Package: hesim (via r-universe)

October 18, 2024

Title Health Economic Simulation Modeling and Decision Analysis
 Version 0.5.5
 Description A modular and computationally efficient R package for parameterizing, simulating, and analyzing health economic simulation models. The package supports cohort discrete time state transition models (Briggs et al. 1998)
 <doi:10.2165/00019053-199813040-00003>, N-state partitioned survival models (Glasziou et al. 1990)
 <doi:10.1002/sim.4780091106>, and individual-level continuous

time state transition models (Siebert et al. 2012) <doi:10.1016/j.jval.2012.06.014>, encompassing both Markov (time-homogeneous and time-inhomogeneous) and semi-Markov processes. Decision uncertainty from a cost-effectiveness analysis is quantified with standard graphical and tabular summaries of a probabilistic sensitivity analysis (Claxton et al. 2005, Barton et al. 2008) <doi:10.1002/hec.985>, <doi:10.1111/j.1524-4733.2008.00358.x>. Use of C++ and data.table make individual-patient simulation, probabilistic sensitivity analysis, and incorporation of patient heterogeneity fast.

URL https://hesim-dev.github.io/hesim/,
 https://github.com/hesim-dev/hesim

BugReports https://github.com/hesim-dev/hesim/issues

License GPL-3 LazyData true

Type Package

LinkingTo Rcpp, RcppArmadillo

Depends R (>= 3.5.0)

Imports data.table, flexsurv, ggplot2, MASS, msm, Rcpp (>= 0.12.16), R6, stats, survival

Suggests covr, kableExtra, knitr, magrittr, mstate, nnet, numDeriv, pracma, rmarkdown, scales, testthat, truncnorm

2 Contents

VignetteBuilder	KIIIU

Roxygen list(markdown = TRUE)

RoxygenNote 7.3.2

Repository https://hesim-dev.r-universe.dev

RemoteUrl https://github.com/hesim-dev/hesim

RemoteRef HEAD

RemoteSha bb523500512f9d6beabfea943625a7fd2465c478

Contents

apply_rr	4
as.data.table.tparams_transprobs	5
as_array3	6
as_pfs_os	8
autoplot.stateprobs	9
autoplot.survival	10
ce	11
	12
CohortDtstm	15
	20
	23
	24
	25
create_IndivCtstmTrans	26
	28
-	30
	32
create_trans_dt	
	35
	37
define_tparams	39
	10
	11
· r	12
	13
	14
8er=meers	14
hesim_data	16
icer	17
	19
IndivCtstm	50
IndivCtstmTrans	54
input_mats	58
mom_beta	50
mom_gamma	51
mstate3 exdata	52

Contents 3

nultinom3_exdata	. 63
nultinom_list	. 65
nc3	. 65
nc3p	. 66
arams	. 67
arams_lm	. 68
arams_mlogit	. 69
arams_mlogit_list	. 70
arams_surv	. 72
arams_surv_list	
lot_ceac	. 75
lot_ceaf	. 76
olot_ceplane	
lot_evpi	. 78
 ?sm	
sm4_exdata	
PsmCurves	
alys	
matrix.matrix	
matrix.msm	
cat	
dirichlet_mat	
ng_distributions	
pwexp	
et_labels	
im_ev	
im_stateprobs.survival	
tateprobs	
tateVals	
tateval_tbl	
ummary.ce	
ummary.eval_rng	
ummary.params	
ummary.tparams_mean	
ummary.tparams_transprobs	
ummary.tpmatrix	
urvival	
urv_quantile	117
ime intervals	
params	
params_mean	
params_transprobs	
pmatrix	
pmatrix_id	
pmatrix_names	
γ	. 120
	127

Index

4 apply_rr

ар	p1	У_	rr
uρ	РΤ	· y –	_, ,

Apply relative risks to transition probability matrices

Description

Elements of transition probability matrices are multiplied by relative risks and the transition probability matrices are adjusted so that rows sum to 1. Operations are vectorized and each relative risk is multiplied by every transition matrix (stored in 3-dimensional arrays).

Usage

```
apply_rr(x, rr, index, complement = NULL)
```

Arguments

x A 3-dimensional array where each slice is a square transition probability matrix.

rr A 2-dimensional tabular object such as a matrix or data frame where each col-

umn is a vector of relative risks to apply to each transition matrix in x.

index The indices of the transition probability matrices that rr is applied to. Should

either be a matrix where the first column denotes a transition probability matrix row and the second column denotes a transition probability matrix column or a list where each element is a vector of length 2 with the first element denoting a transition probability matrix row and the second column denoting a transition

probability matrix column.

complement Denotes indices of transition probability matrices that are "complements" (i.e.,

computed as 1 less the sum of all other elements in that row). Should be in the same format as index. There can be at most one complementary column in each row of a transition probability matrix. If NULL, then the diagonals are assumed

to be the complements.

Details

This function is useful for applying relative treatment effects measured using relative risks to an existing transition probability matrix. For example, a transition probability matrix for the reference treatment strategy may exist or have been estimated from the data. Relative risks estimated from a meta-analysis or network meta-analysis can then be applied to the reference transition probability matrix. If the number of rows in rr exceeds x, then the arrays in x are recycled to the number of rows in rr, which facilitates the application of relative risks from multiple treatment strategies to a reference treatment.

Value

A 3-dimensional array where each slice contains matrices of the same dimension as each matrix in x and the number of slices is equal to the number of rows in rr.

Examples

```
p_12 < c(.7, .5)
p_23 \leftarrow c(.1, .2)
x <- as_array3(tpmatrix(</pre>
  C, p_12, .1,
  0, C,
           p_23,
  0, 0,
            1
))
# There are the same number of relative risk rows and transition probability matrices
rr_12 <- runif(2, .8, 1)
rr_13 <- runif(2, .9, 1)
rr <- cbind(rr_12, rr_13)
apply_rr(x, rr,
         index = list(c(1, 2), c(1, 3)),
         complement = list(c(1, 1), c(2, 2)))
# There are more relative risk rows than transition probability matrices
rr_12 <- runif(4, .8, 1)
rr_13 <- runif(4, .9, 1)
rr <- cbind(rr_12, rr_13)
apply_rr(x, rr,
         index = list(c(1, 2), c(1, 3)),
         complement = list(c(1, 1), c(2, 2)))
```

```
as.data.table.tparams_transprobs

*Coerce to data.table*
```

Description

Creates a data.table that combines the transition probability matrices and ID variables from a tparams_transprobs object. This is often useful for debugging.

Usage

```
## S3 method for class 'tparams_transprobs'
as.data.table(x, ..., prefix = "prob_", sep = "_", long = FALSE)
```

Arguments

```
x A tparams_transprobs object.
... Currently unused.

prefix, sep Arguments passed to tpmatrix_names() for naming the transition probability columns. The states argument is based on the column names (i.e., names of the second dimension) of the $value element of x; if NULL, then states are named $1, ..., sh where h is the number of states. Only used if long = FALSE.
```

6 as_array3

long

If TRUE, then output is returned in a longer format with one row for each transition; if FALSE, then each row contains an entire flattened transition probability matrix.

Value

The output always contains columns for the ID variables and the transition probabilities, but the form depends on on the long argument. If FALSE, then a data.table with one row for each transition probability matrix is returned; otherwise, the data.table contains one row for each transition and columns from (the state being transitioned from) and to (the state being transitioned to) are added.

See Also

```
tparams_transprobs()
```

Examples

```
# Create tparams_transprobs object
hesim_dat <- hesim_data(strategies = data.frame(strategy_id = 1:2),</pre>
                         patients = data.frame(patient_id = 1:3))
input_data <- expand(hesim_dat, by = c("strategies", "patients"))</pre>
tpmat_id <- tpmatrix_id(input_data, n_samples = 2)</pre>
p_12 \leftarrow runif(nrow(tpmat_id), .6, .7) +
  .05 * (tpmat_id$strategy_id == 2)
tpmat <- tpmatrix(</pre>
  C, p_12,
  0, 1
tprobs <- tparams_transprobs(tpmat, tpmat_id)</pre>
# Convert to data.table in "wide" format
as.data.table(tprobs)
as.data.table(tprobs, prefix = "")
as.data.table(tprobs, prefix = "", sep = ".")
# Convert to data.table in "long: format
as.data.table(tprobs, long = TRUE)
```

as_array3

Convert between 2D tabular objects and 3D arrays

Description

Convert a 2-dimensional tabular object where each row stores a flattened square matrix to a 3-dimensional array of square matrices and vice versa. This allows multiple transition matrices to be stored as either tabular objects (e.g., matrices, data frames, etc) or as arrays.

as_array3

Usage

```
as_array3(x)
as_tbl2(
    x,
    output = c("data.table", "data.frame", "matrix", "tpmatrix"),
    prefix = "",
    sep = "_"
)
```

Arguments

x For as_array3() a 2-dimensional tabular object where each row stores a flat-

tened square matrix ordered rowwise. Reasonable classes are matrix, data.frame, data.table, and tpmatrix. For as_tbl2() a 3-dimensional array where each

slice is a square matrix.

output The class of the object returned by the function. Either a data.table, data.frame,

matrix, or tpmatrix.

prefix, sep Arguments passed to tpmatrix_names() for naming the transition probability

columns. The states argument is based on the column names (i.e., names of the second dimension) of array; if NULL, then states are named s1, ..., sh where

h is the number of states.

Value

For as_array3() a 3-dimensional array of square matrices; for as_tb12() a 2-dimensional tabular object as specified by output.

See Also

tpmatrix

```
p_12 <- c(.7, .6)
pmat <- tpmatrix(
    C, p_12,
    0, 1
)
pmat

as_array3(pmat)
as_array3(as.matrix(pmat))
as_tbl2(as_array3(pmat), prefix = "p_", sep = ".")</pre>
```

8 as_pfs_os

as_pfs_os

Convert multi-state data to PFS and OS data

Description

Convert a multi-state dataset with irreversible transitions containing 3 health states to a dataset with one row per patient and progression-free survival (PFS) and overall survival (OS) time-to-event outcomes.

Usage

```
as_pfs_os(
  data,
  patient_vars,
  status = "status",
  time_stop = "time_stop",
  transition = "transition_id"
)
```

Arguments

data A multi-state dataset.

patient_vars Character vector of the names of patient specific variables.

status Character string with the name of the status variable (1 = event, 0 = censored).

time_stop Character string with the name of the stopping time variable (i.e., time patient

transitions from state r to state s).

transition Character string with the name of the variable identifying a transition. The tran-

sition variable should be integer valued with values 1, 2, and 3 for the Stable -> Progression, Stable -> Death, and Progression -> Death transitions, respectively.

Value

A data.table with one row per patient containing each variable in patient_vars as well as a time variable and status indicator for both PFS (pfs_status, pfs_time) and OS (os_time, os_status).

```
as_pfs_os(onc3, patient_vars = c("patient_id", "strategy_name", "female", "age"))
```

autoplot.stateprobs 9

autoplot.stateprobs Plot state probabilities

Description

Quickly plot state probabilities stored in a stateprobs object.

Usage

```
## S3 method for class 'stateprobs'
autoplot(
  object,
  labels = NULL,
  ci = FALSE,
  prob = 0.95,
  ci_style = c("ribbon", "line"),
  geom_alpha = 0.3,
  ...
)
```

Arguments

object	A stateprobs object.
labels	A list of named vectors containing the values and labels of variables. The elements of each vector are the values of a variable and the names are the labels. The names of the list are the names of the variables. See the output returned by get_labels() for an example.
ci	A logical value indicating whether confidence intervals should be plotted. Default is FALSE.
prob	A numeric scalar in the interval (0,1) giving the confidence interval. Default is 0.95 for a 95 percent interval.
ci_style	Style to use for the confidence interval if ci = TRUE. If "line", then dashed lines are used; if "ribbon", then shaded confidence bands are plotted using ggplot2::geom_ribbon().
geom_alpha	The opacity for the shaded confidence bands when ci_style = "ribbon". This is the value of the value of the alpha aesthetic passed to ggplot2::geom_ribbon().
	Further arguments passed to and from methods. Currently unused.

Value

A ggplot object.

Note

If there are multiple patients/groups, then state probabilities are averaged across patients/groups (using the weights in patient_wt if available) prior to plotting.

10 autoplot.survival

See Also

Psm for an example.

autoplot.survival

Plot survival curves

Description

Quickly plot survival curves stored in a survival object.

Usage

```
## S3 method for class 'survival'
autoplot(
  object,
  labels = NULL,
  ci = FALSE,
  prob = 0.95,
  ci_style = c("ribbon", "line"),
  geom_alpha = 0.3,
  ...
)
```

Arguments

object	A survival object.
labels	A list of named vectors containing the values and labels of variables. The elements of each vector are the values of a variable and the names are the labels. The names of the list are the names of the variables. See the output returned by get_labels() for an example.
ci	A logical value indicating whether confidence intervals should be plotted. Default is FALSE.
prob	A numeric scalar in the interval (0,1) giving the confidence interval. Default is 0.95 for a 95 percent interval.
ci_style	Style to use for the confidence interval if ci = TRUE. If "line", then dashed lines are used; if "ribbon", then shaded confidence bands are plotted using ggplot2::geom_ribbon().
geom_alpha	The opacity for the shaded confidence bands when ci_style = "ribbon". This is the value of the value of the alpha aesthetic passed to ggplot2::geom_ribbon().
	Further arguments passed to and from methods. Currently unused.

Value

A ggplot object.

ce 11

Note

If there are multiple patients, then survival probabilities are averaged across patients (using the weights in patient_wt if available) prior to plotting.

See Also

Psm for an example.

ce

A cost-effectiveness object

Description

An object that summarizes simulated measures of clinical effectiveness and costs from a simulation model for use in a cost-effectiveness analysis.

Format

A list containing two elements:

costs Total (discounted) costs by category.

qalys (Discounted) quality-adjusted life-years.

Costs

The costs data. table contains the following columns:

category The cost category.

dr The discount rate.

sample A randomly sampled parameter set from the probabilistic sensitivity analysis (PSA)

strategy_id The treatment strategy ID.

grp_id An optional column denoting a subgroup. If not included, it is assumed that a single subgroup is being analyzed.

costs Costs.

Quality-adjusted life-years

The galys data. table contains the following columns:

dr The discount rate.

sample A randomly sampled parameter set from the probabilistic sensitivity analysis (PSA)

strategy_id The treatment strategy ID.

grp_id An optional column denoting a subgroup. If not included, it is assumed that a single subgroup is being analyzed.

qalys Quality-adjusted life-years

Cost-effectiveness analysis

cea

Description

Conduct cost-effectiveness analysis (CEA) given output of an economic model; that is, summarize a probabilistic sensitivity analysis (PSA), possibly by subgroup.

- cea() computes the probability that each treatment is most cost-effective, output for a cost-effectiveness acceptability frontier, the expected value of perfect information, and the net monetary benefit for each treatment.
- cea_pw() conducts pairwise CEA by comparing strategies to a comparator. Computed quantities include the incremental cost-effectiveness ratio, the incremental net monetary benefit, output for a cost-effectiveness plane, and output for a cost-effectiveness acceptability curve.

Usage

```
cea(x, ...)
cea_pw(x, ...)
## Default S3 method:
cea(x, k = seq(0, 2e+05, 500), sample, strategy, grp = NULL, e, c, ...)
## Default S3 method:
cea_pw(
  Х,
  k = seq(0, 2e+05, 500),
  comparator,
  sample,
  strategy,
  grp = NULL,
  e,
  С,
)
## S3 method for class 'ce'
cea(x, k = seq(0, 2e+05, 500), dr_qalys, dr_costs, ...)
## S3 method for class 'ce'
cea_pw(x, k = seq(0, 2e+05, 500), comparator, dr_qalys, dr_costs, ...)
```

Arguments

Х

An object of simulation output characterizing the probability distribution of clinical effectiveness and costs. If the default method is used, then x must be

cea 13

a data.frame or data.table containing columns of mean costs and clinical effectiveness where each row denotes a randomly sampled parameter set and treatment strategy.

... Further arguments passed to or from other methods. Currently unused.

k Vector of willingness to pay values.

sample Character name of column from x denoting a randomly sampled parameter set.

strategy Character name of column from x denoting treatment strategy.

grp Character name of column from x denoting subgroup. If NULL, then it is assumed

that there is only one group.

e Character name of column from x denoting clinical effectiveness.

c Character name of column from x denoting costs.

comparator Name of the comparator strategy in x.

dr_qalys Discount rate for quality-adjusted life-years (QALYs).

dr_costs Discount rate for costs.

Value

cea() returns a list of four data. table elements.

summary A data.table of the mean, 2.5% quantile, and 97.5% quantile by strategy and group for clinical effectiveness and costs.

mce The probability that each strategy is the most effective treatment for each group for the range of specified willingness to pay values. In addition, the column best denotes the optimal strategy (i.e., the strategy with the highest expected net monetary benefit), which can be used to plot the cost-effectiveness acceptability frontier (CEAF).

evpi The expected value of perfect information (EVPI) by group for the range of specified willingness to pay values. The EVPI is computed by subtracting the expected net monetary benefit given current information (i.e., the strategy with the highest expected net monetary benefit) from the expected net monetary benefit given perfect information.

nmb The mean, 2.5% quantile, and 97.5% quantile of net monetary benefits for the range of specified willingness to pay values.

cea_pw also returns a list of four data.table elements:

summary A data.table of the mean, 2.5% quantile, and 97.5% quantile by strategy and group for incremental clinical effectiveness and costs.

delta Incremental effectiveness and incremental cost for each simulated parameter set by strategy and group. Can be used to plot a cost-effectiveness plane.

ceac Values needed to plot a cost-effectiveness acceptability curve by group. The CEAC plots the probability that each strategy is more cost-effective than the comparator for the specified willingness to pay values.

inmb The mean, 2.5% quantile, and 97.5% quantile of incremental net monetary benefits for the range of specified willingness to pay values.

14 cea

```
library("data.table")
library("ggplot2")
theme_set(theme_bw())
# Simulation output
n_samples <- 30
sim <- data.table(sample = rep(seq(n_samples), 4),</pre>
                  c = c(rlnorm(n_samples, 5, .1), rlnorm(n_samples, 5, .1),
                        rlnorm(n_samples, 11, .1), rlnorm(n_samples, 11, .1)),
                  e = c(rnorm(n_samples, 8, .2), rnorm(n_samples, 8.5, .1),
                        rnorm(n_samples, 11, .6), rnorm(n_samples, 11.5, .6)),
                  strategy_id = rep(1:2, each = n_samples * 2),
                  grp_id = rep(rep(1:2, each = n_samples), 2)
)
# Cost-effectiveness analysis
cea_out <- cea(sim, k = seq(0, 200000, 500), sample = "sample",
               strategy = "strategy_id", grp = "grp_id",
               e = "e", c = "c")
names(cea_out)
## Some sample output
## The probability that each strategy is the most cost-effective
## in each group with a willingness to pay of 20,000
cea_out\mbox{mce}[k == 20000]
# Pairwise cost-effectiveness analysis
cea_pw_out < - cea_pw(sim, k = seq(0, 200000, 500), comparator = 1,
                      sample = "sample", strategy = "strategy_id",
                      grp = "grp_id", e = "e", c = "c")
names(cea_pw_out)
## Some sample output
## The cost-effectiveness acceptability curve
head(cea_pw_out\\ceac[k >= 20000])
# Summarize the incremental cost-effectiveness ratio
labs <- list(strategy_id = c("Strategy 1" = 1, "Strategy 2" = 2),</pre>
             grp_id = c("Group 1" = 1, "Group 2" = 2))
format(icer(cea_pw_out, labels = labs))
# Plots
plot_ceplane(cea_pw_out, label = labs)
plot_ceac(cea_out, label = labs)
plot_ceac(cea_pw_out, label = labs)
plot_ceaf(cea_out, label = labs)
plot_evpi(cea_out, label = labs)
```

CohortDtstm

Cohort discrete time state transition model

Description

Simulate outcomes from a cohort discrete time state transition model.

Format

An R6::R6Class object.

Public fields

```
trans_model The model for health state transitions. Must be an object of class CohortDtstmTrans.
utility_model The model for health state utility. Must be an object of class StateVals.
cost_models The models used to predict costs by health state. Must be a list of objects of class
    StateVals, where each element of the list represents a different cost category.
stateprobs_ An object of class stateprobs simulated using $sim_stateprobs().
qalys_ An object of class qalys simulated using $sim_qalys().
costs_ An object of class costs simulated using $sim_costs().
```

Methods

Public methods:

- CohortDtstm\$new()
- CohortDtstm\$sim_stateprobs()
- CohortDtstm\$sim_qalys()
- CohortDtstm\$sim_costs()
- CohortDtstm\$summarize()
- CohortDtstm\$clone()

Method new(): Create a new CohortDtstm object.

```
Usage:
CohortDtstm$new(trans_model = NULL, utility_model = NULL, cost_models = NULL)
Arguments:
trans_model The trans_model field.
utility_model The utility_model field.
cost_models The cost_models field.
Returns: A new CohortDtstm object.
```

Method sim_stateprobs(): Simulate health state probabilities using CohortDtstmTrans\$sim_stateprobs().

Usage:

CohortDtstm\$sim_stateprobs(n_cycles)

Arguments:

n_cycles The number of model cycles to simulate the model for.

Returns: An instance of self with simulated output of class stateprobs stored in stateprobs_.

Method sim_qalys(): Simulate quality-adjusted life-years (QALYs) as a function of stateprobs_ and utility_model. See sim_qalys() for details.

```
Usage:
```

```
CohortDtstm$sim_qalys(
   dr = 0.03,
   integrate_method = c("trapz", "riemann_left", "riemann_right"),
   lys = TRUE
)
```

Arguments:

dr Discount rate.

integrate_method Method used to integrate state values when computing costs or QALYs. Options are trapz for the trapezoid rule, riemann_left for a left Riemann sum, and riemann_right for a right Riemann sum.

lys If TRUE, then life-years are simulated in addition to QALYs.

Returns: An instance of self with simulated output of class galys stored in galys_.

Method sim_costs(): Simulate costs as a function of stateprobs_ and cost_models. See sim_costs() for details.

Usage:

```
CohortDtstm$sim_costs(
  dr = 0.03,
  integrate_method = c("trapz", "riemann_left", "riemann_right")
)
```

Arguments:

dr Discount rate.

integrate_method Method used to integrate state values when computing costs or QALYs. Options are trapz for the trapezoid rule, riemann_left for a left Riemann sum, and riemann_right for a right Riemann sum.

Returns: An instance of self with simulated output of class costs stored in costs_.

Method summarize(): Summarize costs and QALYs so that cost-effectiveness analysis can be performed. See summarize_ce().

Usage:

```
CohortDtstm$summarize(by_grp = FALSE)
```

Arguments:

by_grp If TRUE, then costs and QALYs are computed by subgroup. If FALSE, then costs and QALYs are aggregated across all patients (and subgroups).

Method clone(): The objects of this class are cloneable with this method.

Usage:

```
CohortDtstm$clone(deep = FALSE)
```

Arguments:

deep Whether to make a deep clone.

References

Incerti and Jansen (2021). See Section 2.1 for a description of a cohort DTSTM and details on simulating costs and QALYs from state probabilities. An example in oncology is provided in Section 4.3.

