Package 'CRM2s'

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Type Package

Title C-Optimality Based Two-Stage Continual Reassessment Method (CRM)

Version 0.1.0

Description
Implements CRM2s, a Two-Stage Continual Reassesment Method based in c-optimality. Simulates and compares this dose-escalation method in phase I clinical trials with the traditional 3+3 design for two types of dose-toxicity models: power with one parameter and logistic with two parameters.

URL https://github.com/alvarocia/CRM2s

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License GPL (>= 3)

Encoding UTF-8

LazyData true

RoxygenNote 7.3.2

Imports lattice

Suggests testthat

Contents

crm2s-imports *Import functions from base packages*

Description

This block imports commonly used base R functions into the package namespace.

export_simulation_table_manual *Export Simulation Summary to LaTeX*

Description

Writes a LaTeX table with MTD and toxicity summaries using cat(), without external dependencies.

Usage

```
export_simulation_table_manual(
  df,
  file_path = "RESULTS/simulation_results.tex"
)
```

Arguments

df	A data frame with simulation summaries for one model (e.g., result_list$power) as returned by simulate_across_n_initial().
file_path	Path to the output .tex file.

Examples

```
result_list <- simulate_across_n_initial()
export_simulation_table_manual(result_list$power, "table_power.tex")
export_simulation_table_manual(result_list$logistic, "table_logistic.tex")
```

logistic_3_3 *3+3 Design Simulation for Logistic model with 2 parameters*

Description

Simulates a single trial using a 3+3 dose-escalation method for estimating the Maximum Tolerated Dose (MTD).

Usage

```
logistic_3_3(
  theta = c(-3, 2),
  theta_0 = c(-3.1, 1.8),
  n_initial = 3,
  p_tox_init = 0.05,
  delta_dosis = 0.092,
  seed = 1234,
  show_plot = FALSE
)
```

Arguments

theta	True value of the vector of parameters for the dose-toxicity curve. Default is c(-3,2).
theta_0	Nominal value for the vector of parameters. Default is c(-3.1,1.8).
n_initial	Number of patients per dose level. Default is 3.
p_tox_init	Initial toxicity probability for computing starting dose. Default is 0.05.
delta_dosis	Step size for dose escalation. Default is 0.05.
seed	Random seed for reproducibility. Default is 1234.
show_plot	Logical. If TRUE, plot dose level vs. patient index. Default is FALSE.

Value

A list with:

n_toxicities Total number of toxicities observed.

mtd_estimated Estimated MTD (last safe dose).

n_patients Total number of patients enrolled.

x Dose levels assigned.

y Observed toxicity outcomes (1 = toxic, 0 = non-toxic).

Examples

```
res <- logistic_3_3()
print(res$mtd_estimated)
```

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power_3_3 *3+3 Design Simulation for power model*

Description

Simulates one trial using a 3+3 dose-escalation method for estimating the Maximum Tolerated Dose (MTD).

Usage

```
power_3_3(
  theta = 3,
  theta_0 = 2.7,
  n_initial = 3,
  p_tox_init = 0.02,
  delta_dosis = 0.05,
  seed = 1234,
  show_plot = FALSE
)
```

Arguments

theta	True value for the dose-toxicity curve. Default is 3.
theta_0	Nominal value for the dose-toxicity curve. Default is 2.7.
n_initial	Number of patients per dose level. Default is 3.
p_tox_init	Initial toxicity probability for computing starting dose. Default is 0.02.
delta_dosis	Step size for dose escalation. Default is 0.05.
seed	Random seed for reproducibility. Default is 1234.
show_plot	Logical. If TRUE, plot dose level vs. patient index. Default is FALSE.

Value

A list with:

n_toxicities Total number of toxicities observed.

mtd_estimated Estimated MTD (last safe dose).

n_patients Total number of patients enrolled.

x Dose levels assigned.

y Observed toxicity outcomes (1 = toxic, 0 = non-toxic).

Examples

```
res <- power_3_3()
print(res$mtd_estimated)
```

---

run_simulation_logistic

Simulation Comparison of 3+3 and CRM2s Designs for a Logistic Model with Two Parameters

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Description

Simulates and compares MTD estimates and toxicity outcomes between the 3+3 design and a two-stage CRM design over multiple replications.

Usage

```
run_simulation_logistic(
  num_rep = 1000,
  seed = 1234,
  save_plot = FALSE,
  p0 = 0.4,
  theta = c(-3, 2),
  theta_0 = c(-3.1, 1.8),
  N = 24,
  n_initial = 1,
  q_0 = 0.05,
  q_2 = 0.4,
  q_1 = 0.9,
  lim_sup_prob = 0.7,
  p_tox_init_3_3 = 0.05,
  delta_dosis_3_3 = 0.092
)
```

