Description

`applied_titecrmts_sim` is used to simulate trials using the two-stage time-to-event continual re-assessment method with specified design options to determine the operating characteristics.

Usage

```
applied_titecrmts_sim(true_tox, prior, target, max_sample_size,
                      num_sims, cohort_size = 1, obswin, minfu, recreate, initdes,
                      dose_func = applied_titecrm, ...)
```

Arguments

<code>true_tox</code>	A vector of 'true' underlying rates of toxicity for each of the dose levels.
<code>prior</code>	A vector of prior estimates of toxicity probabilities for the dose levels.
<code>target</code>	The target DLT rate.
<code>max_sample_size</code>	The maximum number of subjects to be recruited in any simulation.
<code>num_sims</code>	The total number of simulations to be run.
<code>cohort_size</code>	The size of the cohorts. Default is 1.
<code>obswin</code>	The observation period for total subject follow up.
<code>minfu</code>	The minimum amount of follow-up required for each subject.
<code>recreate</code>	The number of subjects recruited per obswin.
<code>initdes</code>	A vector specifying the doses to be assigned to subjects as per the initial design.
<code>dose_func</code>	The function to be employed in executing the CRM. Default is <code>applied_titecrm</code> .
<code>...</code>	Any other arguments detailed in <code>dtpr::applied_titecrm</code> .

Value

A list containing two further lists. The first of these lists contains the operating characteristics of the design, the second contains the underlying data for each of the simulation iterations.

References

O’Quigley, J. O., Pepe, M., and Fisher, L. (1990). Continual reassessment method: A practical design for phase I clinical trials in cancer. *Biometrics* 46:33-48.

Cheung, Y. K. (2011). *Dose Finding by the Continual Reassessment Method*. New York: Chapman & Hall/CRC Press.

Examples

```
# It may take quite long for large num_sims
prior <- c(0.1, 0.3, 0.5)
target <- 0.2
true_tox <- c(0.05, 0.2, 0.35)
first_dose <- 1
num_sims <- 5 # recommend doing 5000 simulations for the final design
obswin = 80

applied_titecrmts_sim(true_tox = true_tox, prior = prior, target = target,
                      max_sample_size = 21, num_sims = num_sims,
                      cohort_size = 3, obswin = obswin, minfu = 20,
                      recreate = 3, initdes = c(rep(1, 3), rep(2, 3), rep(3, 15)),
                      dose_func = applied_titecrm)
```

applied_titecrm_sim	<i>Simulate TITE-CRM trials using specified design options</i>
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Description

applied_titecrm_sim is used to simulate trials using the time-to-event continual reassessment method with specified design options to determine the operating characteristics.

Usage

```
applied_titecrm_sim(true_tox, prior, target, max_sample_size,
                    first_dose, num_sims, cohort_size = 1, obswin, minfu, recreate, dose_func
                    = applied_titecrm, ...)
```

Arguments

true_tox	A vector of 'true' underlying rates of toxicity for each of the dose levels.
prior	A vector of prior estimates of toxicity probabilities for the dose levels.
target	The target DLT rate.
max_sample_size	The maximum number of subjects to be recruited in any simulation.
first_dose	The first dose level to tested.
num_sims	The total number of simulations to be run.

cohort_size	The size of the subject cohorts. Default is 1.
obswin	The observation period for total subject follow up.
minfu	The minimum amount of follow-up required for each subjects.
recreate	The number of subjects recruited per obswin.
dose_func	The function to be employed in executing the CRM. Default is applied_titecrm.
...	Any other arguments detailed in dtp::applied_titecrm.

Value

A list containing two further lists. The first of these lists contains the operating characteristics of the design, the second contains the underlying data for each of the simulation iterations.

References

O'Quigley, J. O., Pepe, M., and Fisher, L. (1990). Continual reassessment method: A practical design for phase I clinical trials in cancer. *Biometrics* 46:33-48.

Cheung, Y. K. (2011). *Dose Finding by the Continual Reassessment Method*. New York: Chapman & Hall/CRC Press.