See Also

CohortDtstm objects can be created from model objects as documented in create_CohortDtstm(). The CohortDtstmTrans documentation describes the class for the transition model and the StateVals documentation describes the class for the cost and utility models. A CohortDtstmTrans object is typically created using create_CohortDtstmTrans().

There are currently three relevant vignettes. vignette("markov-cohort") details a relatively simple Markov model and vignette("markov-inhomogeneous-cohort") describes a more complex time inhomogeneous model in which transition probabilities vary in every model cycle. The vignette("mlogit") shows how a transition model can be parameterized using a multinomial logistic regression model when transition data is collected at evenly spaced intervals.

```
library("data.table")
library("ggplot2")
theme_set(theme_bw())
set.seed(102)
# NOTE: This example replicates the "Simple Markov cohort model"
# vignette using a different approach. Here, we explicitly construct
# the transition probabilities "by hand". In the vignette, the transition
# probabilities are defined using expressions (i.e., by using
# `define_model()`). The `define_model()` approach does (more or less) what
# is done here under the hood.
# (0) Model setup
hesim_dat <- hesim_data(</pre>
 strategies = data.table(
    strategy_id = 1:2,
   strategy_name = c("Monotherapy", "Combination therapy")
 ),
 patients <- data.table(patient_id = 1),</pre>
 states = data.table(
   state_id = 1:3,
    state_name = c("State A", "State B", "State C")
 )
)
n_states <- nrow(hesim_dat$states) + 1</pre>
labs <- get_labels(hesim_dat)</pre>
# (1) Parameters
n_samples <- 10 # Number of samples for PSA
## Transition matrix
### Input data (one transition matrix for each parameter sample,
```

```
treatment strategy, patient, and time interval)
p_id \leftarrow tpmatrix_id(expand(hesim_dat, times = c(0, 2)), n_samples)
N <- nrow(p_id)
### Transition matrices (one for each row in p_id)
p <- array(NA, dim = c(n_states, n_states, nrow(p_id)))</pre>
#### Baseline risk
trans_mono <- rbind(</pre>
  c(1251, 350, 116, 17),
  c(0, 731, 512, 15),
  c(0, 0, 1312, 437),
 c(0, 0, 0, 469)
mono_ind <- which(p_id$strategy_id == 1 | p_id$time_id == 2)</pre>
p[,, mono_ind] <- rdirichlet_mat(n = 2, trans_mono)</pre>
#### Apply relative risks
combo_ind <- setdiff(1:nrow(p_id), mono_ind)</pre>
lrr_se \leftarrow (log(.710) - log(.365))/(2 * qnorm(.975))
rr <- rlnorm(n_samples, meanlog = log(.509), sdlog = lrr_se)</pre>
rr_indices <- list( # Indices of transition matrix to apply RR to</pre>
  c(1, 2), c(1, 3), c(1, 4),
  c(2, 3), c(2, 4),
  c(3, 4)
rr_mat <- matrix(rr, nrow = n_samples, ncol = length(rr_indices))</pre>
p[,, combo_ind] <- apply_rr(p[, , mono_ind],</pre>
                              rr = rr_mat,
                              index = rr_indices)
tp <- tparams_transprobs(p, p_id)</pre>
## Utility
utility_tbl <- stateval_tbl(
  data.table(
    state_id = 1:3,
    est = c(1, 1, 1)
  ),
  dist = "fixed"
## Costs
drugcost_tbl <- stateval_tbl(</pre>
  data.table(
    strategy_id = c(1, 1, 2, 2),
    time_start = c(0, 2, 0, 2),
    est = c(2278, 2278, 2278 + 2086.50, 2278)
 ),
  dist = "fixed"
)
dmedcost_tbl <- stateval_tbl(</pre>
  data.table(
```

```
state_id = 1:3,
   mean = c(A = 1701, B = 1774, C = 6948),
   se = c(A = 1701, B = 1774, C = 6948)
 ),
 dist = "gamma"
)
cmedcost_tbl <- stateval_tbl(</pre>
 data.table(
   state_id = 1:3,
   mean = c(A = 1055, B = 1278, C = 2059),
   se = c(A = 1055, B = 1278, C = 2059)
 dist = "gamma"
)
# (2) Simulation
## Constructing the economic model
### Transition probabilities
transmod <- CohortDtstmTrans$new(params = tp)</pre>
### Utility
utilitymod <- create_StateVals(utility_tbl,</pre>
                                hesim_data = hesim_dat,
                                n = n_samples)
### Costs
drugcostmod <- create_StateVals(drugcost_tbl,</pre>
                                 hesim_data = hesim_dat,
                                 n = n_samples)
dmedcostmod <- create_StateVals(dmedcost_tbl,</pre>
                                 hesim_data = hesim_dat,
                                 n = n_samples)
cmedcostmod <- create_StateVals(cmedcost_tbl,</pre>
                                 hesim_data = hesim_dat,
                                 n = n_samples)
costmods <- list(drug = drugcostmod,</pre>
                 direct_medical = dmedcostmod,
                 community_medical = cmedcostmod)
### Economic model
econmod <- CohortDtstm$new(trans_model = transmod,</pre>
                            utility_model = utilitymod,
                            cost_models = costmods)
## Simulating outcomes
econmod$sim_stateprobs(n_cycles = 20)
autoplot(econmod$stateprobs_, ci = TRUE, ci_style = "ribbon",
         labels = labs)
econmod$sim_qalys(dr = 0, integrate_method = "riemann_right")
econmod$sim_costs(dr = 0.06, integrate_method = "riemann_right")
# (3) Decision analysis
```

20 CohortDtstmTrans

CohortDtstmTrans

Transitions for a cohort discrete time state transition model

Description

Simulate health state transitions in a cohort discrete time state transition model.

Format

An R6::R6Class object.

Public fields

params Parameters for simulating health state transitions. Supports objects of class tparams_transprobs or params_mlogit_list.

input_data An object of class input_mats.

cycle_length The length of a model cycle in terms of years. The default is 1 meaning that model cycles are 1 year long.

absorbing A numeric vector denoting the states that are absorbing states; i.e., states that cannot be transitioned from. Each element should correspond to a state_id, which should, in turn, be the index of the health state.

Active bindings

start_stateprobs A non-negative vector with length equal to the number of health states containing the probability that the cohort is in each health state at the start of the simulation. For example, if there were three states and the cohort began the simulation in state 1, then start_stateprobs = c(1, 0, 0). Automatically normalized to sum to 1. If NULL, then a vector with the first element equal to 1 and all remaining elements equal to 0.

trans_mat A transition matrix describing the states and transitions in a discrete-time multi-state model. Only required if the model is parameterized using multinomial logistic regression. The (i,j) element represents a transition from state i to state j. Each possible transition from row i should be based on a separate multinomial logistic regression and ordered from 0 to K - 1 where K is the number of possible transitions. Transitions that are not possible should be NA. and the reference category for each row should be 0.

CohortDtstmTrans 21

Methods

Public methods:

```
CohortDtstmTrans$new()
```

- CohortDtstmTrans\$sim_stateprobs()
- CohortDtstmTrans\$clone()

Method new(): Create a new CohortDtstmTrans object.

```
Usage:
CohortDtstmTrans$new(
  params,
  input_data = NULL,
  trans_mat = NULL,
  start_stateprobs = NULL,
  cycle_length = 1,
  absorbing = NULL
)
Arguments:
params The params field.
input_data The input_data field.
trans_mat The trans_mat field.
start_stateprobs The start_stateprobs field.
cycle_length The cycle_length field.
absorbing The absorbing field. If NULL, then the constructor will determine which states are
   absorbing automatically; non NULL values will override this behavior.
```

Returns: A new CohortDtstmTrans object.

Method sim_stateprobs(): Simulate probability of being in each health state during each model cycle.

```
Usage:
CohortDtstmTrans$sim_stateprobs(n_cycles)
n_cycles The number of model cycles to simulate the model for.
Returns: An object of class stateprobs.
```

Method clone(): The objects of this class are cloneable with this method.

```
Usage:
CohortDtstmTrans$clone(deep = FALSE)
Arguments:
deep Whether to make a deep clone.
```

See Also

create_CohortDtstmTrans() creates a CohortDtstmTrans object from either a fitted statistical model or a parameter object. A complete economic model can be implemented with the CohortDtstm class.

22 CohortDtstmTrans

```
library("msm")
library("data.table")
set.seed(101)
# We consider two examples that have the same treatment strategies and patients.
# One model is parameterized by fitting a multi-state model with the "msm"
# package; in the second model, the parameters are entered "manually" with
# a "params_mlogit_list" object.
# MODEL SETUP
strategies <- data.table(</pre>
  strategy_id = c(1, 2, 3),
  strategy_name = c("SOC", "New 1", "New 2")
patients <- data.table(patient_id = 1:2)</pre>
hesim_dat <- hesim_data(</pre>
  strategies = strategies,
  patients = patients
# EXAMPLE #1: msm
## Fit multi-state model with panel data via msm
qinit <- rbind(</pre>
 c(0, 0.28163, 0.01239),
 c(0, 0, 0.10204),
  c(0, 0, 0)
fit <- msm(state_id ~ time, subject = patient_id,</pre>
           data = onc3p[patient_id %in% sample(patient_id, 100)],
           covariates = list("1-2" =~ strategy_name),
           qmatrix = qinit)
## Simulation model
transmod_data <- expand(hesim_dat)</pre>
transmod <- create_CohortDtstmTrans(fit,</pre>
                                      input_data = transmod_data,
                                      cycle_length = 1/2,
                                      fixedpars = 2,
                                     n = 2
transmod$sim_stateprobs(n_cycles = 2)
# EXAMPLE #2: params_mlogit_list
## Input data
transmod_data[, intercept := 1]
transmod_data[, new1 := ifelse(strategy_name == "New 1", 1, 0)]
transmod_data[, new2 := ifelse(strategy_name == "New 2", 1, 0)]
## Parameters
n <- 10
transmod_params <- params_mlogit_list(</pre>
```

costs 23

```
## Transitions from stable state (stable -> progression, stable -> death)
 stable = params_mlogit(
   coefs = list(
      progression = data.frame(
       intercept = rnorm(n, -0.65, .1),
        new1 = rnorm(n, log(.8), .02),
       new2 = rnorm(n, log(.7, .02))
      ),
      death = data.frame(
        intercept = rnorm(n, -3.75, .1),
       new1 = rep(0, n),
       new2 = rep(0, n)
   )
 ),
 ## Transition from progression state (progression -> death)
 progression = params_mlogit(
   coefs = list(
      death = data.frame(
       intercept = rnorm(n, 2.45, .1),
       new1 = rep(0, n),
       new2 = rep(0, n)
   )
 )
)
transmod_params
## Simulation model
tmat \leftarrow rbind(c(0, 1, 2),
              c(NA, 0, 1),
              c(NA, NA, NA))
transmod <- create_CohortDtstmTrans(transmod_params,</pre>
                                     input_data = transmod_data,
                                     trans_mat = tmat, cycle_length = 1)
transmodsim_stateprobs(n_cycles = 2)
```

costs

Costs object

Description

An object of class costs returned from methods \$sim_costs() in model classes that store simulated costs.

24 create_CohortDtstm

Components

```
A costs object inherits from data. table and contains the following columns:
```

```
sample A random sample from the PSA.
strategy_id The treatment strategy ID.
patient_id The patient ID.
grp_id The subgroup ID.
state_id The health state ID.
dr The rate used to discount costs.
category The cost category (e.g., drug costs, medical costs, etc).
costs The simulated cost values.
```

create_CohortDtstm

Create CohortDtstm object

Description

A generic function for creating an object of class CohortDtstm.

Usage

```
create_CohortDtstm(object, ...)
## S3 method for class 'model_def'
create_CohortDtstm(
  object,
  input_data,
  cost_args = NULL,
  utility_args = NULL,
  ...
)
```

Arguments

object An object of the appropriate class.

... Further arguments passed to CohortDtstmTrans\$new() in CohortDtstmTrans.

input_data An object of class expanded_hesim_data.

cost_args A list of further arguments passed to StateVals\$new() in StateVals when

initiating cost models.

utility_args A list of further arguments passed to StateVals\$new() in StateVals when

initiating the utility model.

```
create\_CohortDtstmTrans
```

Create CohortDtstmTrans object

Description

A generic function for creating an object of class CohortDtstmTrans.

Usage

```
create_CohortDtstmTrans(object, ...)
## S3 method for class 'multinom_list'
create_CohortDtstmTrans(
  object,
  input_data,
  trans_mat,
 n = 1000,
 uncertainty = c("normal", "none"),
)
## S3 method for class 'msm'
create_CohortDtstmTrans(
 object,
  input_data,
  cycle_length,
  n = 1000,
 uncertainty = c("normal", "none"),
)
## S3 method for class 'params_mlogit_list'
create_CohortDtstmTrans(object, input_data, trans_mat, ...)
```

Arguments

object	An object of the appropriate class containing either a fitted statistical model or model parameters.
	Further arguments passed to CohortDtstmTrans\$new() in CohortDtstmTrans.
input_data	An object of class expanded_hesim_data returned by expand.hesim_data()
trans_mat	A transition matrix describing the states and transitions in a discrete-time multistate model. See CohortDtstmTrans.
n	Number of random observations to draw. Not used if uncertainty = "none".

uncertainty Method determining how parameter uncertainty should be handled. If "normal",

then parameters are randomly drawn from their multivariate normal distribution.

If "none", then only point estimates are returned.

model cycles are 1 year long.

Details

Disease models may either be created from a fitted statistical model or from a parameter object. In the case of the former, input_data is a data frame like object that is used to look for variables from the statistical model that are required for simulation. In this sense, input_data is very similar to the newdata argument in most predict() methods (e.g., see predict.lm()). In other words, variables used in the formula of the statistical model must also be in input_data.

In the case of the latter, the columns of input_data must be named in a manner that is consistent with the parameter object. In the typical case (e.g., with params_surv or params_mlogit), the parameter object contains coefficients from a regression model, usually stored as matrix where rows index parameter samples (i.e., for a probabilistic sensitivity analysis) and columns index model terms. In such instances, there must be one column from input_data with the same name as each model term in the coefficient matrix; that is, the columns in input_data are matched with the columns of the coefficient matrices by name. If there are model terms in the coefficient matrices that are not contained in input_data, then an error will be thrown.

See Also

See CohortDtstmTrans for examples.

```
create_IndivCtstmTrans
```

Create IndivCtstmTrans object

Description

A generic function for creating an object of class IndivCtstmTrans.

Usage

```
## S3 method for class 'flexsurvreg_list'
create_IndivCtstmTrans(
  object,
  input_data,
  trans_mat,
  clock = c("reset", "forward"),
  n = 1000,
  uncertainty = c("normal", "none"),
```

```
## S3 method for class 'flexsurvreg'
create_IndivCtstmTrans(
 object,
 input_data,
 trans_mat,
 clock = c("reset", "forward"),
 n = 1000,
 uncertainty = c("normal", "none"),
)
## S3 method for class 'params_surv'
create_IndivCtstmTrans(
 object,
 input_data,
  trans_mat,
 clock = c("reset", "forward", "mix", "mixt"),
 reset_states = NULL,
 transition_types = NULL,
)
## S3 method for class 'params_surv_list'
create_IndivCtstmTrans(
 object,
 input_data,
 trans_mat,
 clock = c("reset", "forward", "mix", "mixt"),
 reset_states = NULL,
  transition_types = NULL,
)
```

Arguments

object	An object of the appropriate class containing either a fitted multi-state model or parameters of a multi-state model.
	Further arguments passed to IndivCtstmTrans\$new() in IndivCtstmTrans.
input_data	An object of class expanded_hesim_data returned by expand.hesim_data.
trans_mat	The transition matrix describing the states and transitions in a multi-state model in the format from the mstate package. See IndivCtstmTrans.
clock	"reset" for a clock-reset model, "forward" for a clock-forward model, "mix" for a mixture by state, and "mixt" for a mixture by transition of clock-reset and clock-forward models. See the field clock in IndivCtstmTrans.
n	Number of random observations to draw. Not used if uncertainty = "none".

28 create_params

uncertainty Method determining how parameter uncertainty should be handled. If "normal",

then parameters are randomly drawn from their multivariate normal distribution.

If "none", then only point estimates are returned.

reset_states A vector denoting the states in which time resets. See the field reset_states

in IndivCtstmTrans.

transition_types

A vector denoting the type for each transition. See the field transition_types

in IndivCtstmTrans.

Details

Disease models may either be created from a fitted statistical model or from a parameter object. In the case of the former, input_data is a data frame like object that is used to look for variables from the statistical model that are required for simulation. In this sense, input_data is very similar to the newdata argument in most predict() methods (e.g., see predict.lm()). In other words, variables used in the formula of the statistical model must also be in input_data.

In the case of the latter, the columns of input_data must be named in a manner that is consistent with the parameter object. In the typical case (e.g., with params_surv or params_mlogit), the parameter object contains coefficients from a regression model, usually stored as matrix where rows index parameter samples (i.e., for a probabilistic sensitivity analysis) and columns index model terms. In such instances, there must be one column from input_data with the same name as each model term in the coefficient matrix; that is, the columns in input_data are matched with the columns of the coefficient matrices by name. If there are model terms in the coefficient matrices that are not contained in input_data, then an error will be thrown.

Value

Returns an R6::R6Class object of class IndivCtstmTrans.

See Also

See IndivCtstmTrans and IndivCtstm for examples.

create_params

Create a parameter object from a fitted model

Description

create_params is a generic function for creating an object containing parameters from a fitted statistical model. If uncertainty != "none", then random samples from suitable probability distributions are returned.

create_params 29

Usage

```
create_params(object, ...)
## S3 method for class 'lm'
create_params(object, n = 1000, uncertainty = c("normal", "none"), ...)
## S3 method for class 'multinom'
create_params(object, n = 1000, uncertainty = c("normal", "none"), ...)
## S3 method for class 'multinom_list'
create_params(object, n = 1000, uncertainty = c("normal", "none"), ...)
## S3 method for class 'flexsurvreg'
create_params(object, n = 1000, uncertainty = c("normal", "none"), ...)
## S3 method for class 'flexsurvreg_list'
create_params(object, n = 1000, uncertainty = c("normal", "none"), ...)
## S3 method for class 'partsurvfit'
create_params(
 object,
 n = 1000,
 uncertainty = c("normal", "bootstrap", "none"),
 max\_errors = 0,
 silent = FALSE,
)
```

Arguments

object	A statistical model to randomly sample parameters from.
	Currently unused.
n	Number of random observations to draw. Not used if uncertainty = "none".
uncertainty	Method determining how parameter uncertainty should be handled. If "normal", then parameters are randomly drawn from their multivariate normal distribution. If "bootstrap", then parameters are bootstrapped using bootstrap. If "none", then only point estimates are returned.
max_errors	Maximum number of errors that are allowed when fitting statistical models during the bootstrap procedure. This argument may be useful if, for instance, the model fails to converge during some bootstrap replications. Default is 0.
silent	Logical indicating whether error messages should be suppressed. Passed to the silent argument of try().

Value

An object prefixed by params_. Mapping between create_params and the classes of the returned objects are:

30 create_PsmCurves

```
    create_params.lm -> params_lm
    create_params.multinom -> params_mlogit
    create_params.multinom_list -> params_mlogit_list
    create_params.flexsurvreg -> params_surv
    create_params.flexsurvreg_list -> params_surv_list
    create_params.partsurvfit -> params_surv_list
```

See Also

These methods are typically used alongside <code>create_input_mats()</code> to create model objects as a function of input data and a fitted statistical model. For instance, <code>create_PsmCurves()</code> creates the survival model for a partitioned survival model, <code>create_IndivCtstmTrans()</code> creates the transition model for an individual continuous time state transition model, <code>create_CohortDtstmTrans()</code> creates the transition model for a cohort discrete time state transition model, and <code>create_StateVals()</code> creates a health state values model.

Examples

create_PsmCurves

Create PsmCurves object

Description

A generic function for creating a PsmCurves object.

Usage

```
create_PsmCurves(object, ...)
## S3 method for class 'flexsurvreg_list'
create_PsmCurves(
```

create_PsmCurves 31

```
object,
input_data,
n = 1000,
uncertainty = c("normal", "bootstrap", "none"),
est_data = NULL,
...
)

## S3 method for class 'params_surv_list'
create_PsmCurves(object, input_data, ...)
```

Arguments

object	An object of the appropriate class containing either fitted survival models or parameters of survival models.
• • •	Further arguments passed to or from other methods. Passed to create_params.partsurvfit() when object is of class flexsurvreg_list.
input_data	An object of class expanded_hesim_data returned by expand.hesim_data(). Must be expanded by the data tables "strategies" and "patients".
n	Number of random observations to draw. Not used if uncertainty = "none".
uncertainty	Method determining how parameter uncertainty should be handled. If "normal", then parameters are randomly drawn from their multivariate normal distribution. If "bootstrap", then parameters are bootstrapped using bootstrap. If "none", then only point estimates are returned.
est_data	A data.table or data.frame of estimation data used to fit survival models during bootstrap replications.

Details

Disease models may either be created from a fitted statistical model or from a parameter object. In the case of the former, input_data is a data frame like object that is used to look for variables from the statistical model that are required for simulation. In this sense, input_data is very similar to the newdata argument in most predict() methods (e.g., see predict.lm()). In other words, variables used in the formula of the statistical model must also be in input_data.

In the case of the latter, the columns of input_data must be named in a manner that is consistent with the parameter object. In the typical case (e.g., with params_surv or params_mlogit), the parameter object contains coefficients from a regression model, usually stored as matrix where rows index parameter samples (i.e., for a probabilistic sensitivity analysis) and columns index model terms. In such instances, there must be one column from input_data with the same name as each model term in the coefficient matrix; that is, the columns in input_data are matched with the columns of the coefficient matrices by name. If there are model terms in the coefficient matrices that are not contained in input_data, then an error will be thrown.

Value

Returns an R6Class object of class PsmCurves.

32 create_StateVals

See Also

See PsmCurves and Psm for examples. PsmCurves provides an example in which a model is parameterized both with (via create_PsmCurves.flexsurvreg_list()) and without (via create_PsmCurves.params_surv_list access to patient-level data. The Psm example shows how state probabilities, costs, and utilities can be computed from predicted survival curves.

create_StateVals

Create a StateVals object

Description

create_StateVals() is a generic function for creating an object of class StateVals from a fitted statistical model or a stateval_tbl object.

Usage

```
create_StateVals(object, ...)

## S3 method for class 'lm'
create_StateVals(
  object,
  input_data = NULL,
  n = 1000,
  uncertainty = c("normal", "none"),
  ...
)

## S3 method for class 'stateval_tbl'
create_StateVals(object, hesim_data = NULL, n = 1000, ...)
```

Arguments

object	A model object of the appropriate class.
	Further arguments (time_reset and method) passed to StateVals\$new().
input_data	An object of class <code>expanded_hesim_data</code> . Must be expanded by treatment strategies, patients, and health states.
n	Number of random observations of the parameters to draw when parameters are fit using a statistical model.
uncertainty	Method determining how parameter uncertainty should be handled. See documentation in create_params().
hesim_data	A hesim_data object. Only required when object is of class stateval_tbl. See "details".

create_StateVals 33

Details

If object is a stateval_tbl, then a hesim_data object is used to specify treatment strategies, patients, and/or health states not included as columns in the table, or, to match patients in the table to groups. Not required if the table includes one row for each treatment strategy, patient, and health state combination. Patients are matched to groups by specifying both a patient_id and a grp_var column in the patients table.