Arguments

num_rep	Number of replications to run. Default is 1000.
seed	Base random seed for reproducibility. Default is 1234.
save_plot	Logical. If TRUE, saves comparison plots as PDF. Default is FALSE.
p0	Target toxicity probability. Default is 0.4.
theta	True value of the vector of parameters for the dose-toxicity curve. Default is c(-3,2).
theta_0	Nominal value for the vector of parameters. Default is c(-3.1,1.8).
N	Total number of patients in the CRM design. Default is 24.
n_initial	Number of patients per dose level in the CRM design (not used in 3+3). Default is 1.
q_0	Initial toxicity probability for CRM design. Default is 0.05.
q_2	Fraction of patients in CRM stage 1. Default is 0.4.
q_1	Target probability of observing at least one toxicity in CRM stage 1. Default is 0.9.
lim_sup_prob	Maximum probability of toxicity the model allows. Default is 0.7.
p_tox_init_3_3	Initial toxicity probability for the 3+3 model. Default is 0.05.
delta_dosis_3_3	Step size for dose escalation in the 3+3 model. Default is 0.092.

Value

A data.frame with one row per method ("3+3" and "CRM2s") and the following columns:

method Design used ("3+3" or "CRM2s")

mean_pat Mean of patients

median_pat Median of patients

mean_mtd Mean of the estimated MTDs

sd_mtd Standard deviation of the estimated MTDs

median_mtd Median of the estimated MTDs

min_mtd Minimum of the estimated MTDs

q1_mtd First quartile (Q1) of the estimated MTDs

q3_mtd Third quartile (Q3) of the estimated MTDs

max_mtd Maximum of the estimated MTDs

siqr_mtd Semi-interquartile range of the estimated MTDs

mean_tox Mean number of toxicities

sd_tox Standard deviation of the number of toxicities

median_tox Median number of toxicities

min_tox Minimum number of toxicities

q1_tox First quartile (Q1) of the number of toxicities

q3_tox Third quartile (Q3) of the number of toxicities

max_tox Maximum number of toxicities

siqr_tox Semi-interquartile range of the number of toxicities

Examples

```
df <- run_simulation_logistic(num_rep = 100)
head(df)
```

`run_simulation_power` *Run Simulation Comparison Between 3+3 and CRM2s for the power model*

Description

Compares the MTD estimation and toxicity count between the power 3+3 method and the two-stage CRM using multiple replications.

Usage

```
run_simulation_power(
  num_rep = 1000,
  seed = 1234,
  save_plot = FALSE,
  p0 = 0.4,
  theta_0 = 2.7,
  theta = 3,
  N = 24,
  n_initial = 1,
  q_0 = 0.05,
  q_2 = 0.5,
  q_1 = 0.9,
  p_tox_init_3_3 = 0.02,
  delta_dosis_3_3 = 0.055,
  fixed_optimal_dose = 0.2032
)
```

Arguments

num_rep	Number of replications to run. Default is 1000.
seed	Base random seed for reproducibility. Default is 1234.
save_plot	Logical. If TRUE, saves comparison plots as PDF. Default is FALSE.
p0	Target toxicity probability. Default is 0.4.
theta_0	Nominal value of theta used in CRM and 3+3 escalation models. Default is 2.7.
theta	True theta used for generating the MTD reference. Default is 3.
N	Total number of patients in the CRM design. Default is 24.
n_initial	Number of patients per dose level in the CRM design (not used in 3+3). Default is 1.
q_0	Initial toxicity probability for CRM design. Default is 0.05.
q_2	Fraction of patients in CRM stage 1. Default is 0.5.
q_1	Target probability of observing at least one toxicity in CRM stage 1. Default is 0.9.
p_tox_init_3_3	Initial toxicity probability for the 3+3 model. Default is 0.02.
delta_dosis_3_3	Step size for dose escalation in the 3+3 model. Default is 0.055.
fixed_optimal_dose	Reference dose for optimal CRM design. Default is 0.2032.

Value

A `data.frame` with one row per method ("3+3" and "CRM2s") and the following columns:

method Design used ("3+3" or "CRM2s")
mean_pat Mean of patients
median_pat Median of patients
mean_mtd Mean of the estimated MTDs
sd_mtd Standard deviation of the estimated MTDs
median_mtd Median of the estimated MTDs
min_mtd Minimum of the estimated MTDs
q1_mtd First quartile (Q1) of the estimated MTDs
q3_mtd Third quartile (Q3) of the estimated MTDs
max_mtd Maximum of the estimated MTDs
siqr_mtd Semi-interquartile range of the estimated MTDs
mean_tox Mean number of toxicities
sd_tox Standard deviation of the number of toxicities
median_tox Median number of toxicities
min_tox Minimum number of toxicities
q1_tox First quartile (Q1) of the number of toxicities
q3_tox Third quartile (Q3) of the number of toxicities
max_tox Maximum number of toxicities
siqr_tox Semi-interquartile range of the number of toxicities

Examples

```
df <- run_simulation_power(num_rep = 100)
head(df)
```

simulate_across_n_initial

Simulation Study for Different n_initial Values (Power and Logistic Models)

Description

Runs simulations using run_simulation_power() and run_simulation_logistic() with varying n_initial values and summarizes key results.