Examples

```
# It may take quite long for large num_sims
prior <- c(0.1, 0.3, 0.5)
target <- 0.2
true_tox <- c(0.05, 0.2, 0.35)
first_dose <- 1
num_sims <- 5 # recommend doing 5000 simulations for the final design
obswin = 80

applied_titecrm_sim(true_tox = true_tox, prior = prior, target = target,
                    max_sample_size = 21, first_dose = first_dose,
                    num_sims = num_sims, cohort_size = 3,
                    obswin = obswin, minfu = 20, recreate = 3,
                    dose_func = applied_titecrm)
```

calculate_dtps

Produce the Dose Transition Pathways

Description

calculate_dtps is used to produce the dose transition pathways for the continual reassessment method with specified design options. These pathways present the possible model recommendations based on all permutations of trial outcomes.

Usage

```
calculate_dtps(next_dose, cohort_sizes, prev_tox = c(), prev_dose =
  c(), dose_func = applied_crm, ...)
```

Arguments

<code>next_dose</code>	An integer value representing the dose to be assigned to the first cohort of subjects in the pathways.
<code>cohort_sizes</code>	A vector of cohort sizes representing the size of the cohorts to be treated with the recommended dose at each decision point.
<code>prev_tox</code>	A vector of previous subject outcomes; 1 indicates toxicity, 0 otherwise.
<code>prev_dose</code>	A vector of previous subject doses; The length of <code>prev_dose</code> must be equal to that of <code>prev_tox</code> .
<code>dose_func</code>	A function such as <code>applied_crm</code> which produces an object of class 'mtd'. To be used for calculation of the next recommended dose for each pathway permutation.
<code>...</code>	Any other arguments to be passed to <code>dose_func</code> ; for specific arguments related to <code>applied_crm</code> see.

Value

Produces a dataframe containing all possible permutations of outcomes for each cohort based on `cohort_sizes` and the recommended doses for such permutations.

Examples

```
prior <- c(0.1, 0.2, 0.5)
target <- 0.15
prev_tox <- c(0, 0, 0)
prev_dose <- c(2, 2, 2)
cohort_sizes <- c(2, 3)

next_dose = applied_crm(prior = prior, target = target,
  tox = prev_tox, level = prev_dose)$mtd

dose_func <- applied_crm

DTP = calculate_dtps(next_dose, cohort_sizes, prev_tox = prev_tox,
  prev_dose = prev_dose, dose_func = applied_crm,
  prior = prior, target = target)
```

dtpflow	<i>Produce DTP flow diagram</i>
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Description

dtpflow will produce a flow diagram of the possible paths for the next three cohorts of subjects.

Usage

```
dtpflow(dtptable, cohort.labels = c('C1', 'C2', 'C3'))
```

Arguments

dtptable a dataframe produced by `calculate_dtps` where `cohort_sizes` was of length 3.
cohort.labels A vector of length 3, containing character strings for the cohort labels.

Details

The function will produce a visual flow diagram for the first three cohorts of the provided dataframe.

Examples

```
prior <- c(0.1, 0.2, 0.5)
target <- 0.15
prev_tox <- c(0, 0, 0)
prev_dose <- c(2, 2, 2)
cohort_sizes <- c(2, 3, 3)

next_dose = applied_crm(prior = prior, target = target,
                       tox = prev_tox, level = prev_dose)$mtd

dose_func <- applied_crm

DTP = calculate_dtps(next_dose, cohort_sizes, prev_tox = prev_tox,
                    prev_dose = prev_dose, dose_func = applied_crm,
                    prior = prior, target = target)

dtpflow(dtptable = DTP, cohort.labels = c('C1', 'C2', 'C3'))
```

plot_crm

*Plot of posterior estimates from the CRM***Description**

Provides functionality for plotting the posterior estimates of probabilities of toxicity at each dose level for both the most recent update and for past cohort updates if specified.

Usage

```
plot_crm(crm, dose_labels, cohort_sizes = NULL, file = NULL,
         height = 600, width = 750, dose_func = NULL, ...,
         ylim = c(0, 1), lwd = 1, cex.axis = 1, cex.lab = 1,
         cex = 1, cohort.last = F)
```

Arguments

crm	An object of class 'mtd' produced by applied_crm to be plotted.
dose_labels	A vector of character strings detailing the labels to be used for each dose level in the plot.
cohort_sizes	An optional vector of cohort sizes; if provided the previous estimates for each cohort will be plotted in addition.
file	An optional string for the file name; if provided the plot will be saved as a .PNG to the current working directory under the provided file name.
height	A numeric value specifying the vertical pixel count of the plot. Default is 600.
width	A numeric value specifying the horizontal pixel count of the plot. Default is 750.
dose_func	Must be provided if cohort_sizes is provided. The function to be used to when implementing the CRM for previous cohorts.
...	Arguments to be provided to dose_func detailing CRM specification. See applied_crm.
ylim	The y-axis range. Default is c(0, 1)
lwd	line width relative to the default (default=1). 2 is twice as wide. Default is 1.
cex.axis	The magnification to be used for axis annotation relative to the current setting of cex. Default is 1.
cex.lab	The magnification to be used for x and y labels relative to the current setting of cex. Default is 1.
cex	A numerical value giving the amount by which plotting text and symbols should be magnified relative to the default. Default is 1.
cohort.last	If TRUE, the last cohort will have lwd = 6 for emphasis. Default is FALSE.

