Package: cats (via r-universe)

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Type Package

Title Cohort Platform Trial Simulation

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Description Cohort plAtform Trial Simulation whereby every cohort consists of two arms, control and experimental treatment. Endpoints are co-primary binary endpoints and decisions are made using either Bayesian or frequentist decision rules. Realistic trial trajectories are simulated and the operating characteristics of the designs are calculated.

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Encoding UTF-8

Depends R (>= 3.5.0)

RoxygenNote 7.1.2

URL https://el-meyer.github.io/cats/, https://github.com/el-meyer/cats

BugReports https://github.com/el-meyer/cats/issues

Imports dplyr, purrr, ggplot2, plotly, tidyr, parallel, doParallel, foreach, openxlsx, forcats, epitools, zoo, mvtnorm

Suggests knitr, rmarkdown, DT, gtools

Repository https://el-meyer.r-universe.dev

RemoteUrl https://github.com/el-meyer/cats

RemoteRef HEAD

RemoteSha 46b211d8c77fafaea6696e07f9416ec09d186184

Contents

`make_decision_trial` *Checks whether decision criteria are met and updates trial results accordingly.*

Description

Given a res_list object, checks the supplied decision criteria and saves the results in the res_list file.

Usage

```
make_decision_trial(
  res_list,
  which_cohort,
  Bayes_Sup1 = NULL,
  Bayes_Fut1 = NULL,
  Bayes_Sup2 = NULL,
  Bayes_Fut2 = NULL,
  w = 0.5,
  analysis_number,
  beta_prior = 0.5,
  hist_lag,
  endpoint_number,
  analysis_time,
  dataset,
  hist_miss = TRUE,
  sharing_type,
  ...
)
```

Arguments

`res_list`	List item containing individual cohort trial results so far in a format used by the other functions in this package
`which_cohort`	Current cohort that should be evaluated
`Bayes_Sup1`	List of matrices with rows corresponding to number of multiple Bayesian posterior two-arm combination criteria for superiority of histology endpoint 1
`Bayes_Fut1`	List of matrices with rows corresponding to number of multiple Bayesian posterior two-arm combination criteria for futility of histology endpoint 1
`Bayes_Sup2`	List of matrices with rows corresponding to number of multiple Bayesian posterior two-arm combination criteria for superiority of histology endpoint 2
`Bayes_Fut2`	List of matrices with rows corresponding to number of multiple Bayesian posterior two-arm combination criteria for futility of histology endpoint 2
`w`	If dynamic borrowing, what is the prior choice for w. Default is 0.5.

analysis_number	1st, second or third analysis?
beta_prior	Prior parameter for all Beta Distributions. Default is 0.5.
hist_lag	Histology Lag
endpoint_number	Should histology endpoint 1 or 2 be evaluated?
analysis_time	Platform Time of Analysis
dataset	Dataset to be used for analysis
hist_miss	Whether or not to exclude missing histology data
sharing_type	Type of Data Sharing to perform
...	Further arguments inherited from simulate_trial

Value

List containing original res_list and results of decision rules

Examples

```
# Example 1

# Initialize empty data frame
cols <- c("PatID", "ArrivalTime", "Cohort", "Arm", "RespHist1", "RespHist2", "HistMissing")
df <- matrix(nrow = 100, ncol = length(cols))
colnames(df) <- cols
df <- as.data.frame(df)
df$PatID <- 1:100
df$ArrivalTime <- sort(runif(100, min = 0, max = 5))
df$Cohort <- sample(1:2, 100, replace = TRUE)
df$Arm <- sample(c("Combo", "Plac"), 100, replace = TRUE)
df$RespHist1 <- sample(0:1, 100, replace = TRUE)
df$RespHist2 <- sample(0:1, 100, replace = TRUE)
df$HistMissing <- sample(0:1, 100, replace = TRUE, prob = c(0.95, 0.05))

# Initialize res_list Object

res_list <-
rep(
  list(
    list(
      Meta = list(
        decision = rep("none", 3),
        decision_hist1 = rep("none", 3),
        decision_hist2 = rep("none", 3),
        start_n = 0,
        start_time = 0,
        pat_enrolled = 0
      ),
      Arms = rep(
        list(
```

```
          list(
            rr = NULL,
            hist_observed = 0
          )
        ),
        2
      )
    )
  ),
  2
)

arm_names <- c("Comb", "Plac")

for (i in 1:2) {
  names(res_list)[i] <- paste0("Cohort", i)
  names(res_list[[i]]$Arms) <- arm_names

  res_list[[i]]$Arms$Comb$rr <- matrix(c(0.2, 0.2), ncol = 2)
  res_list[[i]]$Arms$Plac$rr <- matrix(c(0.1, 0.1), ncol = 2)
}

sharing_type <- "all"
analysis_number <- 3
which_cohort <- 1
endpoint_number <- 2
hist_lag <- 1
analysis_time <- 6

# Comparison IA1
Bayes_Sup11 <- matrix(nrow = 2, ncol = 2)
Bayes_Sup11[1,] <- c(0.00, 0.95)
Bayes_Sup11[2,] <- c(0.10, 0.80)
# Comparison IA2
Bayes_Sup12 <- matrix(nrow = 2, ncol = 2)
Bayes_Sup12[1,] <- c(0.00, 0.95)
Bayes_Sup12[2,] <- c(NA, NA)
# Comparison IA3
Bayes_Sup13 <- matrix(nrow = 2, ncol = 2)
Bayes_Sup13[1,] <- c(0.00, 0.95)
Bayes_Sup13[2,] <- c(0.10, 0.80)

Bayes_Sup1 <- Bayes_Sup2 <- list(list(Bayes_Sup11), list(Bayes_Sup12), list(Bayes_Sup13))


# DO NOT RUN
res_list2 <-
make_decision_trial(
res_list = res_list, which_cohort = which_cohort,
analysis_number = analysis_number, endpoint_number = endpoint_number,
Bayes_Sup1 = Bayes_Sup1, Bayes_Sup2 = Bayes_Sup2,
dataset = df, analysis_time = analysis_time, hist_lag = hist_lag,
sharing_type = sharing_type
```

```
)
```