Value

A StateVals object.

See Also

See StateVals for documentation of the class and additional examples. An example use case for create_StateVals.stateval_tbl() is provided in the stateval_tbl() documentation.

```
set.seed(10)
# EXAMPLE FOR `create_statevals.lm()`
## Simple example comparing two treatment strategies where
## medical costs vary by sex and health state
## Setup model
hesim_dat <- hesim_data(</pre>
  strategies = data.frame(strategy_id = c(1, 2)),
  patients = data.frame(
    patient_id = c(1, 2),
    female = c(1, 0)
  states = data.frame(
    state_id = c(1, 2, 3),
    state_name = c("state1", "state2", "state3")
  )
)
## Fit model
medcost_estimation_data <- psm4_exdata$costs$medical</pre>
medcost_estimation_data$time5 <- rbinom(nrow(medcost_estimation_data),</pre>
                                          1, .5) # Illustrative time dummy
medcost_fit <- lm(costs ~ female + state_name + time5,</pre>
                   data = medcost_estimation_data)
## Create medical cost model
### Allow medical costs to vary across time in addition to by patient and
### health state
medcost_times <- time_intervals(</pre>
  data.frame(time_start = c(0, 3, 5),
            time5 = c(0, 0, 1)) # Time dummy corresponds to time > 5
)
```

34 create_trans_dt

create_trans_dt

Create a data table of health state transitions

Description

Create a data table of health state transitions from a transition matrix describing the states and transitions in a multi-state model suitable for use with hesim_data.

Usage

```
create_trans_dt(trans_mat)
```

Arguments

trans_mat

A transition matrix in the format from the mstate package. See IndivCtstmTrans.

Value

Returns a data.table::data.table in tidy format with three columns:

transition_id Health state transition ID.

from The starting health state.

to The health state that will be transitions to.

define_model 35

define_model	Define and evaluate model expression	

Description

A model expression is defined by specifying random number generation functions for a probabilistic sensitivity analysis (PSA) and transformations of the sampled parameters as a function of input_data. The unevaluated expressions are evaluated with eval_model() and used to generate the model inputs needed to create an economic model.

Usage

```
define_model(tparams_def, rng_def, params = NULL, n_states = NULL)
eval_model(x, input_data)
```

Arguments

tparams_def	A tparams_def object or a list of tparams_def objects. A list might be considered if time intervals specified with the times argument in define_tparams() vary across parameters. Parameters for a transition probability matrix (tpmatrix), utilities (utility), and/or cost categories (costs) are returned as a named list (see define_tparams() for more details).
rng_def	A rng_def object used to randomly draw samples of the parameters from suitable probability distributions.
params	Either (i) a list containing the values of parameters for random number generation or (ii) parameter samples that have already been randomly generated using eval_rng(). In case (ii), rng_def should be NULL.
n_states	The number of health states (inclusive of all health states including the the death state) in the model. If tpmatrix is an element returned by tparams_def, then it will be equal to the number of states in the transition probability matrix; otherwise it must be specified as an argument.
x	An object of class model_def created with define_model().
input_data	An object of class expanded_hesim_data expanded by patients and treatment strategies.

Details

eval_model() evaluates the expressions in an object of class model_def returned by define_model() and is, in turn, used within functions that instantiate economic models (e.g., create_CohortDtstm()). The direct output of eval_model() can also be useful for understanding and debugging model definitions, but it is not used directly for simulation.

Economic models are constructed as a function of input data and parameters:

1. *Input data*: Objects of class expanded_hesim_data consisting of the treatment strategies and patient population.

36 define_model

2. Parameters: The underlying parameter estimates from the literature are first stored in a list (params argument). Random number generation is then used to sample the parameters from suitable probability distributions for the PSA (rng_def argument). Finally, the sampled parameters are transformed as a function of the input data into values (e.g., elements of a transition probability matrix) used for the simulation (tparams_def argument). The params argument can be omitted if the underlying parameters values are defined inside a define_rng() block.

Value

define_model() returns an object of class model_def, which is a list containing the arguments to the function. eval_model() returns a list containing ID variables identifying parameter samples, treatment strategies, patient cohorts, and time intervals; the values of parameters of the transition probability matrix, utilities, and/or cost categories; the number of health states; and the number of random number generation samples for the PSA.

See Also

```
define_tparams(), define_rng()
```

```
# Data
library("data.table")
strategies <- data.table(strategy_id = 1:2,</pre>
                          strategy_name = c("Monotherapy", "Combination therapy"))
patients <- data.table(patient_id = 1)</pre>
hesim_dat <- hesim_data(strategies = strategies,</pre>
                        patients = patients)
data <- expand(hesim_dat)</pre>
# Model parameters
rng_def <- define_rng({</pre>
  alpha <- matrix(c(1251, 350, 116, 17,
                     0, 731, 512, 15,
                     0, 0, 1312, 437,
                     0, 0, 0, 469),
                   nrow = 4, byrow = TRUE)
  \label{eq:condition} \mbox{rownames(alpha) <- c("A", "B", "C", "D")}
  lrr_mean <- log(.509)
  lrr_se \leftarrow (log(.710) - log(.365))/(2 * qnorm(.975))
  list(
    p_mono = dirichlet_rng(alpha),
    rr_comb = lognormal_rng(lrr_mean, lrr_se),
    u = 1,
    c_zido = 2278,
    c_{1am} = 2086.50,
    c_med = gamma_rng(mean = c(A = 2756, B = 3052, C = 9007),
                       sd = c(A = 2756, B = 3052, C = 9007))
, n = 2
```

define_rng 37

```
tparams_def <- define_tparams({</pre>
 rr = ifelse(strategy_name == "Monotherapy", 1, rr_comb)
 list(
    tpmatrix = tpmatrix(
      C, p_mono$A_B * rr, p_mono$A_C * rr, p_mono$A_D * rr,
      0, C, p_mono$B_C * rr, p_mono$B_D * rr,
      0, 0, C, p_mono$C_D * rr,
      0, 0, 0, 1),
   utility = u,
    costs = list(
      drug = ifelse(strategy_name == "Monotherapy",
                    c_zido, c_zido + c_lam),
      medical = c_med
 )
})
# Simulation
## Define the economic model
model_def <- define_model(</pre>
 tparams_def = tparams_def,
 rng_def = rng_def)
### Evaluate the model expression to generate model inputs
### This can be useful for understanding the output of a model expression
eval_model(model_def, data)
## Create an economic model with a factory function
econmod <- create_CohortDtstm(model_def, data)</pre>
```

define_rng

Define and evaluate random number generation expressions

Description

Random number generation expressions are used to randomly sample model parameters from suitable distributions for probabilistic sensitivity analysis. These functions are typically used when evaluating an object of class model_def defined using define_model().

Usage

```
define_rng(expr, n = 1, ...)
eval_rng(x, params = NULL, check = TRUE)
```

38 define_rng

Arguments

expr	An expression used to randomly draw variates for each parameter of interest in the model. Braces should be used so that the result of the last expression within the braces is evaluated. The expression must return a list where each element is either a vector or tabular object (matrix, data.frame, or data.table). The length of the vector must either be or n and the number of rows in the tabular object must be n.
n	Number of samples of the parameters to draw.
	Additional arguments to pass to the environment used to evaluate expr.
X	An object of class rng_def created with define_rng().
params	A list containing the values of parameters for random number generation. Each element of the list should either be a vector, matrix, data.frame, or data.table
check	Whether to check the returned output so that (i) it returns a list and (ii) each element has the correct length or number of rows. Default is TRUE, meaning that any output can be returned. This is always TRUE when used inside define_model().

Details

hesim contains a number of random number generation functions that return parameter samples in convenient formats and do not typically require the number of samples, n, as arguments (see rng_distributions). The random number generation expressions are evaluated using eval_rng() and used within expr in define_rng(). If a multivariate object is returned by eval_rng(), then the rows are random samples and columns are distinct parameters (e.g., costs for each health state, elements of a transition probability matrix).

Value

define_rng() returns an object of class rng_def, which is a list containing the unevaluated random number generation expressions passed to expr, n, and any additional arguments passed to ... eval_rng() evaluates the rng_def object and returns an eval_rng object containing the evaluated expression.

See Also

Parameters can be conveniently sampled from probability distributions using a number of random number generation functions (see rng_distributions). An economic model can be created with create_CohortDtstm() by using define_rng() (or a previously evaluated eval_rng object) alongside define_tparams() to define a model with define_model(). It can be useful to summarize an evaluated expression with summary.eval_rng().

define_tparams 39

```
rng_def <- define_rng({</pre>
 aecost_mean <- c(500, 800, 1000) # Local object not
                                    # not returned by eval_rng()
 list( # Sampled values of parameters returned by eval_rng()
    p = dirichlet_rng(alpha), # Default column names
    inptcost = gamma_rng(mean = inptcost_mean, # Column names based on
                         sd = inptcost_mean), # named vector
    outptcost = outptcost_mean, # No column names because
                                 # outptcost_mean has none.
    aecost = gamma_rng(mean = aecost_mean, # Explicit naming of columns
                       sd = aecost_mean,
                       names = aecost_colnames)
}, n = 2, aecost\_colnames = c("A", "B", "C")) # Add <math>aecost\_colnames to environment
params_sample <- eval_rng(x = rng_def, params)</pre>
summary(params_sample)
params_sample
```

define_tparams

Define and evaluate transformed parameter expressions

Description

Transformed parameter expressions are used to transform the parameter values sampled with eval_rng() as a function of input data (treatment strategies and patients) and time intervals. These functions are used when evaluating an object of class model_def defined using define_model(). The transformed parameters are ultimately converted into tparams objects and used to simulate outcomes with an economic model.

Usage

```
define_tparams(expr, times = NULL, ...)
eval_tparams(x, input_data, rng_params)
```

Arguments

expr

Expressions used to transform parameters. As with define_rng(), braces should be used so that the result of the last expression within the braces is evaluated. The expression must return a named list with the following possible elements:

- *tpmatrix*: The transition probability matrix used to simulate transition probabilities in the economic model. This should either be the output of tpmatrix() or a 3-dimensional array as in tparams_transprobs().
- *utility*: The utility values to attach to states and used to simulate quality-adjusted life-years in the economic model. Either a vector (in which case utility is the same in each health state) or a data.table/data.frame/matrix with a column for each (non-death) health state.

40 disprog

• *costs*: A named list of costs for each category used to simulate costs in the economic model. Each element of the list must be in the same format as utility.

times Distinct times denoting the stopping time of time intervals.

... Additional arguments to pass to the environment used to evaluate expr.

x An object of class tparams_def.

input_data An object of class expanded_hesim_data (as in eval_model()) expanded by the

distinct times in times.

rng_params Random samples of the parameters returned by eval_rng().

Details

define_tparams() is evaluated when creating economic models as a function of model_def objects defined with define_model(). Operations are "vectorized" in the sense that they are performed for each unique combination of input_data and params. expr is evaluated in an environment including each variable from input_data, all elements of rng_params, and a variable time containing the values from times. The time variable can be used to create models where parameters vary as a function of time. eval_tparams() is not exported and is only meant for use within eval_model().

Value

define_tparams() returns an object of class tparams_def, which is a list containing the unevaluated "transformation" expressions passed to expr, times, and any additional arguments passed to eval_tparams() evaluates the tparams_def object and should return a list of transformed parameter objects.

See Also

```
define_model(), define_rng()
```

disprog

Disease progression object

Description

An object of class disprog returned from methods \$sim_disease() in model classes. It contains simulated trajectories through a multi-state model.

Components

A disprog object inherits from data. table and contains the following columns:

sample A random sample from the PSA.

strategy_id The treatment strategy ID.

patient_id The patient ID.

expand.hesim_data 41

from The health state ID transitioned from.

to The health state ID transitioned to.

final An indicator equal to 1 if a patient is in their final health state during the simulation and 0 otherwise.

time_start The time at the start of the interval.

time_stop The time at the end of the interval.

The object also contains size and absorbing attributes. The size attribute is a numeric vector with the elements n_samples, n_strategies, n_patients, and n_states denoting the number of samples, treatment strategies, patients, and health states The absorbing attribute is a numeric vector containing the absorbing health states; i.e., the health states that cannot be transitioned from. Operationally, an absorbing state is a row in a transition matrix (as in the trans_mat field of the IndivCtstmTrans class) with all NAs.

See Also

A disease progression object can be simulated with either the IndivCtstm or IndivCtstmTrans classes.

expand.hesim_data

Expand hesim_data

Description

Create a data table in long format from all combinations of specified tables from an object of class hesim_data and optionally time intervals. See "Details" for an explanation of how the expansion is done.

Usage

```
## S3 method for class 'hesim_data'
expand(object, by = c("strategies", "patients"), times = NULL)
```

Arguments

object An object of class hesim_data.

by A character vector of the names of the data tables in hesim_data to expand by.

times Either a numeric vector of distinct times denoting the start of time intervals or a

time_intervals object.

Details

This function is similar to expand.grid(), but works for data frames or data tables. Specifically, it creates a data.table from all combinations of the supplied tables in object and optionally the start of times intervals in times. The supplied tables are determined using the by argument. The resulting dataset is sorted by prioritizing ID variables as follows: (i) strategy_id, (ii) patient_id, (iii) the health-related ID variable (either state_id or transition_id, and (iv) the time intervals from times.

42 expmat

Value

An object of class expanded_hesim_data, which is a data.table with an "id_vars" attribute containing the names of the ID variables in the data table and, if times is not NULL, a time_intervals object derived from times.

Examples

expmat

Matrix exponential

Description

This is a wrapper around msm::MatrixExp() that computes the exponential of multiple square matrices.

Usage

```
expmat(x, t = 1, ...)
```

Arguments

x An array of matrices.

t An optional scaling factor for x.

... Arguments to pass to msm::MatrixExp().

Details

This function is most useful when exponentiating transition intensity matrices to produce transition probability matrices. To create transition probability matrices for discrete time state transition models with annual cycles, set t=1. An array of matrices is returned which can be used to create the value element of a tparams_transprobs object. See qmatrix() for an example.

Value

Returns an array of exponentiated matrices. If length(t) > 1, then length(t) arrays are returned for each element in x.

fast_rgengamma 43

See Also

```
qmatrix.msm(), qmatrix.data.table()
```

fast_rgengamma

Random generation for generalized gamma distribution

Description

Draw random samples from a generalized gamma distribution using the parameterization from flexsurv. Written in C++ for speed. Equivalent to flexsurv::rgengamma.

Usage

```
fast\_rgengamma(n, mu = 0, sigma = 1, Q)
```

Arguments

Number of random observations to draw.
 Vector of location parameters. and columns correspond to rates during specified time intervals.
 Vector of scale parameters as described in flexsurv.

Q Vector of shape parameters.

Value

A vector of random samples from the generalized gamma distribution. The length of the sample is determined by n. The numerical arguments other than n are recycled so that the number of samples is equal to n.

```
n <- 1000
m <- 2; s <- 1.7; q <- 1
ptm <- proc.time()
r1 <- fast_rgengamma(n, mu = m, sigma = s, Q = q)
proc.time() - ptm
ptm <- proc.time()
library("flexsurv")
r2 <- flexsurv::rgengamma(n, mu = m, sigma = s, Q = q)
proc.time() - ptm
summary(r1)
summary(r2)</pre>
```

get_labels

flexsurvreg_list

List of flexsurvreg objects

Description

Combine flexsurvreg objects into a list.

Usage

```
flexsurvreg_list(...)
```

Arguments

... Objects of class flexsurvreg, which can be named.

Value

An object of class flexsurvreg_list.

Examples

```
library("flexsurv")
fit1 <- flexsurv::flexsurvreg(formula = Surv(futime, fustat) ~ 1, data = ovarian, dist = "weibull")
fit2 <- flexsurv::flexsurvreg(formula = Surv(futime, fustat) ~ 1, data = ovarian, dist = "exp")
fsreg_list <- flexsurvreg_list(wei = fit1, exp = fit2)
class(fsreg_list)</pre>
```

get_labels

Get value labels

Description

Get value labels for the ID variables in a hesim_data object and create a list of named vectors that can be passed to formatting and plotting functions. This lets users create nice labels for treatment strategies, subgroups, health states, and/or transitions when presenting results.

Usage

```
get_labels(
  object,
  strategy = "strategy_name",
  grp = "grp_name",
  state = "state_name",
  transition = "transition_name",
  death_label = "Death"
)
```

get_labels 45

Arguments

object	An object of class hesim_data created with hesim_data().
strategy	The name of the column in the strategy element of object containing labels for strategy_id.
grp	The name of the column in the patient element of object containing labels for grp_id.
state	The name of the column in the state element of object containing labels for state_id.
transition	The name of the column in the transition element of object containing labels for transition_id.
death_label	The label to use for the death health state. By default a label named "Death" will be concatenated to the labels for the non-death health states. The death state can be omitted from labels for the health states by setting death_label = NULL.

Value

A list of named vectors containing the values and labels of variables. The elements of each vector are the values of a variable and the names are the labels. The names of the list are the names of the ID variables.

See Also

```
hesim_data(), set_labels()
```

```
library("data.table")
strategies <- data.table(</pre>
  strategy_id = c(1, 2),
  strategy_name = c("Strategy 1", "Strategy 2")
patients <- data.table(</pre>
  patient_id = seq(1, 4),
  age = c(50, 55, 60, 65),
  grp_id = c(1, 1, 2, 2),
  grp_name = rep(c("Age 50-59", "Age 60-69"), each = 2)
states <- data.table(</pre>
  state_id = seq(1, 2),
  state_name = c("State 1", "State 2")
)
hesim_dat <- hesim_data(</pre>
  strategies = strategies,
  patients = patients,
  states = states
labs <- get_labels(hesim_dat)</pre>
labs
```

46 hesim_data

hesim_data

Data for health economic simulation modeling

Description

A list of tables required for health economic simulation modeling. This object is used to setup models by defining the treatment strategies, target population, and model structure.

Usage

```
hesim_data(strategies, patients, states = NULL, transitions = NULL)
```

Arguments

strategies

A table of treatment strategies. Must contain the column strategy_id denoting a unique strategy. Other columns are variables describing the characteristics of a treatment strategy.

patients

A table of patients. Must contain the column patient_id denoting a unique patient. The number of rows should be equal to the number of patients in the model. The table may also include columns for grp_id for subgroups and patient_wt specifying the weight to apply to each patient (within a subgroup). If grp_id is NULL, then it is assumed that there is only one subgroup. If patient_wt is NULL, then each patient is given the same weight. Weights cannot be used in individual-level models because each patient should be weighted equally; that is, weights can only be specified in cohort models. Weights within subgroups are normalized to sum to one. Other columns are variables describing the characteristics of a patient.

states

A table of health states. Must contain the column state_id, which denotes a unique health state. The number of rows should be equal to the number of health states in the model. Other columns can describe the characteristics of a health state.

transitions

A table of health state transitions. Must contain the column transition_id, which denotes a unique transition; from, which denotes the starting health state; and to which denotes the state that will be transitioned to.

Value

Returns an object of class hesim_data, which is a list of data tables for health economic simulation modeling.

icer 47

Note

Each table must either be a data.frame or data.table. All ID variables within each table must be numeric vectors of integers and should be of the form 1,2,...N where N is the number of unique values of the ID variable.

See Also

```
expand.hesim_data(), get_labels()
```

Examples

icer

Incremental cost-effectiveness ratio

Description

Generate a tidy table of incremental cost-effectiveness ratios (ICERs) given output from cea_pw() with icer() and format for pretty printing with format.icer().

Usage

```
icer(x, prob = 0.95, k = 50000, labels = NULL, ...)
## S3 method for class 'icer'
format(
    x,
    digits_qalys = 2,
    digits_costs = 0,
    pivot_from = "strategy",
    drop_grp = TRUE,
    pretty_names = TRUE,
    ...
)
```

48 icer

Arguments

x An object of class cea_pw returned by cea_pw().

prob A numeric scalar in the interval (0,1) giving the confidence interval. Default is

0.95 for a 95 percent interval.

k Willingness to pay per quality-adjusted life-year.

labels A list of named vectors containing the values and labels of variables. The ele-

ments of each vector are the values of a variable and the names are the labels. The names of the list are the names of the variables. See the output returned by

get_labels() for an example.

... Further arguments passed to and from methods. Currently unused.

digits_qalys Number of digits to use to report QALYs. digits_costs Number of digits to use to report costs.

pivot_from Character vector denoting a column or columns used to "widen" the data. Should

either be "strategy", "grp", "outcome", or some combination of the three. There will be one column for each value of the variables in pivot_from. Default is to widen so there is a column for each treatment strategy. Set to NULL if you

do not want to widen the table.

drop_grp If TRUE, then the group column will be removed if there is only one subgroup;

other it will be kept. If FALSE, then the grp column is never removed.

pretty_names Logical. If TRUE, then the columns strategy, grp, outcome, and value are

renamed (if they exist) to Strategy, Group, Outcome, and Value.

Details

Note that icer() will report negative ICERs; however, format() will correctly note whether a treatment strategy is dominated by or dominates the reference treatment.

Value

icer() returns an object of class icer that is a tidy data. table with the following columns:

strategy The treatment strategy.

grp The subgroup.

outcome The outcome metric.

estimate The point estimate computed as the average across the PSA samples.

lower The lower limit of the confidence interval.

upper The upper limit of the confidence interval.

format.icer() formats the table according to the arguments passed.

See Also

cea_pw()

incr_effect 49

incr_effect	Incremental treatment effect	

Description

Computes incremental effect for all treatment strategies on outcome variables from a probabilistic sensitivity analysis relative to a comparator.

Usage

```
incr_effect(x, comparator, sample, strategy, grp = NULL, outcomes)
```

Arguments

Х	A data. frame or data. table containing simulation output with information on outcome variables for each randomly sampled parameter set from a PSA. Each row should denote a randomly sampled parameter set and treatment strategy.
comparator	The comparator strategy. If the strategy column is a character variable, then must be a character; if the strategy column is an integer variable, then must be an integer.
sample	Character name of column denoting a randomly sampled parameter set.
strategy	Character name of column denoting treatment strategy.
grp	Character name of column denoting subgroup. If NULL, then it is assumed that there is only one group.
outcomes	Name of columns to compute incremental changes for.

Value

A data.table containing the differences in the values of each variable specified in outcomes between each treatment strategy and the comparator.

```
strategy = "strategy", grp = "grp", outcomes = c("c", "e"))
head(ie)
```

IndivCtstm

Individual-level continuous time state transition model

Description

Simulate outcomes from an individual-level continuous time state transition model (CTSTM). The class supports "clock-reset" (i.e., semi-Markov), "clock-forward" (i.e., Markov), and mixtures of clock-reset and clock-forward multi-state models as described in IndivCtstmTrans.

Format

An R6::R6Class object.