Usage

```
simulate_across_n_initial(num_rep = 500, seed = 1234)
```

Arguments

num_rep	Number of repetitions for each simulation. Default is 500.
seed	Random seed. Default is 1234.

Value

A list of two data frames: $power and $logistic, each containing results for CRM2s at n_initial = 1:4 and 3+3.

Examples

```
result_list <- simulate_across_n_initial()
head(result_list$power)
```

two_stage_crm_logistic

C-optimal based two-stage Continual Reassessment Method (CRM2s) Simulation for logistic model with 2 parameters

Description

Performs one simulation run of a two-stage CRM design for estimating the Maximum Tolerated Dose (MTD) in phase I trials.

Usage

```
two_stage_crm_logistic(
  p0 = 0.4,
  theta = c(-3, 2),
  theta_0 = c(-3.1, 1.8),
  N = 24,
  n_initial = 3,
  q_0 = 0.05,
  q_2 = 0.4,
```

```
  q_1 = 0.9,
  lim_sup_prob = 0.7,
  show_plot = FALSE,
  seed = 1234
)
```

Arguments

p0	Target toxicity probability. Default is 0.4.
theta	True value for the vector of parameters for the dose-toxicity curve. Default is c(-3,2).
theta_0	Nominal value of the vector of parameters. Default is c(-3.1, 1.8).
N	Total number of patients (including both stages). Default is 24.
n_initial	Number of patients per dose in stage 1. Default is 3.
q_0	Toxicity probability at first dose. Default is 0.02.
q_2	Fraction of patients in stage 1. Default is 0.5.
q_1	Target probability of observing at least one toxicity during stage 1. Default is 0.9.
lim_sup_prob	Maximum acceptable probability of toxicity. Default is 0.7.
show_plot	Logical. If TRUE, plots the dose levels for patients in the trial. Default is FALSE.
seed	Random seed for reproducibility. Default is 1234.

Value

A list with:

n_toxicities Total number of toxicities observed.

mtd_estimated Estimated Maximum Tolerated Dose (MTD). If no toxicity is observed in the first stage, the MTD is set to the largest dose level used.

mle_theta Vector of estimated parameters $\theta = (\alpha, \beta)$ for the logistic dose-toxicity model. Set to NA if no toxicity is detected in stage 1.

x Vector of dose levels administered.

y Vector of toxicity outcomes (1 = toxic, 0 = non-toxic).

Note

If no toxicity is observed during the first stage of the trial (i.e., sum(y) == 0), the simulation is terminated. A warning is issued, and the MTD is conservatively estimated as the highest dose level reached. The value of mle_theta is set to NA in this case.

Examples

```
result <- two_stage_crm_logistic(show_plot = TRUE)
print(result$mtd_estimated)
```

`two_stage_crm_power` *C-optimal based two-stage Continual Reassessment Method (CRM2s) Simulation for power model*

Description

Performs one simulation run of a two-stage CRM design for estimating the Maximum Tolerated Dose (MTD) in phase I trials.

Usage

```
two_stage_crm_power(
  p0 = 0.4,
  theta = 3,
  theta_0 = 2.7,
  N = 24,
  n_initial = 3,
  q_0 = 0.02,
  q_2 = 0.5,
  q_1 = 0.9,
  fixed_optimal_dose = 0.2032,
  show_plot = FALSE,
  seed = 1234
)
```

Arguments

`p0`	Target toxicity probability. Default is 0.4.
`theta`	True value for the dose-toxicity curve. Default is 3.
`theta_0`	Nominal value of the dose-toxicity curve parameter (initial guess). Default is 2.7.
`N`	Total number of patients (including both stages). Default is 24.
`n_initial`	Number of patients per dose in stage 1. Default is 3.
`q_0`	Toxicity probability at first dose. Default is 0.02.
`q_2`	Fraction of patients in stage 1. Default is 0.5.
`q_1`	Target probability of observing at least one toxicity during stage 1. Default is 0.9.
`fixed_optimal_dose`	Reference dose for optimal design estimation. Default is 0.2032.
`show_plot`	Logical. If TRUE, plots the dose levels for patients in the trial. Default is FALSE.
`seed`	Random seed for reproducibility. Default is 1234.

Value

A list with:

n_toxicities Total number of toxicities observed.

mtd_estimated Estimated Maximum Tolerated Dose (MTD). If no toxicity is observed in the first stage, the MTD is set to the largest dose level used.

mle_theta Estimated value of the dose-toxicity parameter θ. Set to `NA` if no toxicity is detected in stage 1.

x Vector of dose levels administered.

y Vector of toxicity outcomes (1 = toxic, 0 = non-toxic).

Note

If no toxicity is observed during the first stage of the trial (i.e., `sum(y) == 0`), the simulation is terminated. A warning is issued, and the MTD is conservatively estimated as the highest dose level reached. The value of `mle_theta` is set to `NA` in this case.

Examples

```
result <- two_stage_crm_power(show_plot = TRUE)
print(result$mtd_estimated)
```

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