Details

Produces a plot of current dose-toxicity estimates including the priors and outputs a .png of plot to current directory if 'file' is provided. Potential for history of estimates by cohort if cohort.sizes is provided; dose_func is required to do this.

Examples

```
prior <- c(0.1, 0.3, 0.5)
target <- 0.2
tox <- c(0, 0, 1, 0, 1, 1)
level <- c(1, 1, 1, 2, 2, 2)

crm <- applied_crm(prior, target, tox, level, no_skip_esc = TRUE, no_skip_deesc = TRUE,
  global_coherent_esc = TRUE, stop_func = NULL)

plot_crm(crm, dose_labels = c("1", "2", "3"))
```

stop_for_consensus_reached

Stopping for consensus

Description

This is a function for use with applied_crm for the stop_func argument. The rule will suggest stopping in the scenario that a particular number of patients has already been treated at the current recommended MTD.

Usage

```
stop_for_consensus_reached(x, req_at_mtd)
```

Arguments

x	An object of class 'mtd'.
req_at_mtd	An integer; the number of patients required at current estimate of MTD to suggest stopping for consensus.

Details

This function is an example of a possible stopping function to be used with applied_crm, it will modify the 'mtd' class object produced by applied_crm to include a logical value under the name 'stop' indicting whether or not the trial should stop. The package dtprcm contains a few of these functions for possible use with applied_crm.

Examples

```
prior <- c(0.1, 0.3, 0.5)
target <- 0.2
tox <- c(0, 0, 1, 0, 1, 1)
level <- c(1, 1, 1, 2, 2, 2)

stop_rule <- function(x){
  x <- stop_for_consensus_reached(x, req_at_mtd = 6)
}

crm <- applied_crm(prior, target, tox, level, no_skip_esc = TRUE, no_skip_deesc = TRUE,
  global_coherent_esc = TRUE, stop_func = stop_rule)
```

stop_for_excess_toxicity_empiric

Stopping for excess toxicity - Empiric method

Description

This is a function for use with `applied_crm` for the `stop_func` argument. The rule will suggest stopping in the scenario that the probability of toxicity being greater than a specified value at a defined dose is greater than some further specified certainty value.

Usage

```
stop_for_excess_toxicity_empiric(x, tox_lim, prob_cert, dose = 1,
  nsamps = 10^6, suppress_dose = TRUE)
```

Arguments

<code>x</code>	An object of class 'mtd'.
<code>tox_lim</code>	A numeric; specifying the value for which the estimated toxicity at the selected dose is not to exceed.
<code>prob_cert</code>	A numeric; specifying the probability value to be used when assessing the certainty required that toxicity at the specified dose exceeds <code>tox_lim</code> .
<code>dose</code>	An integer; the dose to be assessed.
<code>nsamps</code>	number of samples used for beta in the underlying normal sampling of beta.
<code>suppress_dose</code>	A logical value indicating if the MTD should be set to NA if trial should stop.

Details

This function is an example of a possible stopping function to be used with `applied_crm`, it will modify the 'mtd' class object produced by `applied_crm` to include a logical value under the name 'stop' indicating whether or not the trial should stop. The package `dtprcm` contains a few of these functions for possible use with `applied_crm`.

Examples

```
prior <- c(0.1, 0.3, 0.5)
target <- 0.2
tox <- c(0, 0, 1, 0, 1, 1)
level <- c(1, 1, 1, 2, 2, 2)

stop_rule <- function(x){
  x <- stop_for_excess_toxicity_empiric(x, tox_lim = 0.25, prob_cert = 0.85)
}

crm <- applied_crm(prior, target, tox, level, no_skip_esc = TRUE, no_skip_deesc = TRUE,
  global_coherent_esc = TRUE, stop_func = stop_rule)
```

stop_for_excess_toxicity_logistic

Stopping for excess toxicity - Logistic method

Description

This is a function for use with `applied_crm` for the `stop_func` argument. The rule will suggest stopping in the scenario that the probability of toxicity being greater than a specified value at a defined dose is greater than some further specified certainty value.