Public fields

```
trans_model The model for health state transitions. Must be an object of class IndivCtstmTrans.
utility_model The model for health state utility. Must be an object of class StateVals.
cost_models The models used to predict costs by health state. Must be a list of objects of class
    StateVals, where each element of the list represents a different cost category.
disprog_ An object of class disprog.
stateprobs_ An object of class stateprobs simulated using $sim_stateprobs().
qalys_ An object of class qalys simulated using $sim_qalys().
costs_ An object of class costs simulated using $sim_costs().
```

Methods

Public methods:

- IndivCtstm\$new()
- IndivCtstm\$sim_disease()
- IndivCtstm\$sim_stateprobs()
- IndivCtstm\$sim_qalys()
- IndivCtstm\$sim_costs()
- IndivCtstm\$summarize()
- IndivCtstm\$clone()

Method new(): Create a new IndivCtstm object.

```
Usage:
IndivCtstm$new(trans_model = NULL, utility_model = NULL, cost_models = NULL)
Arguments:
trans_model The trans_model field.
utility_model The utility_model field.
```

```
cost_models The cost_models field.
```

Returns: A new IndivCtstm object.

Method sim_disease(): Simulate disease progression (i.e., individual trajectories through a multi-state model) using IndivCtstmTrans\$sim_disease().

Usage:

```
IndivCtstm$sim_disease(max_t = 100, max_age = 100, progress = NULL)
```

Arguments:

max_t A scalar or vector denoting the length of time to simulate the model. If a vector, must be equal to the number of simulated patients.

max_age A scalar or vector denoting the maximum age to simulate each patient until. If a vector, must be equal to the number of simulated patients.

progress An integer, specifying the PSA iteration (i.e., sample) that should be printed every progress PSA iterations. For example, if progress = 2, then every second PSA iteration is printed. Default is NULL, in which case no output is printed.

Returns: An instance of self with simulated output stored in disprog_.

Method sim_stateprobs(): Simulate health state probabilities as a function of time using the simulation output stored in disprog.

Usage:

IndivCtstm\$sim_stateprobs(t)

Arguments:

t A numeric vector of times.

Returns: An instance of self with simulated output of class stateprobs stored in stateprobs_.

Method sim_qalys(): Simulate quality-adjusted life-years (QALYs) as a function of disprog_ and utility_model.

```
Usage:
```

```
IndivCtstm$sim_qalys(
  dr = 0.03,
  type = c("predict", "random"),
  lys = TRUE,
  by_patient = FALSE
)
```

Arguments:

dr Discount rate.

type "predict" for mean values or "random" for random samples as in \$sim() in StateVals. lys If TRUE, then life-years are simulated in addition to QALYs.

by_patient If TRUE, then QALYs and/or costs are computed at the patient level. If FALSE, then they are averaged across patients by health state.

Returns: An instance of self with simulated output of class galys stored in galys_.

Method sim_costs(): Simulate costs as a function of disprog_ and cost_models.

```
Usage:
IndivCtstm$sim_costs(
   dr = 0.03,
   type = c("predict", "random"),
   by_patient = FALSE,
   max_t = Inf
)
Arguments:
```

dr Discount rate.

type "predict" for mean values or "random" for random samples as in \$sim() in StateVals. by_patient If TRUE, then QALYs and/or costs are computed at the patient level. If FALSE, then they are averaged across patients by health state.

max_t Maximum time duration to compute costs once a patient has entered a (new) health state. By default, equal to Inf, so that costs are computed over the entire duration that a patient is in a given health state. If time varies by each cost category, then time can also be passed as a numeric vector of length equal to the number of cost categories (e.g., c(1, 2, Inf, 3) for a model with four cost categories).

Returns: An instance of self with simulated output of class costs stored in costs_.

Method summarize(): Summarize costs and QALYs so that cost-effectiveness analysis can be performed. See summarize_ce().

```
Usage:
IndivCtstm$summarize(by_grp = FALSE)
Arguments:
```

by_grp If TRUE, then costs and QALYs are computed by subgroup. If FALSE, then costs and QALYs are aggregated across all patients (and subgroups).

Method clone(): The objects of this class are cloneable with this method.

```
Usage:
IndivCtstm$clone(deep = FALSE)
Arguments:
deep Whether to make a deep clone.
```

References

Incerti and Jansen (2021). See Section 2.2 for a mathematical description of an individual-level CTSTM and Section 4.1 for an example in oncology.

See Also

The IndivCtstmTrans documentation describes the class for the transition model and the StateVals documentation describes the class for the cost and utility models. An IndivCtstmTrans object is typically created using create_IndivCtstmTrans().

There are currently two relevant vignettes. vignette("mstate") shows how to parameterize IndivCtstmTrans objects in cases where patient-level data is available by fitting a multi-state models. vignette("markov-inhomogeneous-indiv") shows how the time inhomogeneous Markov

cohort model in vignette("markov-inhomogeneous-cohort") can be developed as an individual patient simulation; in doing so, it shows how IndivCtstm models can be used even without access to patient-level data.

```
library("flexsurv")
# Treatment strategies, target population, and model structure
strategies <- data.frame(strategy_id = c(1, 2))</pre>
patients <- data.frame(patient_id = seq(1, 3),</pre>
                        age = c(45, 50, 60),
                        female = c(0, 0, 1)
states <- data.frame(state_id = c(1, 2))
hesim_dat <- hesim_data(strategies = strategies,</pre>
                         patients = patients,
                         states = states)
# Parameter estimation
## Multi-state model
tmat <- rbind(c(NA, 1, 2),
              c(3, NA, 4),
              c(NA, NA, NA))
fits <- vector(length = max(tmat, na.rm = TRUE), mode = "list")</pre>
surv_dat <- data.frame(mstate3_exdata$transitions)</pre>
for (i in 1:length(fits)){
  fits[[i]] <- flexsurvreg(Surv(years, status) ~ factor(strategy_id),</pre>
                            data = surv_dat,
                            subset = (trans == i),
                            dist = "weibull")
fits <- flexsurvreg_list(fits)</pre>
## Utility
utility_tbl <- stateval_tbl(data.frame(state_id = states$state_id,
                                         mean = mstate3_exdata$utility$mean,
                                         se = mstate3_exdata$utility$se),
                             dist = "beta")
## Costs
drugcost_tbl <- stateval_tbl(data.frame(strategy_id = strategies$strategy_id,</pre>
                                          est = mstate3_exdata$costs$drugs$costs),
                              dist = "fixed")
medcost_tbl <- stateval_tbl(data.frame(state_id = states$state_id,</pre>
                                         mean = mstate3_exdata$costs$medical$mean,
                                         se = mstate3_exdata$costs$medical$se),
                             dist = "gamma")
# Economic model
n_samples = 2
## Construct model
### Transitions
transmod_data <- expand(hesim_dat)</pre>
```

```
transmod <- create_IndivCtstmTrans(fits, input_data = transmod_data,</pre>
                                     trans_mat = tmat,
                                     n = n_samples)
### Utility
utilitymod <- create_StateVals(utility_tbl, n = n_samples, hesim_data = hesim_dat)
drugcostmod <- create_StateVals(drugcost_tbl, n = n_samples, hesim_data = hesim_dat)</pre>
medcostmod <- create_StateVals(medcost_tbl, n = n_samples, hesim_data = hesim_dat)</pre>
costmods <- list(drugs = drugcostmod,</pre>
                 medical = medcostmod)
### Combine
ictstm <- IndivCtstm$new(trans_model = transmod,</pre>
                          utility_model = utilitymod,
                          cost_models = costmods)
## Simulate outcomes
head(ictstm$sim_disease()$disprog_)
head(ictstm$sim\_stateprobs(t = c(0, 5, 10))$stateprobs_[t == 5])
ictstm$sim_qalys(dr = .03)
ictstm$sim_costs(dr = .03)
### Summarize cost-effectiveness
ce <- ictstm$summarize()</pre>
head(ce)
format(summary(ce), pivot_from = "strategy")
```

IndivCtstmTrans

Transitions for an individual-level continuous time state transition model

Description

Simulate health state transitions in an individual-level continuous time state transition model using parameters from a multi-state model.

Format

An R6::R6Class object.

Super class

hesim::CtstmTrans -> IndivCtstmTrans

Public fields

params An object of class params_surv or params_surv_list.

input_data Input data used to simulate health state transitions by sample from the probabilistic sensitivity analysis (PSA), treatment strategy and patient. Must be an object of class input_mats. If params contains parameters from a list of models (i.e., of class params_surv_list), then input_data must contain a unique row for each treatment strategy and patient; if params contains parameters from a joint model (i.e., of class params_surv), then input_data must contain a unique row for each treatment strategy, patient, and transition.

- trans_mat A transition matrix describing the states and transitions in a multi-state model in the format from the mstate package. See the documentation for the argument "trans" in mstate::msprep.
- start_state A scalar or vector denoting the starting health state. Default is the first health state. If a vector, must be equal to the number of simulated patients.
- start_age A scalar or vector denoting the starting age of each patient in the simulation. Default is 38. If a vector, must be equal to the number of simulated patients.
- death_state The death state in trans_mat. Used with max_age in sim_disease as patients transition to this state upon reaching maximum age. By default, it is set to the final absorbing state (i.e., a row in trans_mat with all NAs).
- clock "reset" for a clock-reset model, "forward" for a clock-forward model, "mix" for a mixture of clock-reset and clock-forward models by state, and "mixt" for a mixture of clock-reset and clock-forward models by transition. A clock-reset model is a semi-Markov model in which transition rates depend on time since entering a state. A clock-forward model is a Markov model in which transition rates depend on time since entering the initial state. If "mix" is used, then reset_states must be specified. If "mixt" is used, then transition_types must be specified.
- reset_states A vector denoting the states in which time resets. Hazard functions are always a function of elapsed time since either the start of the model or from when time was previously reset. Only used if clock = "mix".
- transition_types A vector denoting the type of transition. The vector is of the same length as the number of transitions and takes values "reset", "time" or "age" for hazards that are functions of reset time, time since study entry or age, respectively. Only used if clock = "mixt".

Methods

Public methods:

- IndivCtstmTrans\$new()
- IndivCtstmTrans\$sim_disease()
- IndivCtstmTrans\$sim_stateprobs()
- IndivCtstmTrans\$check()
- IndivCtstmTrans\$clone()

Method new(): Create a new IndivCtstmTrans object.

Usage:

```
IndivCtstmTrans$new(
  params,
  input_data,
  trans_mat,
  start_state = 1,
  start_age = 38,
  death_state = NULL,
  clock = c("reset", "forward", "mix", "mixt"),
  reset_states = NULL,
  transition_types = NULL
)
Arguments:
params The params field.
input_data The input_data field.
trans_mat The trans_mat field.
start_state The start_state field.
start_age The start_age field.
death_state The death_state field.
clock The clock field.
reset_states The reset_states field.
transition_types The transition_types field.
Returns: A new IndivCtstmTrans object.
```

Method sim_disease(): Simulate disease progression (i.e., individual trajectories through a multi-state model using an individual patient simulation).

```
Usage:
```

```
IndivCtstmTrans\$sim\_disease(max\_t = 100, max\_age = 100, progress = NULL)
```

Arguments:

max_t A scalar or vector denoting the length of time to simulate the model. If a vector, must be equal to the number of simulated patients.

max_age A scalar or vector denoting the maximum age to simulate each patient until. If a vector, must be equal to the number of simulated patients.

progress An integer, specifying the PSA iteration (i.e., sample) that should be printed every progress PSA iterations. For example, if progress = 2, then every second PSA iteration is printed. Default is NULL, in which case no output is printed.

Returns: An object of class disprog.

Method sim_stateprobs(): Simulate health state probabilities from a disprog object.

Usage:

```
IndivCtstmTrans$sim_stateprobs(t, disprog = NULL, ...)
```

Arguments:

t A numeric vector of times.

disprog A disprog object. If NULL, then this will be simulated prior to computing state probabilities using IndivCtstm\$sim_disease().

```
... Additional arguments to pass to IndivCtstm$sim_disease() if disprog = NULL.

*Returns: An object of class stateprobs.

Method check(): Input validation for class. Checks that fields are the correct type.

*Usage:*
IndivCtstmTrans$check()

Method clone(): The objects of this class are cloneable with this method.

*Usage:*
```

IndivCtstmTrans\$clone(deep = FALSE)

Arguments:

deep Whether to make a deep clone.

See Also

IndivCtstmTrans objects are conveniently created from either fitted models or parameter objects with create_IndivCtstmTrans(). A complete economic model can be implemented with the IndivCtstm class.

```
library("flexsurv")
# Simulation data
strategies <- data.frame(strategy_id = c(1, 2, 3))
patients <- data.frame(patient_id = seq(1, 3),</pre>
                        age = c(45, 50, 60),
                        female = c(0, 0, 1)
# Multi-state model with transition specific models
tmat <- rbind(c(NA, 1, 2),
              c(NA, NA, 3),
              c(NA, NA, NA))
fits <- vector(length = max(tmat, na.rm = TRUE), mode = "list")</pre>
for (i in 1:length(fits)){
  fits[[i]] <- flexsurvreg(Surv(years, status) ~ 1,</pre>
                            data = bosms3[bosms3$trans == i, ],
                            dist = "exp")
fits <- flexsurvreg_list(fits)</pre>
# Simulation model
hesim_dat <- hesim_data(strategies = strategies,</pre>
                         patients = patients)
fits_data <- expand(hesim_dat)</pre>
transmod <- create_IndivCtstmTrans(fits, input_data = fits_data,</pre>
                                     trans_mat = tmat,
                                     n = 2
head(transmod$hazard(c(1, 2, 3)))
head(transmod$cumhazard(c(1, 2, 3)))
```

58 input_mats

```
## Simulate disease progression and state probabilities together transmod\sin_s tateprobs(t = c(0, 5, 10))[t == 5]
## Simulate disease progression and state probabilities separately disprog <- transmod\sin_d tease(max_t = 10) transmod\sin_s tateprobs(t = c(0, 5, 10), disprog = disprog)[t == 5]
```

input_mats

Input matrices for a statistical model

Description

An object of class input_mats contains input matrices for simulating a statistical model. Consists of (i) input matrices, X, and (ii) metadata used to index each matrix in X.

Once created, an input_mats object can be converted to a data.table::data.table with as.data.table(), which is a helpful way to check that the object is as expected. The print() method summarizes the object and prints it to the console.

More details are provided under "Details" below.

Usage

```
input_mats(X, ...)
## S3 method for class 'input_mats'
as.data.table(x, ...)
## S3 method for class 'input_mats'
print(x, ...)
```

Arguments

X	A list of input matrices for predicting the values of each parameter in a statistical model. May also be a list of lists of input matrices when a list of separate models is fit (e.g., with flexsurvreg_list()).
	For input_mats(), arguments to pass to id_attributes(). For print(), arguments to pass to data.table::print.data.table().
Х	An input_mats object.

Details

input_mats objects are used with params objects to simulate disease models, cost models, and/or utility models. Each column of \$X contains variables from the params object and a given row corresponds to a combination of the ID variables. An input matrix must always have rows for the treatment strategies (strategy_id) and patients (patient_id); it may optionally have rows for health variables (state_id or transition_id) and time intervals (time_id). The rows must be

input_mats 59

sorted by prioritizing (i) strategy_id, (ii) patient_id, (iii) the health related ID variable (either state_id or transition_id) and (iv) time_id.

While input_mats objects can be created directly with input_mats(), it is rarely a good idea to do so. They are typically created as the input_data field when creating model objects (e.g., with create_IndivCtstmTrans(), create_CohortDtstmTrans(), and create_PsmCurves()). Internally, these functions create the input matrices using create_input_mats() methods, which ensure that they are in the correct format. Users may also use create_input_mats() methods, but there is not usually a good reason to do so.

as.data.table.input_mats() will convert input matrices into a single data.table() that column binds the ID variables and the unique combinations of variables contained in the elements of \$X. print.input_mats() prints a call to as.data.table() and provides additional information about the ID variables.

See Also

See IndivCtstmTrans() and PsmCurves() for examples in which the input_data field of an instance of a model class is an input_mats object.

```
library("data.table")
# Input matrices are typically created as part of model objects
# Let's illustrate with a partitioned survival model (PSM)
## Model setup
strategies <- data.frame(strategy_id = c(1, 2),</pre>
                         new_strategy = c(0, 1)
patients <- data.frame(patient_id = seq(1, 3),</pre>
                        age = c(45, 47, 60),
                        female = c(1, 0, 0),
                        group = factor(c("Good", "Medium", "Poor")))
hesim_dat <- hesim_data(strategies = strategies,</pre>
                         patients = patients)
## Create survival models for PSM
### Parameters
n < -2
survmod_params <- params_surv_list(</pre>
 # Progression free survival (PFS)
 pfs = params_surv(
    coefs = list(
      rate = data.frame(intercept = rnorm(n, log(1/5), 1),
                         new\_strategy = rnorm(n, log(.8), 1))
      ),
    dist = "exp"
 ),
 # Overall survival (OS)
 os = params_surv(
   coefs = list(
```

60 mom_beta

```
rate = data.frame(intercept = rnorm(n, log(1/10), 1))
),
dist = "exp"
)

### Input data
survmod_input_data <- expand(hesim_dat)[, intercept := 1]

### Model object
survmod <- create_PsmCurves(survmod_params, input_data = survmod_input_data)

## Inspect input data
survmod$input_data # Print "input_mats" object to console
as.data.table(survmod$input_data) # Convert "input_mats" object to data.table</pre>
```

mom_beta

Method of moments for beta distribution

Description

Compute the parameters shape1 and shape2 of the beta distribution using method of moments given the mean and standard deviation of the random variable of interest.

Usage

```
mom_beta(mean, sd)
```

Arguments

mean

Mean of the random variable.

sd

Standard deviation of the random variable.

Details

If μ is the mean and σ is the standard deviation of the random variable, then the method of moments estimates of the parameters shape1 = $\alpha > 0$ and shape2 = $\beta > 0$ are:

$$\alpha = \mu \left(\frac{\mu(1-\mu)}{\sigma^2} - 1 \right)$$

and

$$\beta = (1 - \mu) \left(\frac{\mu(1 - \mu)}{\sigma^2} - 1 \right)$$

Value

A list containing the parameters shape1 and shape2.

mom_gamma 61

Examples

```
mom_beta(mean = .8, sd = .1)
# The function is vectorized.
mom_beta(mean = c(.6, .8), sd = c(.08, .1))
```

mom_gamma

Method of moments for gamma distribution

Description

Compute the shape and scale (or rate) parameters of the gamma distribution using method of moments for the random variable of interest.

Usage

```
mom_gamma(mean, sd, scale = TRUE)
```

Arguments

mean Mean of the random variable.

sd Standard deviation of the random variable.

scale Logical. If TRUE (default), then the scale parameter is returned; otherwise, the

rate parameter is returned.

Details

If μ is the mean and σ is the standard deviation of the random variable, then the method of moments estimates of the parameters shape = $\alpha > 0$ and scale = $\theta > 0$ are:

$$\theta = \frac{\sigma^2}{\mu}$$

and

$$\alpha = \frac{\mu}{\theta}$$

The inverse of the scale parameter, $\beta = 1/\theta$, is the rate parameter.

Value

If scale = TRUE, then a list containing the parameters shape and scale; otherwise, if scale = FALSE, then a list containing the parameters shape and rate.

```
mom_gamma(mean = 10000, sd = 2000)
# The function is vectorized.
mom_gamma(mean = c(8000, 10000), sd = c(1500, 2000))
```

62 mstate3_exdata

mstate3_exdata

Example data for a reversible 3-state multi-state model

Description

Example multi-state data for parameterizing a continuous time state transition model. Costs and utility are also included to facilitate cost-effectiveness analysis.

Usage

mstate3_exdata

Format

A list containing the following elements:

transitions A data frame containing the times at which patient transitions between health states based on the prothr dataset from the mstate package.

costs A list of data frames. The first data frame contains summary medical cost estimates and the second data frame contains drug cost data.

utility A data frame of summary utility estimates.

Transitions data

The data frame has the following columns:

strategy_id Treatment strategy identification number.

patient_id Patient identification number.

age Patient age (in years).

female 1 if a patient is female; 0 if male.

from Starting state.

to Receiving state.

trans Transition number.

Tstart Starting time.

Tstop Transition time.

years Elapsed years between Tstart and Tstop.

status Status variable; 1=transition, 0=censored.

multinom3_exdata 63

Cost data

The cost list contains two data frames. The first data frame contains data on the drug costs associated with each treatment strategy.

strategy_id The treatment strategy identification number.

costs Annualized drug costs.

The second data frame contains summary data on medical costs by health state, and contains the following columns:

state_id The health state identification number.

mean Mean costs.

se Standard error of medical costs.

Utility data

The data frame has the following columns:

state_id The health state identification number.

mean Mean utility

se Standard error of utility

multinom3_exdata

Example data for a 3-state multinomial model

Description

Example discrete time health state transitions data simulated using multinomial logistic regression. Costs and utility are also included to facilitate cost-effectiveness analysis.

Usage

multinom3_exdata

Format

A list containing the following elements:

transitions A data frame containing patient transitions between health states at discrete time intervals (i.e., on a yearly basis).

costs A list of data frames. The first data frame contains drug cost data and the second contains summary medical cost estimates.

utility A data frame of summary utility estimates.

64 multinom3_exdata

Transitions data

The data frame has the following columns:

patient_id Patient identification number.

strategy_id Treatment strategy identification number.

strategy_name Treatment strategy name.

age Patient age (in years).

age_cat A factor variable with 3 age groups: (i) age less than 40, (ii) age at least 40 and less than 60, and (iii) age at least 60.

female 1 if a patient is female; 0 if male.

year The year since the start of data collection with the first year equal to 1.

state_from State making a transition from.

state_to State making a transition to.

year_cat Factor variable for year with 3 categories: (i) year 3 and below, (ii) year between 3 and 6, and (iii) year 7 and above.

Cost data

The cost list contains two data frames. The first data frame contains data on the drug costs associated with each treatment strategy.

strategy_id The treatment strategy identification number.

strategy_name The treatment strategy name.

costs Annualized drug costs.

The second data frame contains summary data on medical costs by health state, and contains the following columns:

state_id The health state identification number.

state_name The name of the health state.

mean Mean medical costs.

se Standard error of medical costs.

Utility data

The data frame has the following columns:

state id The health state identification number.

state name The name of the health state.

mean Mean utility

se Standard error of utility.

multinom_list 65

multinom_list

List of multinom objects

Description

Combine multinom objects into a list.

Usage

```
multinom_list(...)
```

Arguments

... Objects of class multinom, which can be named.

Value

An object of class multinom_list.

Examples

onc3

Multi-state oncology data for 3-state model

Description

Simulated 3-state dataset in oncology with three health states (Stable, Progression, and Death) and three possible transitions (Stable -> Progression, Stable -> Death, and Progression -> Death).

Usage

onc3

onc3p

Format

A data. table with the following columns:

from Health state making a transition from.

to Health state making a transition to.

strategy_name Standard of care (SOC), new treatment 1 (New 1), or new treatment 2 (New 2).

female 1 if a patient is female; 0 if male.

age Patient age (in years).

patient_id Patient identification number.

time_start Starting time.

time_stop Stopping time.

status Status indicator: 1=transition, 0=censored.

transition_id Integer denoting transition: 1 = Stable -> Progression, 2 = Stable -> Death, 3 = Progression -> Death.

strategy_id Strategy identification number.

time Elapsed years between time_start and time_stop.

See Also

onc3p

Examples

head(onc3)

onc3p

Multi-state panel oncology data for 3-state model

Description

The same dataset as onc3 converted into a panel data format in which health states are recorded at a finite series of times.