`simulate_trial` *Simulates the cohort trial.*

Description

Simulates the cohort trial.

Usage

```
simulate_trial(
  n_fin,
  cohorts_start = 1,
  composite = "or",
  rr_comb1,
  rr_plac1,
  rr_comb2,
  rr_plac2,
  random_type = NULL,
  random = FALSE,
  correlation,
  prob_comb1_rr = NULL,
  prob_plac1_rr = NULL,
  prob_comb2_rr = NULL,
  prob_plac2_rr = NULL,
  stage_data = FALSE,
  cohort_random = NULL,
  cohorts_max = 4,
  sr_drugs_pos = 1,
  sr_pats = cohorts_max * (n_fin + 3 * cohorts_max),
  sr_first_pos = FALSE,
  cohort_offset = 0,
  sharing_type = "all",
  safety_prob = 0,
  cohorts_sim = Inf,
  missing_prob = 0,
  cohort_fixed = NULL,
  accrual_type = "fixed",
  accrual_param = 9,
  hist_lag = 48,
  analysis_times = c(0.5, 0.75, 1),
  time_trend = time_trend,
  ...
)
```

Arguments

n_fin	Sample size per cohort at final
cohorts_start	Number of cohorts to start the platform with
composite	Rule for deriving the composite endpoint. By default "or", otherwise "and"
rr_comb1	Response rates of treatment, histology endpoint 1
rr_plac1	Response rate of the SoC, histology endpoint 1
rr_comb2	Response rates of treatment, histology endpoint 2
rr_plac2	Response rate of the SoC, histology endpoint 2
random_type	How should the response rates be drawn randomly? Options are: "absolute": Specify absolute response rates that will be drawn with a certain probability "risk_difference": Specify absolute response rates for placebo which will be drawn randomly, plus specify vectors for absolute treatment effects of mono therapies over placebo and for combo over the mono therapies. "risk_ratio": Specify absolute response rates for placebo which will be drawn randomly, plus specify vectors for relative treatment effects of mono therapies over placebo and for combo over the mono therapies. "odds_ratios": Specify response rate for placebo, specify odds-ratios for mono therapies (via rr_back and rr_mono) and respective probabilities. On top, specify interaction for the combination therapy via rr_comb with prob_rr_comb. Set: odds_combo = odds_plac * or_mono1 * or_mono2 * rr_comb. If rr_comb > 1 -> synergistic, if rr_comb = 1 -> additive. If rr_comb < 1 -> antagonistic. Default is "NULL".
random	Should the response rates of the arms be randomly drawn from rr_exp? Default is FALSE.
correlation	Correlation between histology endpoints
prob_comb1_rr	If random == TRUE, what are the probabilities with which the elements of rr_comb1 should be drawn?
prob_plac1_rr	If random == TRUE, what are the probabilities with which the elements of rr_plac1 should be drawn?
prob_comb2_rr	If random == TRUE, what are the probabilities with which the elements of rr_comb2 should be drawn?
prob_plac2_rr	If random == TRUE, what are the probabilities with which the elements of rr_plac2 should be drawn?
stage_data	Should individual stage data be passed along? Default is TRUE
cohort_random	If not NULL, indicates that new arms/cohorts should be randomly started. For every timestep, there is a cohort_random probability that a new cohort will be started.
cohorts_max	Maximum number of cohorts that are allowed to be added throughout the trial
sr_drugs_pos	Stopping rule for successful experimental arms; Default = 1
sr_pats	Stopping rule for total number of patients; Default = cohorts_max * n_fin + error term based on randomization