Usage

```
stop_for_excess_toxicity_logistic(x, tox_lim, prob_cert, dose = 1,
  nsamps = 10^6, suppress_dose = TRUE)
```

Arguments

<code>x</code>	An object of class 'mtd'.
<code>tox_lim</code>	A numeric; specifying the value for which the estimated toxicity at the selected dose is not to exceed.
<code>prob_cert</code>	A numeric; specifying the probability value to be used when assessing the certainty required that toxicity at the specified dose exceeds <code>tox_lim</code> .
<code>dose</code>	An integer; the dose to be assessed.
<code>nsamps</code>	Number of samples used for beta in the underlying normal sampling of beta.
<code>suppress_dose</code>	A logical value indicating if the MTD should be set to NA if trial should stop.

Details

This function is an example of a possible stopping function to be used with `applied_crm`, it will modify the 'mtd' class object produced by `applied_crm` to include a logical value under the name 'stop' indicating whether or not the trial should stop. The package `dtprcm` contains a few of these functions for possible use with `applied_crm`.

Examples

```
prior <- c(0.1, 0.3, 0.5)
target <- 0.2
tox <- c(0, 0, 1, 0, 1, 1)
level <- c(1, 1, 1, 2, 2, 2)

stop_rule <- function(x){
  x <- stop_for_excess_toxicity_logistic(x, tox_lim = 0.25, prob_cert = 0.85)
}

crm <- applied_crm(prior, target, tox, level, no_skip_esc = TRUE, no_skip_deesc = TRUE,
  global_coherent_esc = TRUE, stop_func = stop_rule)
```

stop_for_sample_size *Stopping for sample size reached*

Description

This is a function for use with `applied_crm` for the `stop_func` argument. The rule will suggest stopping in the scenario that a maximum number of subjects has been recruited.

Usage

```
stop_for_sample_size(x, max_sample_size)
```

Arguments

`x` An object of class 'mtd'.

`max_sample_size` An integer; specifying the maximum number of subjects to be recruited.

Details

This function is an example of a possible stopping function to be used with `applied_crm`, it will modify the 'mtd' class object produced by `applied_crm` to include a logical value under the name 'stop' indicating whether or not the trial should stop. The package `dtprcm` contains a few of these functions for possible use with `applied_crm`.

Examples

```
prior <- c(0.1, 0.3, 0.5)
target <- 0.2
tox <- c(0, 0, 1, 0, 1, 1)
level <- c(1, 1, 1, 2, 2, 2)

stop_rule <- function(x){
  x <- stop_for_sample_size(x, max_sample_size = 20)
```



```

}

crm <- applied_crm(prior, target, tox, level, no_skip_esc = TRUE, no_skip_deesc = TRUE,
                  global_coherent_esc = TRUE, stop_func = stop_rule)

```

summary_crm

*Provide a summary of applied_crm output***Description**

summary_crm is used to return a dataframe of the summary of the output from applied_crm.

Usage

```
summary_crm(x)
```

Arguments

x An object assigned to be the output from applied_crm.

Details

This function takes an object of class "mtd" and produces a dataframe containing a summary of information within the object. Specifically it shows the dose levels, prior probabilities, number of evaluable patients, number of DLTs and the posterior probability estimates along with confidence/probability intervals if estimated in the underlying object.

Value

Dataframe of the summary of the output from applied_crm.

References

O'Quigley, J. O., Pepe, M., and Fisher, L. (1990). Continual reassessment method: A practical design for phase I clinical trials in cancer. *Biometrics* 46:33-48.

Cheung, Y. K. (2011). *Dose Finding by the Continual Reassessment Method*. New York: Chapman & Hall/CRC Press.

Examples

```

prior <- c(0.1, 0.3, 0.5)
target <- 0.2
tox    <- c(0, 0, 1, 0, 1, 1)
level  <- c(1, 1, 1, 2, 2, 2)

crm_obj <- applied_crm(prior, target, tox, level, no_skip_esc = TRUE, no_skip_deesc = TRUE,
                      global_coherent_esc = TRUE, stop_func = NULL)

```

```
summary_crm(crm_obj)
```

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