Usage

onc3p

params 67

Format

```
A data. table with the following columns:
```

```
state The name of the health state (Stable, Progression, and Death).
```

strategy_name Standard of care (SOC), new treatment 1 (New 1), or new treatment 2 (New 2).

female 1 if a patient is female; 0 if male.

age Patient age (in years).

patient_id Patient identification number.

time Time that state was recorded.

strategy_id Strategy identification number.

state_id The health state identification number.

See Also

onc3

Examples

head(onc3p)

params

Parameter object

Description

Objects prefixed by "params_" are lists containing the parameters of a statistical model used for simulation modeling. The parameters are used to simulate outcomes as a function of covariates contained in input matrices (input_mats).

See Also

tparams

68 params_lm

params_lm

Parameters of a linear model

Description

Create a list containing the parameters of a fitted linear regression model.

Usage

```
params_lm(coefs, sigma = 1)
```

Arguments

coefs Samples of the coefficients under sampling uncertainty. Must be a matrix or any object coercible to a matrix such as data. frame or data. table. sigma A vector of samples of the standard error of the regression model. Default value is 1 for all samples. Only used if the model is used to randomly simulate values

(rather than to predict means).

Details

Fitted linear models are used to predict values, y, as a function of covariates, x,

$$y = x^T \beta + \epsilon$$
.

Predicted means are given by $x^T \hat{\beta}$ where $\hat{\beta}$ is the vector of estimated regression coefficients. Random samples are obtained by sampling the error term from a normal distribution, $\epsilon \sim N(0, \hat{\sigma}^2)$.

Value

An object of class params_lm, which is a list containing coefs, sigma, and n_samples. n_samples is equal to the number of rows in coefs. The coefs element is always converted into a matrix.

See Also

This parameter object is useful for modeling health state values when values can vary across patients and/or health states as a function of covariates. In many cases it will, however, be simpler, and more flexible to use a stateval_tbl. For an example use case see the documentation for create_StateVals.lm().

```
library("MASS")
n <- 2
params <- params_lm(</pre>
  coefs = mvrnorm(n, mu = c(.5, .6),
                   Sigma = matrix(c(.05, .01, .01, .05), nrow = 2)),
  sigma <- rgamma(n, shape = .5, rate = 4)</pre>
```

params_mlogit 69

```
)
summary(params)
params
```

params_mlogit

Parameters of a multinomial logit model

Description

Store the parameters of a fitted multinomial logistic regression model. The model is used to predict probabilities of K classes, which represent the probability of transitioning to particular health state in a discrete time state transition model. Can be used as an element of a params_mlogit_list to parameterize a CohortDtstmTrans object.

Usage

```
params_mlogit(coefs)
```

Arguments

coefs

A 3D array of stacked matrices containing samples of the regression coefficients under sampling uncertainty. May also be a list of objects (e.g., data frames) that can be coerced into matrices with as.matrix(). Each matrix must have the same number of columns and the number of matrices must be equal to K-1.

Details

Multinomial logit models are used to predict the probability of membership for subject i in each of K classes as a function of covariates:

$$Pr(y_i = c) = \frac{e^{\beta_c x_i}}{\sum_{k=1}^{K} e^{\beta_k x_i}}$$

Value

An object of class params_mlogit, which is a list containing coefs and n_samples, where n_samples is equal to the number of rows in each element of coefs. The coefs element is always converted into a 3D array of stacked matrices.

See Also

```
summary.params_mlogit(), params_mlogit_list(), CohortDtstmTrans
```

70 params_mlogit_list

Examples

```
# Consider a sick-sicker model and model transitions from the sick state
## We can instantiate from a list of data frames
params <- params_mlogit(</pre>
 coefs = list(
    ### Transition from sick to sicker
   sicker = data.frame(
      intercept = c(-0.33, -.2, -.15),
      treat = c(\log(.75), \log(.8), \log(.9))
   ),
   ### Transition from sick to death
   death = data.frame(
      intercept = c(-1, -1.2, -.5),
      treat = c(\log(.6), \log(.65), \log(.55))
 )
)
summary(params)
params
## We can also instantiate from an array
coefs_sicker <- data.frame(</pre>
 intercept = c(-0.33, -.2, -.15),
 treat = c(log(.75), log(.8), log(.9))
)
coefs_death <- data.frame(</pre>
 intercept = c(-1, -1.2, -.5),
 treat = c(\log(.6), \log(.65), \log(.55))
)
params2 <- params_mlogit(</pre>
 coefs <- array(</pre>
    data = c(as.matrix(coefs_sicker),
             as.matrix(coefs_death)),
   dim = c(3, 2, 2),
    dimnames = list(NULL, c("intercept", "treat"), c("sicker", "death"))
 )
)
params2
```

Description

Create a list containing the parameters of multiple fitted multinomial logit models. Can be used to parameterize state transitions in a discrete time transition model by passing to the params field of a CohortDtstmTrans object.

params_mlogit_list 71

Usage

```
params_mlogit_list(...)
```

Arguments

... Objects of class params_mlogit, which can be named.

Value

An object of class params_mlogit_list, which is a list containing params_mlogit objects.

See Also

```
summary.params_mlogit_list(), params_mlogit(), CohortDtstmTrans
```

```
# Consider a sick-sicker model
params <- params_mlogit_list(</pre>
  ## Transitions from sick state (sick -> sicker, sick -> death)
  sick = params_mlogit(
   coefs = list(
      sicker = data.frame(
        intercept = c(-0.33, -.2),
        treat = c(log(.75), log(.8))
      death = data.frame(
        intercept = c(-1, -1.2),
        treat = c(log(.6), log(.65))
      )
   )
  ),
  ## Transitions from sicker state (sicker -> death)
  sicker = params_mlogit(
   coefs = list(
      death = data.frame(
        intercept = c(-1.5, -1.4),
        treat = c(log(.5), log(.55))
   )
 )
)
summary(params)
params
```

72 params_surv

params_surv

Parameters of a survival model

Description

Create a list containing the parameters of a single fitted parametric or flexible parametric survival model

Usage

```
params_surv(coefs, dist, aux = NULL)
```

Arguments

coefs	A list of length equal to the number of parameters in the survival distribution. Each element of the list is a matrix of samples of the regression coefficients under sampling uncertainty used to predict a given parameter. All parameters are expressed on the real line (e.g., after log transformation if they are defined as positive). Each element of the list may also be an object coercible to a matrix such as a data.frame or data.table.
dist	Character vector denoting the parametric distribution. See "Details".
aux	Auxiliary arguments used with splines, fractional polynomial, or piecewise exponential models. See "Details".

Details

Survival is modeled as a function of L parameters α_l . Letting F(t) be the cumulative distribution function, survival at time t is given by

$$1 - F(t|\alpha_1(x_1), \ldots, \alpha_L(x_L)).$$

The parameters are modeled as a function of covariates, x_l , with an inverse transformation function $g^{-1}()$,

 $\alpha_l = g^{-1}(x_l^T \beta_l).$

 $g^{-1}()$ is typically exp() if a parameter is strictly positive and the identity function if the parameter space is unrestricted.

The types of distributions that can be specified are:

exponential **or** exp Exponential distribution. coef must contain the rate parameter on the log scale and the same parameterization as in stats::Exponential.

weibull **or** weibull.quiet Weibull distribution. The first element of coef is the shape parameter (on the log scale) and the second element is the scale parameter (also on the log scale). The parameterization is that same as in stats::Weibull.

weibullPH Weibull distribution with a proportional hazards parameterization. The first element of coef is the shape parameter (on the log scale) and the second element is the scale parameter (also on the log scale). The parameterization is that same as in flexsurv::WeibullPH.

params_surv 73

gamma Gamma distribution. The first element of coef is the shape parameter (on the log scale) and the second element is the rate parameter (also on the log scale). The parameterization is that same as in stats::GammaDist.

- Inorm Lognormal distribution. The first element of coef is the meanlog parameter (i.e., the mean of survival on the log scale) and the second element is the sdlog parameter (i.e., the standard deviation of survival on the log scale). The parameterization is that same as in stats::Lognormal. The coefficients predicting the meanlog parameter are untransformed whereas the coefficients predicting the sdlog parameter are defined on the log scale.
- gompertz Gompertz distribution. The first element of coef is the shape parameter and the second element is the rate parameter (on the log scale). The parameterization is that same as in flexsurv::Gompertz.
- llogis Log-logistic distribution. The first element of coef is the shape parameter (on the log scale) and the second element is the scale parameter (also on the log scale). The parameterization is that same as in flexsurv::Llogis.
- gengamma Generalized gamma distribution. The first element of coef is the location parameter mu, the second element is the scale parameter sigma (on the log scale), and the third element is the shape parameter Q. The parameterization is that same as in flexsurv::GenGamma.
- survspline Survival splines. Each element of coef is a parameter of the spline model (i.e. gamma_0, gamma_1, ...) with length equal to the number of knots (including the boundary knots). See below for details on the auxiliary arguments. The parameterization is that same as in flexsurv::Survspline.
- fracpoly Fractional polynomials. Each element of coef is a parameter of the fractional polynomial model (i.e. gamma_0, gamma_1, ...) with length equal to the number of powers plus 1. See below for details on the auxiliary arguments (i.e., powers).
- pwexp Piecewise exponential distribution. Each element of coef is rate parameter for a distinct time interval. The times at which the rates change should be specified with the auxiliary argument time (see below for more details).
- fixed A fixed survival time. Can be used for "non-random" number generation. coef should contain a single parameter, est, of the fixed survival times.

Auxiliary arguments for spline models should be specified as a list containing the elements:

knots A numeric vector of knots.

- scale The survival outcome to be modeled as a spline function. Options are "log_cumhazard" for the log cumulative hazard; "log_hazard" for the log hazard rate; "log_cumodds" for the log cumulative odds; and "inv_normal" for the inverse normal distribution function.
- timescale If "log" (the default), then survival is modeled as a spline function of log time; if "identity", then it is modeled as a spline function of time.

Auxiliary arguments for fractional polynomial models should be specified as a list containing the elements:

powers A vector of the powers of the fractional polynomial with each element chosen from the following set: -2. -1, -0.5, 0, 0.5, 1, 2, 3.

Auxiliary arguments for piecewise exponential models should be specified as a list containing the element:

74 params_surv_list

time A vector equal to the number of rate parameters giving the times at which the rate changes.

Furthermore, when splines (with scale = "log_hazard") or fractional polynomials are used, numerical methods must be used to compute the cumulative hazard and for random number generation. The following additional auxiliary arguments can therefore be specified:

cumhaz_method Numerical method used to compute cumulative hazard (i.e., to integrate the hazard function). Always used for fractional polynomials but only used for splines if scale = "log_hazard". Options are "quad" for adaptive quadrature and "riemann" for Riemann sum

random_method Method used to randomly draw from an arbitrary survival function. Options are "invcdf" for the inverse CDF and "discrete" for a discrete time approximation that randomly samples events from a Bernoulli distribution at discrete times.

step Step size for computation of cumulative hazard with numerical integration. Only required when using "riemann" to compute the cumulative hazard or using "discrete" for random number generation.

Value

An object of class params_surv, which is a list containing coefs, dist, and n_samples. n_samples is equal to the number of rows in each element of coefs, which must be the same. The coefs element is always converted into a list of matrices. The list may also contain aux if a spline, fractional polynomial, or piecewise exponential model is used.

Examples

```
n <- 10
params <- params_surv(
    coefs = list(
        shape = data.frame(
            intercept = rnorm(n, .5, .23)
        ),
        scale = data.frame(
            intercept = rnorm(n, 12.39, 1.49),
            age = rnorm(n, -.09, .023)
        )
        ),
        dist = "weibull"
)
summary(params)
params</pre>
```

params_surv_list

Parameters of a list of survival models

Description

Create a list containing the parameters of multiple fitted parametric survival models.

plot_ceac 75

Usage

```
params_surv_list(...)
```

Arguments

... Objects of class params_surv, which can be named.

Value

An object of class params_surv_list, which is a list containing params_surv objects.

See Also

```
create_params()
```

Examples

```
n <- 5
params <- params_surv_list(</pre>
  # Model for progression free survival
  pfs = params_surv(
   coefs = list(
      rate = data.frame(intercept = rnorm(n, log(.5), .5),
                        new_strategy = rnorm(n, log(.8), .1))
  ),
   dist = "exp"
  ),
  # Model for overall survival
  os = params_surv(
   coefs = list(
      rate = data.frame(intercept = rnorm(n, log(.3) , .5))
   ),
    dist = "exp"
  )
summary(params)
params
```

plot_ceac

Plot cost-effectiveness acceptability curve

Description

Plot a cost-effectiveness curve from either the output of cea() or cea_pw() using ggplot2::ggplot. The former compares all treatment strategies simultaneously and uses the probabilistic sensitivity analysis (PSA) to compute the probability that each strategy is the most cost-effective at a given willingness to pay value, while the latter uses the PSA to compute the probability that each treatment is cost-effective relative to a comparator.

76 plot_ceaf

Usage

```
plot_ceac(x, ...)
## S3 method for class 'cea_pw'
plot_ceac(x, labels = NULL, ...)
## S3 method for class 'cea'
plot_ceac(x, labels = NULL, ...)
```

Arguments

x An object of the appropriate class.

... Further arguments passed to and from methods. Currently unused.

labels A list of named vectors containing the values and labels of variables. The ele-

ments of each vector are the values of a variable and the names are the labels. The names of the list are the names of the variables. See the output returned by

get_labels() for an example.

Details

See the cea() documentation for an example. If there are multiple subgroups, then a faceted plot is produced with one plot for each subgroup.

plot_ceaf

Plot cost-effectiveness acceptability frontier

Description

Plot a cost-effectiveness acceptability frontier (CEAF) from the output of cea using ggplot2::ggplot. The CEAF plots the probability that the optimal treatment strategy (i.e., the strategy with the highest expected net monetary benefit) is cost-effective.

Usage

```
plot_ceaf(x, labels = NULL)
```

Arguments

x A cea object produced by cea.

labels A list of named vectors containing the values and labels of variables. The ele-

ments of each vector are the values of a variable and the names are the labels. The names of the list are the names of the variables. See the output returned by

get_labels() for an example.

plot_ceplane 77

Details

See the cea() documentation for an example. If there are multiple subgroups, then a faceted plot is produced with one plot for each subgroup.

Value

A ggplot object.

plot_ceplane

Plot cost-effectiveness plane

Description

Plot a cost-effectiveness plane from the output of cea_pw() using ggplot2::ggplot. Each point is a random draw of incremental costs (y-axis) and incremental QALYs (x-axis) from a probabilistic sensitivity analysis.

Usage

```
plot_ceplane(x, k = 50000, labels = NULL)
```

Arguments

x A cea_pw object produced by cea_pw().

k Willingness to pay per QALY.

labels A list of named vectors containing the values and labels of variables. The ele-

ments of each vector are the values of a variable and the names are the labels. The names of the list are the names of the variables. See the output returned by

get_labels() for an example.

Details

See the cea_pw() documentation for an example. If there are multiple subgroups, then a faceted plot is produced with one plot for each subgroup.

Value

A ggplot object.

plot_evpi

Plot expected value of perfect information

Description

Plot the expected value of perfect information (EVPI) from the output of cea() using ggplot2::ggplot. Intuitively, the EVPI provides an estimate of the amount that a decision maker would be willing to pay to collect additional data and completely eliminate uncertainty.

Usage

```
plot_evpi(x, labels = NULL)
```

Arguments

x A cea object produced by cea().

labels A list of named vectors containing the values and labels of variables. The ele-

ments of each vector are the values of a variable and the names are the labels. The names of the list are the names of the variables. See the output returned by

get_labels() for an example.

Details

See the cea() documentation for an example. If there are multiple subgroups, then a faceted plot is produced with one plot for each subgroup.

Value

A ggplot object.

Psm

N-state partitioned survival model

Description

Simulate outcomes from an N-state partitioned survival model.

Format

An R6::R6Class object.

Public fields

survival_models The survival models used to predict survival curves. Must be an object of class PsmCurves.

utility_model The model for health state utility. Must be an object of class StateVals.

cost_models The models used to predict costs by health state. Must be a list of objects of class StateVals, where each element of the list represents a different cost category.

n_states Number of states in the partitioned survival model.

t_ A numeric vector of times at which survival curves were predicted. Determined by the argument t in \$sim_curves().

```
survival_ An object of class survival simulated using sim_survival().
stateprobs_ An object of class stateprobs simulated using $sim_stateprobs().
qalys_ An object of class qalys simulated using $sim_qalys().
costs_ An object of class costs simulated using $sim_costs().
```

Methods

Public methods:

- Psm\$new()
- Psm\$sim_survival()
- Psm\$sim_stateprobs()
- Psm\$sim_qalys()
- Psm\$sim_costs()
- Psm\$summarize()
- Psm\$clone()

Method new(): Create a new Psm object.

```
Usage:
```

```
Psm$new(survival_models = NULL, utility_model = NULL, cost_models = NULL)
```

Arguments:

survival_models The survival_models field.

utility_model The utility_model field.

cost_models The cost_models field.

Details: n_states is set equal to the number of survival models plus one.

Returns: A new Psm object.

Method sim_survival(): Simulate survival curves as a function of time using PsmCurves\$survival().

Usage:

Psm\$sim_survival(t)

Arguments:

t A numeric vector of times. The first element must be 0.

Returns: An instance of self with simulated output from PsmCurves\$survival() stored in survival_.

Method sim_stateprobs(): Simulate health state probabilities from survival_using a partitioned survival analysis.

Usage:

Psm\$sim_stateprobs()

Returns: An instance of self with simulated output of class stateprobs stored in stateprobs_.

Method sim_qalys(): Simulate quality-adjusted life-years (QALYs) as a function of stateprobs_ and utility_model. See sim_qalys() for details.

```
Usage:
```

```
Psm$sim_qalys(
   dr = 0.03,
   integrate_method = c("trapz", "riemann_left", "riemann_right"),
   lys = TRUE
)
```

Arguments:

dr Discount rate.

integrate_method Method used to integrate state values when computing costs or QALYs. Options are trapz for the trapezoid rule, riemann_left for a left Riemann sum, and riemann_right for a right Riemann sum.

lys If TRUE, then life-years are simulated in addition to QALYs.

Returns: An instance of self with simulated output of class qalys stored in qalys_.

Method sim_costs(): Simulate costs as a function of stateprobs_ and cost_models. See sim_costs() for details.

```
Usage:
```

```
Psm$sim_costs(
  dr = 0.03,
  integrate_method = c("trapz", "riemann_left", "riemann_right")
)
```

Arguments:

dr Discount rate.

integrate_method Method used to integrate state values when computing costs or QALYs. Options are trapz for the trapezoid rule, riemann_left for a left Riemann sum, and riemann_right for a right Riemann sum.

Returns: An instance of self with simulated output of class costs stored in costs_.

Method summarize(): Summarize costs and QALYs so that cost-effectiveness analysis can be performed. See summarize_ce().

Usage:

```
Psm$summarize(by_grp = FALSE)
```

Arguments:

by_grp If TRUE, then costs and QALYs are computed by subgroup. If FALSE, then costs and QALYs are aggregated across all patients (and subgroups).

```
Method clone(): The objects of this class are cloneable with this method.
    Usage:
    Psm$clone(deep = FALSE)
    Arguments:
    deep Whether to make a deep clone.
```

References

Incerti and Jansen (2021). See Section 2.3 for a mathematical description of a PSM and Section 4.2 for an example in oncology. The mathematical approach used to simulate costs and QALYs from state probabilities is described in Section 2.1.

See Also

The PsmCurves documentation describes the class for the survival models and the StateVals documentation describes the class for the cost and utility models. A PsmCurves object is typically created using create_PsmCurves(). The PsmCurves documentation provides an example in which the model is parameterized from parameter objects (i.e., without having the patient-level data required to fit a model with R). A longer example is provided in vignette("psm").

```
library("flexsurv")
library("ggplot2")
theme_set(theme_bw())
# Model setup
strategies <- data.frame(strategy_id = c(1, 2, 3),</pre>
                          strategy_name = paste0("Strategy ", 1:3))
patients <- data.frame(patient_id = seq(1, 3),</pre>
                        age = c(45, 50, 60),
                        female = c(0, 0, 1)
states <- data.frame(state_id = seq(1, 3),
                      state_name = paste0("State ", seq(1, 3)))
hesim_dat <- hesim_data(strategies = strategies,</pre>
                         patients = patients,
                         states = states)
labs <- c(
  get_labels(hesim_dat),
  list(curve = c("Endpoint 1" = 1,
                  "Endpoint 2" = 2,
                  "Endpoint 3" = 3)
n_samples <- 2
# Survival models
surv_est_data <- psm4_exdata$survival</pre>
fit1 <- flexsurvreg(Surv(endpoint1_time, endpoint1_status) ~ factor(strategy_id),</pre>
                     data = surv_est_data, dist = "exp")
fit2 <- flexsurvreg(Surv(endpoint2_time, endpoint2_status) ~ factor(strategy_id),</pre>
                     data = surv_est_data, dist = "exp")
```

82 psm4_exdata

```
fit3 <- flexsurvreg(Surv(endpoint3_time, endpoint3_status) ~ factor(strategy_id),</pre>
                     data = surv_est_data, dist = "exp")
fits <- flexsurvreg_list(fit1, fit2, fit3)</pre>
surv_input_data <- expand(hesim_dat, by = c("strategies", "patients"))</pre>
psm_curves <- create_PsmCurves(fits, input_data = surv_input_data,</pre>
                                uncertainty = "bootstrap", est_data = surv_est_data,
                                n = n_{samples}
# Cost model(s)
cost_input_data <- expand(hesim_dat, by = c("strategies", "patients", "states"))</pre>
fit_costs_medical <- lm(costs ~ female + state_name,</pre>
                         data = psm4_exdata$costs$medical)
psm_costs_medical <- create_StateVals(fit_costs_medical,</pre>
                                        input_data = cost_input_data,
                                        n = n_samples)
# Utility model
utility_tbl <- stateval_tbl(tbl = data.frame(state_id = states$state_id,
                                               min = psm4_exdata$utility$lower,
                                               max = psm4_exdata$utility$upper),
                             dist = "unif")
psm_utility <- create_StateVals(utility_tbl, n = n_samples,</pre>
                                 hesim_data = hesim_dat)
# Partitioned survival decision model
psm <- Psm$new(survival_models = psm_curves,</pre>
               utility_model = psm_utility,
               cost_models = list(medical = psm_costs_medical))
psm$sim_survival(t = seq(0, 5, 1/12))
autoplot(psm$survival_, labels = labs, ci = FALSE, ci_style = "ribbon")
psm$sim_stateprobs()
autoplot(psm$stateprobs_, labels = labs)
psm$sim_costs(dr = .03)
head(psm$costs_)
head(psm\$sim\_qalys(dr = .03)\$qalys\_)
```

psm4_exdata

Example data for a 4-state partitioned survival model

Description

A collection of example datasets containing simulated survival, costs, and utility data for a 4-state partitioned survival model.

Usage

psm4_exdata

psm4_exdata 83

Format

A list containing the following elements:

Survival A data frame containing patient information and time to 3 separate survival endpoints.

Costs A list of data frames. The first data frame contains medical cost data and the second data frame contains drug cost data.