sr_first_pos	Stopping rule for first successful cohort; if TRUE, after first cohort was found to be successful, no further cohorts will be included but cohorts will finish evaluating, unless other stopping rules reached prior. Default is FALSE.
cohort_offset	Minimum number of time between adding new cohorts
sharing_type	Which backbone and placebo data should be used for arm comparisons; Default is "all". Another option is "concurrent" or "dynamic" or "cohort".
safety_prob	Probability for a random stopping after every patient
cohorts_sim	Maximum number of cohorts that can run simultaneously
missing_prob	Probability for a missing value at final (independent of treatment)
cohort_fixed	If not NULL, fixed timesteps after which a cohort will be included
accrual_type	Type of patient accrual; choices are "fixed", "poisson" or "exponential"
accrual_param	Parameter used for patient accrual
hist_lag	Time until histology outcome is observed
analysis_times	Vector of information fractions needed for first interim, second interim and final
time_trend	Additive term by which response rates increase at every time step
...	Further arguments to be passed to decision function, such as decision making criteria

Value

List containing: Responses and patients on experimental and control arm, total treatment successes and failures and final p-value

Examples

```
random <- TRUE

rr_comb1 <- 0.10
prob_comb1_rr <- 1
rr_comb2 <- 0.45
prob_comb2_rr <- 1
rr_plac1 <- 0.10
prob_plac1_rr <- 1
rr_plac2 <- 0.20
prob_plac2_rr <- 1

correlation <- 0.8

cohorts_start <- 2
cohorts_max <- 5
safety_prob <- 0
sharing_type <- "concurrent"
sr_drugs_pos <- 5
sr_first_pos <- FALSE
n_fin <- 100
stage_data <- TRUE
cohort_random <- 0.01
```

```
cohort_offset <- 0
cohorts_sim <- Inf
random_type <- "absolute"
missing_prob <- 0.2
cohort_fixed <- 5
hist_lag <- 48
analysis_times <- c(0.5, 0.75, 1)
accrual_type <- "fixed"
accrual_param <- 9
time_trend <- 0.001
composite <- "or"

# Comparison IA1
Bayes_Sup11 <- matrix(nrow = 2, ncol = 2)
Bayes_Sup11[1,] <- c(0.00, 0.95)
Bayes_Sup11[2,] <- c(0.10, 0.80)
# Comparison IA2
Bayes_Sup12 <- matrix(nrow = 2, ncol = 2)
Bayes_Sup12[1,] <- c(0.00, 0.95)
Bayes_Sup12[2,] <- c(0.10, 0.80)
# Comparison IA3
Bayes_Sup13 <- matrix(nrow = 2, ncol = 2)
Bayes_Sup13[1,] <- c(0.00, 0.95)
Bayes_Sup13[2,] <- c(0.10, 0.80)

Bayes_Sup1 <- Bayes_Sup2 <- list(list(Bayes_Sup11), list(Bayes_Sup12), list(Bayes_Sup13))

# Comparison IA1
Bayes_Fut11 <- matrix(nrow = 1, ncol = 2)
Bayes_Fut11[1,] <- c(0.00, 0.20)
# Comparison IA2
Bayes_Fut12 <- matrix(nrow = 1, ncol = 2)
Bayes_Fut12[1,] <- c(0.00, 0.30)
# Comparison IA3
Bayes_Fut13 <- matrix(nrow = 1, ncol = 2)
Bayes_Fut13[1,] <- c(NA, NA)
# Endpoint 1+2
Bayes_Fut1 <- Bayes_Fut2 <- list(list(Bayes_Fut11), list(Bayes_Fut12), list(Bayes_Fut13))

simulate_trial(
 n_fin = n_fin, random_type = random_type, composite = composite,
 rr_comb1 = rr_comb1, rr_comb2 = rr_comb2, rr_plac1 = rr_plac1, rr_plac2 = rr_plac2,
 random = random, prob_comb1_rr = prob_comb1_rr, prob_comb2_rr = prob_comb2_rr,
 prob_plac1_rr = prob_plac1_rr, prob_plac2_rr = prob_plac2_rr, correlation = correlation,
 stage_data = stage_data, cohort_random = cohort_random, cohorts_max = cohorts_max,
 sr_drugs_pos = sr_drugs_pos, sharing_type = sharing_type, Bayes_Fut1 = Bayes_Fut1,
 safety_prob = safety_prob, Bayes_Sup1 = Bayes_Sup1, Bayes_Sup2 = Bayes_Sup2,
 cohort_offset = cohort_offset, sr_first_pos = sr_first_pos, Bayes_Fut2 = Bayes_Fut2,
 missing_prob = missing_prob, cohort_fixed = cohort_fixed, accrual_type = accrual_type,
 accrual_param = accrual_param, hist_lag = hist_lag, analysis_times = analysis_times,
 time_trend = time_trend, cohorts_start = cohorts_start, cohorts_sim = cohorts_sim
)
```