Survival data

The survival data frame contains a list of 3 survival curves, each containing the following columns.

female An indicator variable equal to 1 if the patient is female and 0 otherwise.

age The age of the patient in years.

strategy_id The id of the treatment strategy used.

endpoint1_time Follow up time with right censored data to survival endpoint 1.

endpoint1_status A status indicator for survival endpoint 1 equal to 0 if alive and 1 if dead.

endpoint2_time Follow up time with right censored data to survival endpoint 2.

endpoint2_status A status indicator for survival endpoint 2 equal to 0 if alive and 1 if dead.

endpoint3_time Follow up time with right censored data to survival endpoint 3.

endpoint3_status A status indicator for survival endpoint 3 equal to 0 if alive and 1 if dead.

Cost data

The cost list contains two data frames. The first data frame contains data on the medical costs by patient and health state, and contains the following columns:

patient_id An integer denoting the id of the patient.

female An indicator variable equal to 1 if the patient is female and 0 otherwise.

state_name A categorical variable denoting the three possible health states.

costs Annualized medical costs.

The second data frame contains data on the drug costs associated with each treatment strategy.

strategy_id The id of each treatment strategy.

costs Annualized drug costs.

84 PsmCurves

PsmCurves

Partitioned survival curves

Description

Summarize N-1 survival curves for an N-state partitioned survival model.

Format

An R6::R6Class object.

Public fields

```
params An object of class params_surv_list.
```

input_data An object of class input_mats. Each row in X must be a unique treatment strategy and patient.

Methods

Public methods:

- PsmCurves\$new()
- PsmCurves\$hazard()
- PsmCurves\$cumhazard()
- PsmCurves\$survival()
- PsmCurves\$rmst()
- PsmCurves\$quantile()
- PsmCurves\$check()
- PsmCurves\$clone()

Method new(): Create a new PsmCurves object.

Usage:

PsmCurves\$new(params, input_data)

Arguments:

params The params field.

input_data The input_data field.

Returns: A new PsmCurves object.

Method hazard(): Predict the hazard function for each survival curve as a function of time.

Usage:

PsmCurves\$hazard(t)

Arguments:

t A numeric vector of times.

Returns: A data.table with columns sample, strategy_id, patient_id, grp_id, curve (the curve number), t, and hazard.

Method cumhazard(): Predict the cumulative hazard function for each survival curve as a function of time.

Usage:

PsmCurves\$cumhazard(t)

Arguments:

t A numeric vector of times.

Returns: A data.table with columns sample, strategy_id, patient_id, grp_id, curve, t, and cumhazard.

Method survival(): Predict survival probabilities for each survival curve as a function of time.

Usage:

PsmCurves\$survival(t)

Arguments:

t A numeric vector of times.

Returns: An object of class survival.

Method rmst(): Predict the restricted mean survival time up until time points t for each survival curve.

Usage:

PsmCurves\$rmst(t, dr = 0)

Arguments:

t A numeric vector of times.

dr Discount rate.

 $\textit{Returns:} \; \; A \; \text{data.table with columns sample, strategy_id, patient_id, grp_id, curve, t, and rmst.}$

Method quantile(): Predict quantiles of the survival distribution for each survival curve.

Usage:

PsmCurves\$quantile(p)

Arguments:

p A numeric vector of probabilities for computing quantiles.

Returns: A data.table with columns sample, strategy_id, patient_id, grp_id, curve, p and quantile.

Method check(): Input validation for class. Checks that fields are the correct type.

Usage:

PsmCurves\$check()

Method clone(): The objects of this class are cloneable with this method.

Usage:

PsmCurves\$clone(deep = FALSE)

Arguments:

deep Whether to make a deep clone.

86 PsmCurves

See Also

PsmCurves are conveniently created from either fitted models or parameter objects with create_PsmCurves(). A complete economic model can be implemented with the Psm class. A longer example is provided in vignette("psm").

```
library("flexsurv")
N_SAMPLES <- 5 # Number of parameter samples for PSA
# Consider a 3-state model where there is a
# progression-free survival (PFS) and an
# overall survival (OS) endpoint
# (0) Model setup
hesim_dat <- hesim_data(</pre>
  strategies = data.frame(
    strategy_id = c(1, 2),
    strategy_name = c("SOC", "New 1")
  patients = data.frame(
    patient_id = 1
  )
)
# (1) Parameterize survival models
## (1.1) If patient-level data is available,
## we can fit survival models
### (1.1.1) Data for estimation (for simplicity, only use 2 strategies)
surv_est_data <- as_pfs_os(</pre>
  onc3[strategy_name != "New 2"],
  patient_vars = c("patient_id", "strategy_name")
surv_est_data$strategy_name <- droplevels(surv_est_data$strategy_name)</pre>
### (1.1.2) Fit models
fit_pfs <- flexsurvreg(Surv(pfs_time, pfs_status) ~ strategy_name,</pre>
                        data = surv_est_data, dist = "exp")
fit_os <- flexsurvreg(Surv(os_time, os_status) ~ strategy_name,</pre>
                      data = surv_est_data, dist = "exp")
fits <- flexsurvreg_list(pfs = fit_pfs, os = fit_os)</pre>
## (1.2) If patient-level data is NOT available,
## we can construct the parameter objects "manually"
### (1.2.1) Baseline hazard:
### Assume that we know the (log) rate parameters for both PFS and OS
### for SOC (i.e., the intercept) and their standard error
logint_pfs_est <- -1.7470900
logint_pfs_se <- 0.03866223
logint_os_est <- -2.7487675
```

PsmCurves 87

```
logint_os_se <- 0.04845015
### (1.2.2) Relative treatment effect:
### Assume we know the log hazard ratios (and their standard errors)
### for comparing the new interventions to the SOC
loghr_pfs_est_new1 <- -0.1772028
loghr_pfs_se_new1 <- 0.05420119
loghr_os_est_new1 <- -0.1603632
loghr_os_se_new1 <- 0.06948962
### (1.2.3) Create "params_surv_list" object by combining the baseline hazard
### and relative treatment effects
params <- params_surv_list(</pre>
 #### Model for PFS
 pfs = params_surv(
   coefs = list(
      rate = data.frame( # coefficients predict log rate
        intercept = rnorm(N_SAMPLES, logint_pfs_est, logint_pfs_se),
        new1 = rnorm(N_SAMPLES, loghr_pfs_est_new1, loghr_pfs_se_new1)
      )
   ),
   dist = "exp"
 ),
 #### Model for OS
 os = params_surv(
   coefs = list(
      rate = data.frame(
       intercept = rnorm(N_SAMPLES, logint_os_est, logint_os_se),
        new1 = rnorm(N_SAMPLES, loghr_os_est_new1, loghr_os_se_new1)
     )
   ),
    dist = "exp"
 )
)
#### The print (and summary) methods for the "params_surv_list" object will
#### summarize each of the model terms, which is a good way to check
#### if it's been setup correctly
params
# (2) Simulation
## (2.1) Construct the model
### (2.1.1) Case where patient-level data was available
### Use create_PsmCurves.params_flexsurvreg_list() method
surv_input_data <- expand(hesim_dat, by = c("strategies", "patients"))</pre>
psm_curves1 <- create_PsmCurves(fits, input_data = surv_input_data,</pre>
                                n = N_SAMPLES,
                                uncertainty = "normal",
                                est_data = surv_est_data)
### (2.1.2) Case where patient-level data was NOT available
### Use create_PsmCurves.params_surv_list() method
```

88 qalys

```
surv_input_data$intercept <- 1</pre>
surv_input_data$new1 <- ifelse(surv_input_data$strategy_name == "New 1",</pre>
                                1, 0)
psm_curves2 <- create_PsmCurves(params, input_data = surv_input_data)</pre>
## (2.2) Summarize survival models
## There are minor discrepancies between the case where models were fit
## with flexsurvreg() and the case where the "params_surv_list" object
## was constructed manually due to differences in the random draws
## of the parameter samples. These differences are decreasing in the size
## of N_SAMPLES
times \leftarrow seq(0, 10, 1/12) # Monthly times
### Quantiles
head(psm\_curves1$quantile(p = c(.25, .5, .75)))
head(psm\_curves2$quantile(p = c(.25, .5, .75)))
### Survival curves
head(psm_curves1$survival(t = times))
head(psm_curves2$survival(t = times))
### Restricted mean survival
head(psm\_curves1\$rmst(t = c(2, 5)))
head(psm\_curves2\$rmst(t = c(2, 5)))
```

qalys

Quality-adjusted life-years object

Description

An object of class qalys returned from methods \$sim_qalys() in model classes that store simulated quality-adjusted life-years (QALYs).

Components

A qalys object inherits from data. table and contains the following columns:

```
sample A random sample from the PSA.
strategy_id The treatment strategy ID.
patient_id The patient ID.
grp_id The subgroup ID.
state_id The health state ID.
dr The rate used to discount QALYs.
category A single category always equal to "qalys".
qalys The simulated values of QALYs.
```

If the argument lys = TRUE, then the data.table also contains a column lys containing simulated life-years.

qmatrix.matrix 89

ama	tr	1 X	. ma	t.	rıx

Transition intensity matrix from tabular object

Description

Creates transition intensity matrices where elements represent the instantaneous risk of moving between health states.

Usage

```
## S3 method for class 'matrix'
qmatrix(x, trans_mat, ...)
## S3 method for class 'data.table'
qmatrix(x, trans_mat, ...)
## S3 method for class 'data.frame'
qmatrix(x, trans_mat, ...)
```

Arguments

X	A two-dimensional tabular object containing elements of the transition intensity matrix. A column represents a transition from state r to state s . Each row represents elements of a different transition intensity matrix. See "Details" for more information.
trans_mat	Just as in IndivCtstmTrans, a transition matrix describing the states and transitions in a multi-state model.
	Further arguments passed to or from other methods. Currently unused.

Details

The object x must only contain non-zero and non-diagonal elements of a transition intensity matrix. The diagonal elements are automatically computed as the negative sum of the other rows.

Value

An array of transition intensity matrices with the third dimension equal to the number of rows in x.

See Also

```
qmatrix.msm()
```

90 qmatrix.msm

Examples

```
# 3 state irreversible model
tmat <- rbind(c(NA, 1, 2),
              c(NA, NA, 3),
              c(NA, NA, NA))
q12 <- c(.8, .7)
q13 < -c(.2, .3)
q23 <- c(1.1, 1.2)
q <- data.frame(q12, q13, q23)</pre>
qmat <- qmatrix(q, trans_mat = tmat)</pre>
print(qmat)
# Matrix exponential of each matrix in array
expmat(qmat)
```

qmatrix.msm

Transition intensity matrix from msm object

Description

Draw transition intensity matrices for a probabilistic sensitivity analysis from a fitted msm object.

Usage

```
## S3 method for class 'msm'
qmatrix(x, newdata = NULL, uncertainty = c("normal", "none"), n = 1000, ...)
```

Arguments

X	A msm::msm object.
newdata	A data frame to look for variables with which to predict. A separate transition intensity matrix is predicted based on each row in newdata. Can be NULL if no covariates are included in the fitted msm object.
uncertainty	Method used to draw transition intensity matrices. If "none", then point estimates are used. If "normal", then samples are drawn from the multivariate normal distribution of the regression coefficients.
n	Number of random observations of the parameters to draw.
	Further arguments passed to or from other methods. Currently unused.

Value

An array of transition intensity matrices with the third dimension equal to the number of rows in newdata.

See Also

```
qmatrix.matrix()
```

rcat 91

Examples

rcat

Random generation for categorical distribution

Description

Draw random samples from a categorical distribution given a matrix of probabilities. rcat is vectorized and written in C++ for speed.

Usage

```
rcat(n, prob)
```

Arguments

n Number of random observations to draw.

A matrix of probabilities where rows correspond to observations and columns correspond to categories.

Value

A vector of random samples from the categorical distribution. The length of the sample is determined by n. The numerical arguments other than n are recycled so that the number of samples is equal to n.

```
p \leftarrow c(.2, .5, .3)

n \leftarrow 10000

pmat \leftarrow matrix(rep(p, n), nrow = n, ncol = length(p), byrow = TRUE)
```

92 rdirichlet_mat

```
# rcat
set.seed(100)
ptm <- proc.time()
samp1 <- rcat(n, pmat)
proc.time() - ptm
prop.table(table(samp1))

# rmultinom from base R
set.seed(100)
ptm <- proc.time()
samp2 <- t(apply(pmat, 1, rmultinom, n = 1, size = 1))
samp2 <- apply(samp2, 1, function(x) which(x == 1))
proc.time() - ptm
prop.table(table(samp2))</pre>
```

rdirichlet_mat

Random generation for multiple Dirichlet distributions

Description

Draw random samples from multiple Dirichlet distributions for use in transition probability matrices.

Usage

```
rdirichlet_mat(
  n,
  alpha,
  output = c("array", "matrix", "data.frame", "data.table")
)
```

Arguments

n Number of samples to draw.

alpha A matrix where each row is a separate vector of shape parameters.

output The class of the object returned by the function. Either an array, matrix,

data.frame, or data.table.

Details

This function is meant for representing the distribution of transition probabilities in a transition matrix. The (i,j) element of alpha is a transition from state i to state j. It is vectorized and written in C++ for speed.

rng_distributions 93

Value

If output = "array", then an array of matrices is returned where each row of each matrix is a sample from the Dirichlet distribution. If output results in a two dimensional object (i.e., a matrix, data.frame, or data.table, then each row contains all elements of the sampled matrix from the Dirichlet distribution ordered rowwise; that is, each matrix is flattened. In these cases, the number of rows must be less than or equal to the number of columns.

Examples

```
alpha <- matrix(c(100, 200, 500, 50, 70, 75), ncol = 3, nrow = 2, byrow = TRUE)
samp <- rdirichlet_mat(100, alpha)
print(samp[, , 1:2])</pre>
```

rng_distributions

Random number generation distributions

Description

A collection of functions for randomly generating deviates from probability distributions with define_rng().

Usage

```
beta_rng(
  shape1 = 1,
  shape2 = 1,
 mean = NULL,
  sd = NULL,
 names = NULL,
 n = parent.frame()$n
)
dirichlet_rng(alpha, names = NULL, n = parent.frame()$n)
fixed(est, names = NULL, n = parent.frame()$n)
custom(x, names = NULL, n = parent.frame()$n)
gamma_rng(mean, sd, names = NULL, n = parent.frame()$n)
lognormal_rng(meanlog, sdlog, names = NULL, n = parent.frame()$n)
multi_normal_rng(mu, Sigma, names = NULL, n = parent.frame()$n, ...)
normal_rng(mean, sd, names = NULL, n = parent.frame()$n)
uniform_rng(min, max, names = NULL, n = parent.frame()$n)
```

94 rng_distributions

Arguments

shape1, shape2 Non-negative parameters of the Beta distribution. Mean and standard deviation of the random variable. mean, sd Names for columns if an object with multiple columns is returned by the funcnames The number of random samples of the parameters to draw. Default is the value n of n in the environment in which the function is called, which can be useful when used inside define_rng because it means that a value does not need to be explicitly passed to n. alpha A matrix where each row is a separate vector of shape parameters. est A vector of estimates of the variable of interest. A numeric vector, matrix, data.frame, or data.table containing random Х samples of the variable of interest from a suitable probability distribution. This would typically be a posterior distribution from a Bayesian analysis. meanlog, sdlog Mean and standard deviation of the distribution on the log scale. mu, Sigma mu is a vector giving the means of the variables and Sigma is a positive-definite symmetric matrix specifying the covariance matrix of the variables. Additional arguments to pass to underlying random number generation functions. See "details". Lower and upper limits of the distribution. Must be finite. min, max

Details

These functions are not exported and are meant for use with define_rng(). They consequently assume that the number of samples to draw, n, is defined in the parent environment. Convenience random number generation functions include:

- beta_rng() If mean and sd are both not NULL, then parameters of the beta distribution are derived using the methods of moments with mom_beta(). Beta variates are generated with
 stats::rbeta().
- custom() Use previously sampled values from a custom probability distribution. There are three possibilities: (i) if n is equal to the number previously sampled values (say n_samples), then x is returned as is; (ii) if n < n_samples, then samples from x are sampled without replacement; and (iii) if n > n_samples, then samples from x are sampled with replacement and a warning is provided.
- dirichlet_rng() Dirichlet variates for each row in the matrix are generated with rdirichlet_mat(). The sampled values are stored in a data.table where there is a column for each element of alpha (with elements ordered rowwise).
- fixed() This function should be used when values of the variable of interest are fixed (i.e., they
 are known with certainty). If length(est) > 1, an n by length(est) data.table is returned
 meaning that each element of est is repeated n times; otherwise (if length(est) == 1), a
 vector is returned where est is repeated n times.
- gamma_rng() The parameters of the gamma distribution are derived using the methods of moments with mom_gamma() and gamma variates are generated with stats::rgamma().

rpwexp 95

```
lognormal_rng() Lognormal variates are generated with stats::rlnorm().
multi_normal_rng() Multivariate normal variates are generated with MASS::mvrnorm().
normal_rng() Normal variates are generated with stats::rnorm().
uniform_rng() Uniform variates are generated with stats::runif().
```

Value

Functions either return a vector of length n or an n by k data.table. Multivariate distributions always return a data.table. If a univariate distribution is used, then a data.table is returned if each parameter is specified as a vector with length greater than 1; otherwise, if parameters are scalars, then a vector is returned. In the data.table case, k is equal to the length of the parameter vectors entered as arguments. For example, if the probability distribution contained mean as an argument and mean were of length 3, then an n by 3 matrix would be returned. The length of all parameter vectors must be the same. For instance, if the vector mean were of length 3 then all additional parameters (e.g., sd) must also be of length 3.

If a data.table is returned by a distribution, then its column names are set according to the following hierarchy:

- 1. With the names argument if it is not NULL
- 2. With the names of the parameter vectors if they are named vectors. If there are multiple parameter vector arguments, then the names of the first parameter vector with non NULL names is used. For instance, if mean and sd are both arguments to a random number generation function and mean is a named vector, then the names from the vector mean are used.
- 3. As v1, ..., vk if the names argument is NULL and there are no named parameter vectors.

See Also

define_rng()

rpwexp

Random generation for piecewise exponential distribution

Description

Draw random samples from an exponential distribution with piecewise rates. rpwexp is vectorized and written in C++ for speed.

Usage

```
rpwexp(n, rate = 1, time = 0)
```

Arguments

n	Number of random observations to draw.
rate	A matrix of rates where rows correspond to observations and columns correspond to rates during specified time intervals.
time	A vector equal to the number of columns in rate giving the times at which the rate changes

96 set_labels

Value

A vector of random samples from the piecewise exponential distribution. The length of the sample is determined by n. The numerical arguments other than n are recycled so that the number of samples is equal to n.

Examples

set_labels

Set value labels

Description

Update existing variables or create new ones that replace existing values with more informative labels as in factor(). All modifications are performed by reference (see data.table::set() for more information about assignment by reference).

Usage

```
set_labels(x, labels, new_names = NULL, as_factor = TRUE)
```

Arguments

x A data.table.

labels A list of named vectors containing the values and labels of variables. The ele-

ments of each vector are the values of a variable and the names are the labels. The names of the list are the names of the variables. See the output returned by

get_labels() for an example.

new_names A character vector of the same length as labels where each element denotes

the name of a new variable to create for the corresponding element in labels. If NULL, then the variables in labels are modified and no new variables are created; otherwise, the existing variables are not modified and new variables are

created instead.

as_factor If TRUE factor variables are created; otherwise character vectors are created.

Value

x is modified by reference and returned invisibly.

See Also

```
get_labels()
```

Examples

sim_ev

Expected values from state probabilities

Description

Simulate expected values as a function of simulated state occupancy probabilities, with simulation of costs and quality-adjusted life-years (QALYs) as particular use cases.

Usage

```
## S3 method for class 'stateprobs'
sim_ev(
 object,
 models = NULL,
 dr = 0.03,
  integrate_method = c("trapz", "riemann_left", "riemann_right"),
  value_name = "value",
  outcome_name = "outcome",
)
sim_qalys(
  object,
 model,
  dr = 0.03,
  integrate_method = c("trapz", "riemann_left", "riemann_right"),
  lys = TRUE
)
sim_costs(
```

```
object,
models,
dr = 0.03,
integrate_method = c("trapz", "riemann_left", "riemann_right")
```

Arguments

object A stateprobs object.

dr Discount rate.

integrate_method

Method used to integrate state values when computing costs or QALYs. Options are trapz (the default) for the trapezoid rule, riemann_left left for a left

Riemann sum, and riemann_right right for a right Riemann sum.

value_name Name of the column containing values of the outcome. Default is "value".

outcome_name Name of the column indicating the outcome corresponding to each model. Only

used if models is a list. Default is "outcome".

... Currently unused.

model, models An object or list of objects of class StateVals used to model state values. When

using sim_qalys(), this should be a single model for utility. With sim_costs(), a list of models should be used with one model for each cost category. Finally, with sim_ev(), this may either be a single model or a list of models. May also be NULL, in which case length of stay is computed based on the state probabilities

contained in object.

lys If TRUE, then life-years are simulated in addition to QALYs.

Details

Expected values in cohort models (i.e., those implemented with the CohortDtstm and Psm classes) are mean outcomes for patients comprising the cohort. The method used to simulate expected values depends on the \$method field in the StateVals object(s) stored in model(s). If \$method = "starting", then state values represent a one-time value that occurs at time 0.

The more common use case is \$method = "wlos", or a "weighted length of stay". That is, expected values for each health state can be thought of as state values weighted by the time a patient spends in each state (and discounted by a discount factor that depends on the discount rate dr). The precise computation proceeds in four steps. In the first step, the probability of being in each health state at each discrete time point is simulated (this is the output contained in the stateprobs object). Second, a StateVals model is used to predict state values at each time point. Third an expected value at each time point is computed by multiplying the state probability, the state value, and the discount factor. Fourth, the expected values at each time point are summed across all time points.

The summation in the fourth step can be thought of as a discrete approximation of an integral. In particular, the limits of integration can be partitioned into time intervals, with each interval containing a start and an end. The integrate_method argument determines the approach used for this approximation:

 A left Riemann sum (integrate_method = "riemann_left") uses expected values at the start of each time interval.

A right Riemann sum (integrate_method = "riemann_right") uses expected values at the end of each time interval.

3. The trapezoid rule (integrate_method = "trapz") averages expected values at the start and end of each time interval. (This will generally be the most accurate and is recommended.)

Mathematical details are provided in the reference within the "References" section below.

Value

```
sim_ev() returns a data.table with the following columns:
```

sample A random sample from the PSA.

strategy_id The treatment strategy ID.

patient_id The patient ID.

grp_id The subgroup ID.

state id The health state ID.

dr The rate used to discount costs.

outcome The outcome corresponding to each model in models. Only included if models is a list.

value The expected value.

The names of the outcome and value columns may be changed with the value_name and outcome_name arguments. sim_costs() and sim_qalys() return similar objects, that are of class costs and qalys, respectively.

Note

The ID variables in the state value models in models must be consistent with the ID variables contained in object. In particular, the models should predict state values for each non-absorbing health state in object; that is, the number of health states modeled with the models should equal the number of health states in object less the number of absorbing states.

The absorbing states are saved as an attribute named absorbing to stateprobs objects. When simulating state probabilities with a CohortDtstmTrans object, the absorbing state is determined by the absorbing field in the class; in a Psm (or with sim_stateprobs.survival()), the absorbing state is always equal to the final health state.