`trial_ocs` *Calculates the operating characteristics of the cohort trial*

Description

Given the trial specific design parameters, performs a number of simulations of the trial and saves the result in an Excel file

Usage

```
trial_ocs(
  iter,
  coresnum = 1,
  save = FALSE,
  path = NULL,
  filename = NULL,
  ret_list = FALSE,
  ret_trials = FALSE,
  plot_ocs = FALSE,
  export = NULL,
  ...
)
```

Arguments

`iter`	Number of program simulations that should be performed
`coresnum`	How many cores should be used for parallel computing
`save`	Indicator whether simulation results should be saved in an Excel file
`path`	Path to which simulation results will be saved; if NULL, then save to current path
`filename`	Filename of saved Excel file with results; if NULL, then name will contain design parameters
`ret_list`	Indicator whether function should return list of results
`ret_trials`	Indicator whether individual trial results should be saved as well
`plot_ocs`	Should OCs stability plots be drawn?
`export`	Should any other variables be exported to the parallel tasks?
`...`	All other design parameters for chosen program

Value

List containing: Responses and patients on experimental and control arm, total treatment successes and failures and final p-value

Examples

```
random <- TRUE

rr_comb1 <- 0.25
prob_comb1_rr <- 1
rr_comb2 <- 0.20
prob_comb2_rr <- 1
rr_plac1 <- 0.10
prob_plac1_rr <- 1
rr_plac2 <- 0.10
prob_plac2_rr <- 1

correlation <- 0.8

cohorts_start <- 2
cohorts_max <- 5
safety_prob <- 0
sharing_type <- "concurrent"
sr_drugs_pos <- 5
sr_first_pos <- FALSE
n_fin <- 100
stage_data <- TRUE
cohort_random <- 0.01
cohort_offset <- 0
cohorts_sim <- Inf
random_type <- "absolute"
missing_prob <- 0.2
cohort_fixed <- 5
hist_lag <- 48
analysis_times <- c(0.5, 0.75, 1)
accrual_type <- "fixed"
accrual_param <- 9
time_trend <- 0.001
composite <- "or"

# Comparison IA1
Bayes_Sup11 <- matrix(nrow = 2, ncol = 2)
Bayes_Sup11[1,] <- c(0.00, 0.95)
Bayes_Sup11[2,] <- c(0.10, 0.80)
# Comparison IA2
Bayes_Sup12 <- matrix(nrow = 2, ncol = 2)
Bayes_Sup12[1,] <- c(0.00, 0.95)
Bayes_Sup12[2,] <- c(0.10, 0.80)
# Comparison IA3
Bayes_Sup13 <- matrix(nrow = 2, ncol = 2)
Bayes_Sup13[1,] <- c(0.00, 0.95)
Bayes_Sup13[2,] <- c(0.10, 0.80)

Bayes_Sup1 <- Bayes_Sup2 <- list(list(Bayes_Sup11), list(Bayes_Sup12), list(Bayes_Sup13))

ocs <- trial_ocs(
n_fin = n_fin, random_type = random_type, composite = composite,
```

```
rr_comb1 = rr_comb1, rr_comb2 = rr_comb2, rr_plac1 = rr_plac1, rr_plac2 = rr_plac2,
random = random, prob_comb1_rr = prob_comb1_rr, prob_comb2_rr = prob_comb2_rr,
prob_plac1_rr = prob_plac1_rr, prob_plac2_rr = prob_plac2_rr,
stage_data = stage_data, cohort_random = cohort_random, cohorts_max = cohorts_max,
sr_drugs_pos = sr_drugs_pos, sharing_type = sharing_type, correlation = correlation,
safety_prob = safety_prob, Bayes_Sup1 = Bayes_Sup1, Bayes_Sup2 = Bayes_Sup2,
cohort_offset = cohort_offset, sr_first_pos = sr_first_pos,
missing_prob = missing_prob, cohort_fixed = cohort_fixed, accrual_type = accrual_type,
accrual_param = accrual_param, hist_lag = hist_lag, analysis_times = analysis_times,
time_trend = time_trend, cohorts_start = cohorts_start, cohorts_sim = cohorts_sim,
iter = 2, coresnum = 1, save = FALSE, ret_list = TRUE, plot_ocs = TRUE
)
```

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