References

Incerti and Jansen (2021). See Section 2.1 for mathematical details.

See Also

State probabilities can be simulated using the \$sim_stateprobs() methods from either the CohortDtstmTrans (or CohortDtstm) or Psm classes. State probabilities can also be computed directly from survival curves with the generic method sim_stateprobs.survival().

Costs and QALYs are typically computed within the R6 model classes using the \$sim_costs() and \$sim_qalys() methods. For instance, see the documentation and examples for the CohortDtstm and Psm classes. The sim_qalys() and sim_costs() functions are exported to give users additional

flexibility when creating their own modeling pipelines. sim_ev() may be useful for computing outcomes other than costs or QALYs.

costs and qalys objects can be passed to summarize_ce() to create a cost-effectiveness object for performing a cost-effectiveness analysis with cea(). Although note that typically the \$summarize() method belonging to the CohortDtstm or Psm classes would be used instead.

Use the IndivCtstm class to simulate costs and QALYs with an individual continuous-time state transition model.

```
# We need (i) a state probability object and (ii) a model for state values
## We should start by setting up our decision problem
hesim_dat <- hesim_data(strategies = data.frame(strategy_id = 1:2),</pre>
                          patients = data.frame(patient_id = 1:3),
                          states = data.frame(state_id = 1))
input_data <- expand(hesim_dat, by = c("strategies", "patients"))</pre>
## (i) Simulate a state probability object
tpmat_id <- tpmatrix_id(input_data, n_samples = 2)</pre>
p_12 <- ifelse(tpmat_id$strategy_id == 1, .15, .1)</pre>
tpmat <- tpmatrix(</pre>
 C, p_12,
 0, 1
transmod <- CohortDtstmTrans$new(params = tparams_transprobs(tpmat, tpmat_id))</pre>
stprobs <- transmod$sim_stateprobs(n_cycles = 3)</pre>
## Construct model for state values
outcome_tbl <- stateval_tbl(</pre>
 data.frame(
   state_id = 1,
    est = 5000
 ),
 dist = "fixed"
)
outmod <- create_StateVals(outcome_tbl, n = 2, hesim_data = hesim_dat)</pre>
# We can then simulate expected values
## The generic expected values function
sim_ev(stprobs, models = outmod)
## We can also pass a list of models
sim_ev(stprobs, models = list(`Outcome 1` = outmod))
## Suppose the outcome were a cost category. Then we might
## prefer the following:
sim_costs(stprobs, models = list(drug = outmod))
## Length of stay is computed if there is no state value model
sim_ev(stprobs)
```

sim_stateprobs.survival 101

```
sim_stateprobs.survival
```

Simulate state probabilities from survival curves

Description

Simulate health state probabilities from a survival object using partitioned survival analysis.

Usage

```
## S3 method for class 'survival'
sim_stateprobs(x, ...)
```

Arguments

x An object of class survival.

... Further arguments passed to or from other methods.

Details

In an N-state partitioned survival model there are N-1 survival curves and $S_n(t)$ is the cumulative survival function denoting the probability of survival to health state n or a lower indexed state beyond time t. The probability that a patient is in health state 1 at time t is simply $S_1(t)$. State membership in health states $2,\ldots,N-1$ is calculated as $S_n(t)-S_{n-1}(t)$. Finally, the probability of being in the final health state N (i.e., the death state) is $1-S_{N-1}(t)$, or one minus the overall survival curve.

In some cases, the survival curves may cross. hesim will issue a warning but the function will still run. Probabilities will be set to 0 in a health state if the prior survival curve lies above the curve for state n; that is, if $S_n(t) < S_{n-1}(t)$, then the probability of being in state n is set to 0 and $S_n(t)$ is adjusted to equal $S_{n-1}(t)$. The probability of being in the final health state is also adjusted if necessary to ensure that probabilities sum to 1.

Value

A stateprobs object.

See Also

survival

```
library("data.table")
library("survival")

# This example shows how to simulate a partitioned survival model by
# manually constructing a "survival" object. We will consider a case in which
# Cox proportional hazards models from the survival package---which are not
```

```
# integrated with hesim---are used for parameter estimation. We will use
# point estimates in the example, but bootstrapping, Bayesian modeling,
# or other techniques could be used to draw samples for a probabilistic
# sensitivity analysis.
# (0) We first setup our model per usual by defining the treatment strategies,
# target population, and health states
hesim_dat <- hesim_data(</pre>
 strategies = data.table(strategy_id = 1:3,
                           strategy_name = c("SOC", "New 1", "New 2")),
 patients = data.table(patient_id = 1:2,
                         female = c(0, 1),
                         grp_id = 1),
 states = data.table(state_id = 1:2,
                       state_name = c("Stable", "Progression"))
)
# (1) Next we will estimate Cox models with survival::coxph(). We illustrate
# by predicting progression free survival (PFS) and overall survival (OS)
## Fit models
onc3_pfs_os <- as_pfs_os(onc3, patient_vars = c("patient_id", "female",</pre>
                                                  "strategy_name"))
fit_pfs <- coxph(Surv(pfs_time, pfs_status) ~ strategy_name + female,</pre>
                 data = onc3_pfs_os)
fit_os <- coxph(Surv(os_time, pfs_status) ~ strategy_name + female,</pre>
                data = onc3_pfs_os)
## Predict survival on input data
surv_input_data <- expand(hesim_dat)</pre>
times <- seq(0, 14, 1/12)
predict_survival <- function(object, newdata, times) {</pre>
 surv <- summary(survfit(object, newdata = newdata, se.fit = FALSE),</pre>
                  t = times)
 pred <- newdata[rep(seq_len(nrow(newdata)), each = length(times)), ]</pre>
 pred[, sample := 1] # Point estimates only in this example
 pred[, time := rep(surv$time, times = nrow(newdata))]
 pred[, survival := c(surv$surv)]
 return(pred[, ])
pfs <- predict_survival(fit_pfs, newdata = surv_input_data, times = times)</pre>
os <- predict_survival(fit_os, newdata = surv_input_data, times = times)
surv <- rbind(</pre>
 as.data.table(pfs)[, curve := 1L],
 as.data.table(os)[, curve := 2L]
)
## Convert predictions to a survival object
surv <- survival(surv, t = "time")</pre>
## Not run: autoplot(surv)
# (2) We can then compute state probabilities from the survival object
stprobs <- sim_stateprobs(surv)</pre>
```

103 stateprobs

```
# (3) Finally, we can use the state probabilities to compute QALYs and costs
## A dummy utility model to illustrate
utility_tbl <- stateval_tbl(
  data.table(state_id = 1:2,
             est = c(1, 1)
  dist = "fixed"
utilitymod <- create_StateVals(utility_tbl,</pre>
                                 hesim_data = hesim_dat,
                                 n = 1
## Instantiate Psm class and compute QALYs
psm <- Psm$new(utility_model = utilitymod)</pre>
psm$stateprobs_ <- stprobs</pre>
psm$sim_qalys()
psm$qalys_
```

stateprobs

State probability object

Description

An object of class stateprobs returned by sim_stateprobs() or from \$sim_stateprobs() methods in model classes.

Components

A stateprobs object inherits from data, table and contains the following columns:

```
sample A random sample from the PSA.
strategy_id The treatment strategy ID.
patient_id The patient ID.
grp_id The subgroup ID.
state_id The health state ID.
```

t The time at which a state probability is computed.

prob The probability of being in a given health state.

When simulating individual-level models, the patient_id column is not included as state probabilities are computed by averaging across patients.

In cohort models, the object also contains size and absorbing attributes. The size attribute is a numeric vector with the elements n_samples, n_strategies, n_patients, n_states, and n_times denoting the number of samples, treatment strategies, patients, health states, and times. The absorbing attribute is a numeric vector containing the absorbing health states (see the absorbing field of the CohortDtstmTrans class for more details).

104 State Vals

StateVals

Model for state values

Description

Simulate values (i.e., utility or costs) associated with health states in a state transition or partitioned survival model.

Public fields

params Parameters for simulating state values. Currently supports objects of class tparams_mean or params_lm.

input_data An object of class input_mats. Only used for params_lm objects.

method The method used to simulate costs and quality-adjusted life-years (QALYs) as a function of state values. If wlos, then costs and QALYs are simulated by weighting state values by the length of stay in a health state. If starting, then state values represent a one-time value that occurs when a patient enters a health state. When starting is used in a cohort model, the state values only accrue at time 0; in contrast, in an individual-level model, state values accrue each time a patient enters a new state and are discounted based on time of entrance into that state.

time_reset If FALSE then time intervals are based on time since the start of the simulation. If TRUE, then time intervals reset each time a patient enters a new health state. This is relevant if, for example, costs vary over time within health states. Only used if method = wlos.

Methods

Public methods:

- StateVals\$new()
- StateVals\$sim()
- StateVals\$check()
- StateVals\$clone()

Method new(): Create a new StateVals object.

```
Usage:
StateVals$new(
   params,
   input_data = NULL,
   method = c("wlos", "starting"),
   time_reset = FALSE
)
Arguments:
params The params field.
input_data The input_data field.
method The method field.
```

State Vals 105

```
time_reset The time_reset field.
Returns: A new StateVals object.
```

Method sim(): Simulate state values with either predicted means or random samples by treatment strategy, patient, health state, and time t.

```
nent strategy, patient, health state, and time t.

Usage:
StateVals$sim(t, type = c("predict", "random"))

Arguments:
t A numeric vector of times.
type "predict" for mean values or "random" for random samples.

Returns: A data.table of simulated state values with columns for sample, strategy_id, patient_id, state_id, time, and value.
```

Method check(): Input validation for class. Checks that fields are the correct type.

Usage:

StateVals\$check()

Method clone(): The objects of this class are cloneable with this method.

Usage:

StateVals\$clone(deep = FALSE)

Arguments:

deep Whether to make a deep clone.

```
# Simple sick-sicker example where drug costs vary by treatment strategy
# and over time. Prior to time = 5, costs are $10,000 for treatment strategy
# 1 and $5,000 for treatment strategy 2. After time = 5, costs are $2,000
# for both treatment strategies
## Setup the model
hesim_dat <- hesim_data(</pre>
  strategies = data.frame(strategy_id = c(1, 2)),
  patients = data.frame(patient_id = 1:3),
  states = data.frame(state_id = c(1, 2), # Non-death states
                      state_name = c("sick", "sicker"))
)
## Drug costs vary by health state and time interval
drugcost_tbl <- stateval_tbl(</pre>
  data.frame(
   strategy_id = c(1, 1, 2, 2),
   time_start = c(0, 5, 0, 5),
   est = c(10000, 2000, 5000, 2000)
  dist = "fixed"
drugcost_tbl
```

106 stateval_tbl

```
## Create drug cost model
drugcostmod <- create_StateVals(drugcost_tbl, n = 1, hesim_data = hesim_dat)
## Explore predictions from the drug cost model
drugcostmod$sim(t = c(2, 6), type = "predict")</pre>
```

stateval_tbl

Table to store state value parameters

Description

Create a table for storing parameter estimates used to simulate costs or utility in an economic model by treatment strategy, patient, health state, and (optionally) time interval.

Usage

```
stateval_tbl(
  tbl,
  dist = c("norm", "beta", "gamma", "lnorm", "unif", "fixed", "custom"),
  hesim_data = NULL,
  grp_var = NULL
)
```

Arguments

tbl	A data.frame or data.table for storing parameter values. See "Details" for specifics.
dist	Probability distribution used to sample parameters for a probabilistic sensitivity analysis (PSA).
hesim_data	A hesim_data object. This argument is deprecated and should be passed to create_StateVals.stateval_tbl() instead.
grp_var	The name of the variable used to group patients.

Details

tbl is a tabular object containing columns for treatment strategies (strategy_id), patients (patient_id), health states (state_id), and/or the start of time intervals (time_start). The table must contain at least one column named strategy_id, patient_id, or state_id, but does not need to contain all of them. Each row denotes a unique treatment strategy, patient, health state, and/or time interval pair. tbl may also contain a column with the name specified in grp_var (rather than patient_id) so that state values are assigned to groups of patients.

tbl must also contain columns summarizing the state values for each row, which depend on the probability distribution selected with dist. Available distributions include the normal (norm), beta (beta), gamma (gamma), lognormal (lnorm), and uniform (unif) distributions. In addition, the option fixed can be used if estimates are known with certainty and custom can be used if parameter

stateval_tbl 107

values for a PSA have been previously sampled from an arbitrary probability distribution. The columns in tbl that must be included, by distribution, are:

norm mean and sd

beta mean and se or shape1 and shape2

gamma mean and se, shape and rate, or shape and scale

lnorm meanlog or sdlog

unif min and max

fixed est

custom sample and value

Note that if dist = "custom", then tbl must include a column named sample (an integer vector denoting a unique random draw) and value (denoting the value of the randomly sampled parameter). In this case, there is a unique row in tbl for each random draw (sample) and each combination of strategies, patients, health states, and/or time intervals. Again, tbl must contain at least one column named strategy_id, patient_id (or grp_var), or state_id, but does not need to contain them all.

Value

An object of class stateval_tbl, which is a data.table of parameter values with attributes for dist and grp_var.

See Also

```
create_StateVals(), StateVals
```

```
strategies <- data.frame(strategy_id = c(1, 2))</pre>
patients <- data.frame(patient_id = seq(1, 3),</pre>
                        grp = c(1, 1, 2),
                        age = c(45, 50, 60),
                        female = c(0, 0, 1)
states <- data.frame(state_id = c(1, 2))</pre>
hesim_dat <- hesim_data(strategies = strategies,</pre>
                         patients = patients,
                         states = states)
# Utility varies by health state and patient group
utility_tbl <- stateval_tbl(data.frame(state_id = rep(states$state_id, 2),
                                         grp = rep(rep(c(1, 2)), each = nrow(states)),
                                         mean = c(.8, .7, .75, .55),
                                         se = c(.18, .12, .10, .06)),
                             dist = "beta",
                             grp_var = "grp")
print(utility_tbl)
utilmod <- create_StateVals(utility_tbl, n = 2, hesim_data = hesim_dat)</pre>
```

108 summary.ce

summary.ce

Summary method for cost-effectiveness object

Description

Summarize a ce object by producing confidence intervals for quality-adjusted life-years (QALYs) and each cost category with summary.ce() and format for pretty printing with format.summary.ce().

Usage

```
## S3 method for class 'ce'
summary(object, prob = 0.95, labels = NULL, ...)

## S3 method for class 'summary.ce'
format(
    x,
    digits_qalys = 2,
    digits_costs = 0,
    dr_qalys = NULL,
    dr_costs = NULL,
    pivot_from = "strategy",
    drop_grp = TRUE,
    pretty_names = TRUE,
    ...
)
```

Arguments

object	A ce object.
prob	A numeric scalar in the interval (0,1) giving the confidence interval. Default is 0.95 for a 95 percent interval.
labels	A list of named vectors containing the values and labels of variables. The elements of each vector are the values of a variable and the names are the labels. The names of the list are the names of the variables. See the output returned by get_labels() for an example.
	Further arguments passed to or from other methods. Currently unused.
.,	A commence of this of

x A summary.ce object.

summary.ce 109

digits_qalys Number of digits to use to report QALYs.

digits_costs Number of digits to use to report costs.

dr_qalys Discount rate to subset to for quality-adjusted life-years (QALYs).

dr_costs Discount rate to subset to for costs.

pivot_from Character vector denoting a column or columns used to "widen" the data. Should

either be "strategy", "grp", "outcome", or some combination of the three. There will be one column for each value of the variables in pivot_from. Default is to widen so there is a column for each treatment strategy. Set to NULL if you

do not want to widen the table.

drop_grp If TRUE, then the group column will be removed if there is only one subgroup;

other it will be kept. If FALSE, then the grp column is never removed.

pretty_names Logical. If TRUE, then the columns strategy, grp, outcome, dr, and value

are renamed (if they exist) to Strategy, Group, Outcome, Discount rate, and

Value.

Details

For an example, see IndivCtstm.

Value

summary.ce() returns an object of class summary.ce that is a tidy data.table with the following columns:

dr The discount rate.

strategy The treatment strategy.

grp The patient subgroup.

type Either "QALYs" or "Costs".

category Category is always "QALYs" when type == "QALYs"; otherwise, it is the cost category.

estimate The point estimate computed as the average across the PSA samples.

lower The lower limit of the confidence interval.

upper The upper limit of the confidence interval.

format.summary.ce() formats the table according to the arguments passed.

110 summary.eval_rng

ng <i>object</i>	
------------------	--

Description

Summarize the model parameters randomly sampled for probabilistic sensitivity analysis with eval_rng().

Usage

```
## S3 method for class 'eval_rng'
summary(object, probs = c(0.025, 0.975), sep = "_", ...)
## S3 method for class 'eval_rng'
print(x, ...)
```

Arguments

object, x	An eval_rng object.
probs	A numeric vector of probabilities with values in $[0,1]$ used to compute quantiles with stats::quantile().
sep	When a list element returned by eval_rng is a tabular object, the parameter name is created by concatenating the name of the list element with the columns of the tabular object. The sep argument determines the character string used to separate the terms.
	For the print method, arguments to pass to summary.eval_rng().

Value

summary.eval_rng() returns a data.table::data.table with columns for (i) the name of the parameter (param), (ii) the mean of the parameter samples (mean), (iii) the standard deviation of the parameter samples (sd), and (iv) quantiles of the parameter samples corresponding to the probs argument.print.eval_rng() prints the output of summary.eval_rng() to the console.

See Also

See eval_rng() for an example.

summary.params 111

summary.params

Summarize parameter objects

Description

Summarize the coefficients of a parameter object by computing the mean, standard deviation, and quantiles for each model term. This is a convenient way to check whether a parameter object has been specified correctly and sampling distributions of the coefficients are as expected.

Usage

```
## S3 method for class 'params_lm'
summary(object, probs = c(0.025, 0.975), ...)
## S3 method for class 'params_mlogit'
summary(object, probs = c(0.025, 0.975), ...)
## S3 method for class 'params_mlogit_list'
summary(object, probs = c(0.025, 0.975), ...)
## S3 method for class 'params_surv'
summary(object, probs = c(0.025, 0.975), ...)
## S3 method for class 'params_surv_list'
summary(object, probs = c(0.025, 0.975), ...)
```

Arguments

object	An object of the appropriate class.
probs	A numeric vector of probabilities with values in [0,1] used to compute quantiles. By default, the 2.5th and 97.5th percentiles are computed.
	Additional arguments affecting the summary. Currently unused.

Value

A data.table::data.table that always contains the following columns:

term The regression term.

mean The mean value of the regression term.

sd The standard deviation of the values of the regression term.

In addition, the probs argument determines the quantiles that are computed. By default, the columns 2.5% and 97.5% are returned corresponding to the 2.5th and 97.5th percentiles.

Finally, the following columns may also be present:

parameter The name of the parameter of interest. This is relevant for any parametric model in which the underlying probability distribution has multiple parameters. For instance, both params_surv and params_surv_list store regression coefficients that are used to model the underlying parameters of the survival distribution (e.g., shape and scale for a Weibull model). Similarly, there are two parameters (mean and sd) for params_lm objects.

model The name of the statistical model. This is used for a params_surv_list object, where each list element represents a separate model. In a state transition model, each model is a unique health state transition and in a partitioned survival model, there is a separate model for each curve.

to The health state that is being transitioned to. In params_mlogit and params_mlogit_list objects, there are coefficients for each health state that can be transitioned to.

from The health state that is being transitions from. This is used for a params_mlogit_list objects where a different multinomial logistic regression is used for each state that can be transitioned from.

See Also

For examples, see the underlying parameter object functions: params_lm(), params_surv(), params_surv_list(), params_mlogit(), and params_mlogit_list().

```
summary.tparams_mean Summarize tparams_mean object
```

Description

The summary() method summarizes a tparams_mean object containing predicted means; summary statistics are computed for each combination of the ID variables. The print() method summarizes the object using summary.tparams_mean() and prints it to the console.

Usage

```
## $3 method for class 'tparams_mean'
summary(object, probs = c(0.025, 0.975), ...)
## $3 method for class 'tparams_mean'
print(x, ...)
```

Arguments

```
object, x A tparams_mean object.

A numeric vector of probabilities with values in [0,1] used to compute quantiles. By default, the 2.5th and 97.5th percentiles are computed.

Currently unused.
```

Value

A data.table with columns for (i) the ID variables, (ii) the mean of each parameter across parameter samples (mean), (iii) the standard deviation of the parameter samples (sd), and (iv) quantiles of the parameter samples corresponding to the probs argument.

See Also

See tparams_mean for an example use of the summary and print methods.

```
summary.tparams_transprobs 
 Summarize \ \ \ \ transprobs \ \ object
```

Description

The summary() method summarizes a tparams_transprobs object containing predicted transition probabilities; summary statistics are computed for each possible transition by the relevant ID variables.

Usage

```
## S3 method for class 'tparams_transprobs'
summary(object, probs = NULL, unflatten = FALSE, ...)
```

Arguments

object A tparams_transprobs object.

probs A numeric vector of probabilities with values in [0,1] used to compute quan-

tiles. Computing quantiles can be slow when object is large, so the default is

NULL, meaning that no quantiles are computed.

unflatten If FALSE, then each column containing a summary statistic is a vector and the

generated table contains one row (for each set of ID variables) for each possible transition; if TRUE, then each column stores a list of matrix objects containing transition probability matrices formed by "unflattening" the one-dimensional

vectors. See "Value" below for additional details.

... Additional arguments affecting the summary. Currently unused.

Value

If unflatten = "FALSE" (the default), then a data.table::data.table is returned with columns for (i) the health state that is being transitioned from (from), (ii) the health state that is being transitioned to (to) (iii) the mean of each parameter across parameter samples (mean), (iv) the standard deviation of the parameter samples (sd), and (v) quantiles of the parameter samples corresponding to the probs argument.

If, on the other hand, unflatten = "TRUE", then the parameters are unflattened to form transition probability matrices; that is, the mean, sd, and quantile columns are (lists of) matrices.

In both cases, the ID variables are also returned as columns.

114 summary.tpmatrix

See Also

See tparams_transprobs for an example use of the summary method.

summary.tpmatrix

Summarize transition probability matrix

Description

Summarize a tpmatrix object storing transition probability matrices. Summary statistics are computed for each possible transition.

Usage

```
## S3 method for class 'tpmatrix'
summary(object, id = NULL, probs = NULL, unflatten = FALSE, ...)
```

Arguments

object	A tpmatrix object.
id	A tpmatrix_id object for which columns contain the ID variables for each row in object. If not NULL, then transition probability matrices are summarized by the ID variables in id.
probs	A numeric vector of probabilities with values in $[0,1]$ used to compute quantiles. Computing quantiles can be slow when object is large, so the default is NULL, meaning that no quantiles are computed.
unflatten	If FALSE, then each column containing a summary statistic is a vector and the generated table contains one row (for each set of ID variables) for each possible transition; if TRUE, then each column stores a list of matrix objects containing transition probability matrices formed by "unflattening" the one-dimensional vectors. See "Value" below for additional details.
	Additional arguments affecting the summary. Currently unused.

Value

If unflatten = "FALSE" (the default), then a data.table::data.table is returned with columns for (i) the health state that is being transitioned from (from), (ii) the health state that is being transitioned to (to) (iii) the mean of each parameter across parameter samples (mean), (iv) the standard deviation of the parameter samples (sd), and (v) quantiles of the parameter samples corresponding to the probs argument.

If, on the other hand, unflatten = "TRUE", then the parameters are unflattened to form transition probability matrices; that is, the mean, sd, and quantile columns are (lists of) matrices.

In both cases, if id is not NULL, then the ID variables are also returned as columns.

survival 115

Examples

```
library("data.table")
hesim_dat <- hesim_data(strategies = data.table(strategy_id = 1:2),</pre>
                                  patients = data.table(patient_id = 1:3))
input_data <- expand(hesim_dat, by = c("strategies", "patients"))</pre>
# Summarize across all rows in "input_data"
p_12 <- ifelse(input_data$strategy_id == 1, .8, .6)</pre>
p <- tpmatrix(</pre>
 C, p_{12}
  0, 1
)
## Summary where each column is a vector
summary(p)
summary(p, probs = c(.025, .975))
## Summary where each column is a matrix
ps <- summary(p, probs = .5, unflatten = TRUE)</pre>
ps
ps$mean
# Summarize by ID variables
tpmat_id <- tpmatrix_id(input_data, n_samples = 2)</pre>
p_12 <- ifelse(tpmat_id$strategy_id == 1, .8, .6)</pre>
p <- tpmatrix(</pre>
  C, p_12,
  0, 1
)
## Summary where each column is a vector
summary(p, id = tpmat_id)
## Summary where each column is a matrix
ps <- summary(p, id = tpmat_id, unflatten = TRUE)</pre>
ps
ps$mean
```

survival

Survival object

Description

An object of class survival stores survival probabilities. It is typically returned by Psm\$sim_survival() or PsmCurves\$survival(); however, it can also be constructed "manually" from existing data using the survival() function as described below. The latter option is useful if survival modeling has been performed by an R package other than those that integrate with hesim(currently flexsurv). In this case a simulation model can still be developed by using sim_stateprobs.survival() to compute simulated state probabilities and then simulating quality-adjusted life-years and costs in a typical fashion.

116 survival

Usage

```
survival(
  data,
  sample = "sample",
  strategy_id = "strategy_id",
  patient_id = "patient_id",
  grp_id = "grp_id",
  curve = "curve",
  t = "t",
  survival = "survival"
)
```

Arguments

data A tabular object that can be coerced to a data.table with as.data.table(). The name of the column corresponding to sample. sample strategy_id The name of the column corresponding to strategy_id. patient_id The name of the column corresponding to patient_id. The name of the column corresponding to grp_id. grp_id The name of the column corresponding to curve. curve t. The name of the column corresponding to t. survival The name of the column corresponding to survival.

Value

An object of class survival that inherits from data. table and contains the following columns:

```
sample A random sample from the PSA.
```

strategy_id The treatment strategy ID.

patient id The patient ID.

grp_id The subgroup ID.

curve One of the N-1 survival curves in an N-state partitioned survival model. Each curve corresponds to unique endpoint.

t The time at which a survival probability is computed.

survival The probability of surviving to time t.

The object also contains a size attribute that contains the elements n_samples, n_strategies, n_patients, n_states, and n_times denoting the number of samples, treatment strategies, patients, health states, and times.

See Also

survival objects are returned by methods in the Psm and PsmCurves classes. An example in which a survival object is constructed "manually" (presumably from a preexisting survival model fit using software other than flexsurv) is provided in the documentation to sim_stateprobs.survival().

surv_quantile 117

surv_quantile	Survival quantiles
---------------	--------------------

Description

Compute quantiles from survival curves.

Usage

```
surv_quantile(x, probs = 0.5, t, surv_cols, by)
```

Arguments

x	A data.table or data.frame.
probs	A numeric vector of probabilities with values in [0,1].
t	A character scalar of the name of the time column.
surv_cols	A character vector of the names of columns containing survival curves.
by	A character vector of the names of columns to group by.

Value

A data.table of quantiles of each survival curve in surv_cols by each group in by.

Examples

time_intervals

Time intervals

Description

Create a table of time intervals given a vector or data frame of unique times. This would typically be passed to id_attributes.

118 tparams

Usage

```
time_intervals(times)
```

Arguments

times

Either a vector of starting times for each interval or a data. frame with at least one column named time_start.

Value

An object of class time_intervals that inherits from data.table in the same format as time_intervals as described in id_attributes.

See Also

id attributes

Examples

```
\label{eq:time_intervals} \begin{tabular}{ll} time_intervals(c(0, 3, 5)) \\ time_intervals(data.frame(time_start = c(0, 3, 5), \\ time_cat = c("Time <= 3", "3 < Time <= 5", \\ "Time > 5"))) \end{tabular}
```

tparams

Transformed parameter object

Description

Objects prefixed by "tparams_" are lists containing transformed parameters used to simulate outcomes. The parameters have presumably already been transformed as a function of input data and consequently do not need to be used alongside input matrices. In other words, transformed parameters are parameters that have already been predicted as a function of covariates.

See Also

params

tparams_mean 119

tparams_mean

Predicted means

Description

Create a list containing means predicted from a statistical model.

Usage

```
tparams_mean(value, ...)
```

Arguments

value Matrix of samples from the distribution of the mean. Columns denote random

samples and rows denote means for different observations.

Arguments to pass to id_attributes. Each row in value must be a prediction for a strategy_id, patient_id, state_id, and optionally time_id combination.

Value

An object of class tparams_mean, which is a list containing value, n_samples, and the ID attributes passed to id attributes.

Note

The tparams_mean() constructor would not normally be used by users; instead, a tparams_mean object is typically created automatically as part of the StateVals class with create_StateVals().

See Also

A tparams_mean object is a type of transformed parameter object and is a supported class type of the params field of the StateVals class. See the documentation for create_StateVals() and stateval_tbl() for examples of how to createStateVals objects. Predicted means can be summarized across parameter samples using summary.tparams_mean().

```
# Setup model
hesim_dat <- hesim_data(
    strategies = data.frame(strategy_id = c(1, 2)),
    patients = data.frame(patient_id = c(1, 2)),
    states = data.frame(
        state_id = c(1, 2, 3),
        state_name = c("state1", "state2", "state3")
)
# Cost model</pre>
```

120 tparams_transprobs

tparams_transprobs

Transition probabilities

Description

Create a list containing predicted transition probabilities at discrete times. Since the transition probabilities have presumably already been predicted based on covariate values, no input data is required for simulation. The class can be instantiated from either an array, a data.table, a data.frame, or a tpmatrix. This is the object in hesim used to specify the transition probabilities required to simulate Markov chains with the CohortDtstmTrans class.

Usage

```
tparams_transprobs(object, ...)

## S3 method for class 'array'
tparams_transprobs(
  object,
  tpmatrix_id = NULL,
  times = NULL,
  grp_id = NULL,
  patient_wt = NULL,
  ...
)

## S3 method for class 'data.table'
tparams_transprobs(object, ...)

## S3 method for class 'data.frame'
tparams_transprobs(object, ...)

## S3 method for class 'tpmatrix'
tparams_transprobs(object, tpmatrix_id, ...)
```

tparams_transprobs 121

Arguments

object An object of the appropriate class.

... Further arguments passed to or from other methods. Currently unused.

tpmatrix_id An object of class tpmatrix_id (or an equivalent data.table with the same

ID columns as returned by tpmatrix_id()).

times An optional numeric vector of distinct times to pass to time intervals represent-

ing time intervals indexed by the 4th dimension of the array. May either be the start or the end of intervals. This argument is not required if there is only one

time interval.

grp_id An optional numeric vector of integers denoting the subgroups. Must be the

same length as the 3rd dimension of the array.

patient_wt An optional numeric vector denoting the weight to apply to each patient within

a subgroup. Must be the same length as the 3rd dimension of the array.

Details

The format of object depends on its class:

array Either a 3D or a 6D array is possible.

• If a 3D array, then each slice is a square transition probability matrix. In this case tpmatrix_id is required and each matrix slice corresponds to the same numbered row in tpmatrix_id. The number of matrix slices must equal the number of rows in tpmatrix_id.

• If a 6D array, then the dimensions of the array should be indexed as follows: 1st (sample), 2nd (strategy_id), 3rd (patient_id), 4th (time_id), 5th (rows of transition matrix), and 6th (columns of transition matrix). In other words, an index of [s, k, i, t] represents the transition matrix for the sth sample, kth treatment strategy, ith patient, and tth time interval.

data.table Must contain the following:

- ID columns for the parameter sample (sample), treatment strategy (strategy_id), and patient (patient_id). If the number of time intervals is greater than 1 it must also contain the column time_start denoting the starting time of a time interval. A column patient_wt may also be used to denote the weight to apply to each patient.
- Columns for each element of the transition probability matrix. They should be prefixed with "prob_" and ordered rowwise. For example, the following columns would be used for a 2x2 transition probability matrix: prob_1 (1st row, 1st column), prob_2 (1st row, 2nd column), prob_3 (2nd row, 1st column), and prob_4 (2nd row, 2nd column).

data.frame Same as data.table.

tpmatrix An object of class tpmatrix.

A tparams_transprobs object is also instantiated when creating a cohort discrete time state transition model using define_model().

Value

An object of class tparams_transprobs, which is a list containing value and relevant ID attributes. The element value is an array of predicted transition probability matrices from the probability distribution of the underlying statistical model. Each matrix in value is a prediction for a sample, strategy_id, patient_id, and optionally time_id combination.

122 tparams_transprobs

See Also

A tparams_transprobs object is used to store the "parameters" of the transition component of a cohort discrete time state transition model (cDTSTM). You can create such an object with CohortDtstmTran\$new().

tpmatrix() and tpmatrix_id() provide a convenient way to construct a tparams_transprobs object in a flexible way. define_model() is, in turn, a convenient way to construct a tpmatrix object using mathematical expressions; in this case, an entire cDTSTM can be instantiated from a model definition using create_CohortDtstm.model_def(). Detailed examples are provided in vignette("markov-cohort") and vignette("markov-inhomogeneous-cohort")

The output of a tparams_transprobs object is rather verbose. It can be helpful to check the output by converting it to a data.table (containing both the ID variables and flattened transition probability matrices) with as.data.table.tparams_transprobs(). Transition probabilities can also be summarized (across parameter samples) using summary.tparams_transprobs().

```
hesim_dat <- hesim_data(strategies = data.frame(strategy_id = 1:2),</pre>
                         patients = data.frame(patient_id = 1:3))
input_data <- expand(hesim_dat, by = c("strategies", "patients"))</pre>
# tpmatrix objects provide a convenient way to construct
# tparams_transprobs() objects
tpmat_id <- tpmatrix_id(input_data, n_samples = 2)</pre>
p_12 \leftarrow runif(nrow(tpmat_id), .6, .7) +
  .05 * (tpmat_id$strategy_id == 2)
tpmat <- tpmatrix(</pre>
 C, p_12,
 0, 1
)
tprobs <- tparams_transprobs(tpmat, tpmat_id)</pre>
names(tprobs) # Names of list elements
# Convert to data.table in wide format
as.data.table(tprobs)
# Convert to data.table in long format
as.data.table(tprobs, long = TRUE)
# Summary where each column is a vector
summary(tprobs)
summary(tprobs, probs = c(.025, .975))
# Summary where each column is a matrix
ps <- summary(tprobs, id = tpmat_id, unflatten = TRUE)</pre>
ps
ps$mean
```

tpmatrix 123

tpmatrix

Transition probability matrix

Description

tpmatrix() both defines and evaluates a transition probability matrix in which elements are expressions. It can be used within define_tparams() to create a transition probability matrix or directly to create a tparams_transprobs() object. These are, in turn, ultimately used to create a CohortDtstmTrans object for simulating health state transitions.

Usage

```
tpmatrix(..., complement = NULL, states = NULL, prefix = "", sep = "_")
```

Arguments

. . .

Named values of expressions defining elements of the matrix. Each element of ... should either be a vector or a 2-dimensional tabular object such as a data frame. See "Details" and the examples below.

complement

Either a character vector or a numeric vector denoting the transitions (i.e., the columns of the tabular object formed from ...) that are complementary (see "Details" below). If a character vector, each element should be the name of a column in the tabular object; if a numeric vector, each element should be the index of a column in the tabular object.

states, prefix, sep

Arguments passed to tpmatrix_names() for naming the columns. If states = NULL (the default), then the states are named s1, ..., sh where h is the number of health states.

Details

A tpmatrix is a 2-dimensional tabular object that stores flattened square transition probability matrices in each row. Each transition probability matrix is filled rowwise. The complementary probability (equal to 1 minus the sum of the probabilities of all other elements in a row of a transition probability matrix) can be conveniently referred to as C or specified with the complement argument. There can only be one complement for each row in a transition probability matrix.

Value

Returns a tpmatrix object that inherits from data. table where each column is an element of the transition probability matrix with elements ordered rowwise.

See Also

A tpmatrix is useful because it provides a convenient way to construct a tparams_transprobs object, which is the object in hesim used to specify the transition probabilities required to simulate

124 tpmatrix

Markov chains with the CohortDtstmTrans class. See the tparams_transprobs documentation for more details.

The summary.tpmatrix() method can be used to summarize a tpmatrix across parameter samples.

```
p_12 \leftarrow c(.7, .6)
tpmatrix(
  C, p_12,
  0, 1
)
tpmatrix(
 C, p_12,
  C, 1
)
# Pass matrix
pmat \leftarrow matrix(c(.5, .5, .3, .7), byrow = TRUE, ncol = 4)
tpmatrix(pmat)
# Pass vectors and data frames
p1 <- data.frame(</pre>
 p_12 = c(.7, .6),
 p_13 = c(.1, .2)
p2 <- data.frame(</pre>
  p_21 = 0,
 p_22 = c(.4, .45),
 p_23 = c(.6, .55)
p3 <- data.frame(
 p_31 = c(0, 0),
 p_32 = c(0, 0),
 p_33 = c(1, 1)
tpmatrix(
 C, p1,
 p2,
 р3
)
# Use the 'complement' argument
pmat \leftarrow data.frame(s1\_s1 = 0, s1\_s2 = .5, s2\_s1 = .3, s2\_s2 = 0)
tpmatrix(pmat, complement = c("s1_s1", "s2_s2"))
tpmatrix(pmat, complement = c(1, 4)) # Can also pass integers
# Can control column names
```

tpmatrix_id 125

tpmatrix_id

Transition probability matrix IDs

Description

Creates ID variables for each row returned by tpmatrix(). This function is most conveniently used along with tpmatrix() to construct a tparams_transprobs() object.

Usage

```
tpmatrix_id(object, n_samples)
```

Arguments

object An object of class expanded_hesim_data returned by expand.hesim_data().

This dataset must be expanded by treatment strategies, patients, and optionally

time intervals.

n_samples The number of parameters samples used for the probabilistic sensitivity analysis

(PSA).

Value

Returns a tpmatrix_id object that inherits from data.table with the same columns in object repeated n_samples times. That is, to facilitate creation of a tparams_transprobs() object, there is one row for each parameter sample, treatment strategy, patient, and optionally time interval.

See Also

```
tpmatrix(), tparams_transprobs(), expand.hesim_data()
```

tpmatrix_names

toma	striv	names	
LUIII	1 L I I I	t Hailles	

Names for elements of a transition probability matrix

Description

Create names for all elements of a transition probability matrix given names for the health states. This is useful for flattening a transition probability matrix (rowwise) into a vector and naming the resulting vector. The name of an element of the flattened vector representing a transition from the ith state to the jth state is of the form paste0(prefix, states[i], sep, states[j]).

Usage

```
tpmatrix_names(states, prefix = "p_", sep = "_")
```

Arguments

states	A character vector of the names of health states in the transition matrix.
prefix	A prefix that precedes the described transitions between states used to name a transition. For example, if prefix = "p_" (and sep = "_"), then a transition between state i and state j will be of the form "p_states[i]_states[j]"; similarly, if prefix = "", then the same transition will be named "states[i]_states[j]".
sep	A character string to separate the terms representing state i and state j. For instance, if sep = ".", the resulting name will be of the form "states[i].states[j]".

Value

A character vector containing a name for each element of the transition probability matrix encompassing all possible transitions.

See Also

See tpmatrix(), which uses tpmatrix_names() to name the columns of the returned object.

```
tpmatrix_names(LETTERS[1:4])
tpmatrix_names(LETTERS[1:4], prefix = "")
tpmatrix_names(LETTERS[1:4], prefix = "", sep = ".")
```

Index

* datasets	<pre>create_IndivCtstmTrans(), 30, 52, 57, 59</pre>
mstate3_exdata, 62	create_input_mats(), 30, 59
multinom3_exdata, 63	create_params, 28
onc3, 65	create_params(), 32, 75
onc3p, 66	<pre>create_params.partsurvfit(), 31</pre>
psm4_exdata, 82	create_PsmCurves, 30
· - /	create_PsmCurves(), 30, 59, 81, 86
apply_rr,4	create_StateVals, 32
as.data.table(), 116	create_StateVals(), 30, 107, 119
as.data.table.input_mats(input_mats),	create_StateVals.lm(), 68
58	<pre>create_StateVals.stateval_tbl(), 33,</pre>
as.data.table.tparams_transprobs,5	106
as.data.table.tparams_transprobs(),	create_trans_dt, 34
122	custom (rng_distributions), 93
as_array3, 6	77
as_pfs_os, 8	data.table::data.table, 34, 58, 110, 111,
as_tbl2 (as_array3), 6	113, 114
autoplot.stateprobs, 9	<pre>data.table::print.data.table(),58</pre>
autoplot.survival, 10	data.table::set(),96
	define_model, 35
beta_rng(rng_distributions),93	define_model(), 37-40, 121, 122
bootstrap, 29, 31	define_rng, 37
Braces, <i>38</i>	define_rng(), 36, 39, 40, 93-95
braces, <i>39</i>	define_tparams, 39
	define_tparams(), 35, 36, 38, 40, 123
ce, 11, <i>108</i>	dirichlet_rng (rng_distributions), 93
cea, 12, 76	disprog, 40, 50, 56
cea(), 12, 13, 75–78, 100	
cea_pw (cea), 12	eval_model (define_model), 35
cea_pw(), 12, 47, 48, 75, 77	$eval_model(), 40$
CohortDtstm, 15, 21, 24, 98–100	eval_rng, <i>110</i>
CohortDtstmTrans, <i>15</i> , <i>17</i> , 20, 21, 24–26,	eval_rng(define_rng), 37
69–71, 99, 103, 120, 123, 124	eval_rng(), <i>39</i> , <i>40</i> , <i>110</i>
costs, 15, 16, 23, 50, 52, 79, 80, 99, 100	eval_tparams (define_tparams), 39
create_CohortDtstm, 24	$eval_tparams(), 40$
$create_CohortDtstm(), 17, 35, 38$	expand.grid(),41
<pre>create_CohortDtstm.model_def(), 122</pre>	expand.hesim_data, 27, 41
<pre>create_CohortDtstmTrans, 25</pre>	expand.hesim_data(), 25, 31, 47, 125
$create_CohortDtstmTrans(), 17, 21, 30, 59$	expanded_hesim_data, 24, 32, 35, 40
<pre>create_IndivCtstmTrans, 26</pre>	expmat, 42

128 INDEX

factor(), 96	mstate3_exdata, 62
fast_rgengamma, 43	mstate::msprep, 55
fixed (rng_distributions), 93	multi_normal_rng (rng_distributions), 93
flexsurv::GenGamma, 73	multinom, 65
flexsurv::Gompertz, 73	multinom3_exdata, 63
flexsurv::Llogis, 73	multinom_list, 65
flexsurv::Survspline, 73	_ ,
flexsurv::WeibullPH, 72	<pre>normal_rng (rng_distributions), 93</pre>
flexsurvreg, 44	- · · · · · · · · · · · · · · · · · · ·
flexsurvreg_list, 31, 44	onc3, 65, 66, 67
flexsurvreg_list(), 58	onc3p, 66, 66
format.icer(icer), 47	
format.summary.ce (summary.ce), 108	params, 58, 67, 118
formula, 26, 28, 31	params_lm, 30, 68, 104, 112
101 110	params_lm(), 112
<pre>gamma_rng (rng_distributions), 93</pre>	params_mlogit, 26, 28, 30, 31, 69, 71, 112
get_labels, 44	params_mlogit(), 71, 112
get_labels(), 9, 10, 47, 48, 76–78, 96, 97,	params_mlogit_list, 20, 30, 69, 70, 112
108	params_mlogit_list(), 69, 112
	params_surv, 26, 28, 30, 31, 55, 72, 75, 112
ggplot2::ggplot, <i>75–78</i>	params_surv(), 112
haalth atata walusa 60	params_surv_list, 30, 55, 74, 84, 112
health state values, 68	params_surv_list(), 112
hesim::CtstmTrans, 54	
hesim_data, 32–34, 41, 46, 106	plot_ceac, 75
$hesim_data(), 45$	plot_ceaf, 76
. 47	plot_ceplane, 77
icer, 47	plot_evpi, 78
ID, 36	predict(), 26, 28, 31
id_attributes, 117-119	predict.lm(), 26, 28, 31
id_attributes(), 58	print.eval_rng(summary.eval_rng), 110
incr_effect, 49	<pre>print.input_mats(input_mats), 58</pre>
IndivCtstm, 28, 41, 50, 57, 100, 109	<pre>print.params_mlogit(params_mlogit), 69</pre>
IndivCtstmTrans, 26–28, 34, 41, 50, 52, 54,	<pre>print.params_surv(params_surv), 72</pre>
89	<pre>print.tparams_mean</pre>
<pre>IndivCtstmTrans(), 59</pre>	(summary.tparams_mean), 112
input_mats, 20, 55, 58, 58, 67, 84, 104	<pre>print.tparams_transprobs</pre>
input_mats(), 59	(tparams_transprobs), 120
	prothr, 62
<pre>lognormal_rng (rng_distributions), 93</pre>	Psm, 10, 11, 32, 78, 86, 98–100, 116
	psm4_exdata, 82
MASS::mvrnorm(), 95	PsmCurves, 30-32, 79, 81, 84, 116
metadata, 58	PsmCurves(), 59
mom_beta, 60	• •
mom_beta(), 94	qalys, 15, 16, 50, 51, 79, 80, 88, 99, 100
mom_gamma, 61	qmatrix(), 42
mom_gamma(), 94	qmatrix.data.frame (qmatrix.matrix), 89
msm::MatrixExp(), 42	qmatrix.data.table (qmatrix.matrix), 89
msm::msm, 90	qmatrix.data.table(), 43
mstate. 27. 34. 55. 62	qmatrix.matrix.89
1110 000 00, 47, 0 1, 00, 04	91114 CI IX 1 1114 CI IX 1 U/

INDEX 129

qmatrix.msm, 90	<pre>summary.params_surv_list</pre>
qmatrix.msm(), 43, 89	(summary.params), 111
	summary.tparams_mean, 112
R6::R6Class, 15, 20, 28, 50, 54, 78, 84	$summary.tparams_mean(), 119$
rcat, 91	summary.tparams_transprobs, 113
rdirichlet_mat, 92	<pre>summary.tparams_transprobs(), 122</pre>
rdirichlet_mat(), 94	summary.tpmatrix, 114
rng_def, <i>35</i>	<pre>summary.tpmatrix(), 124</pre>
rng_distributions, 38, 93	surv_quantile, 117
rpwexp, 95	survival, 10, 79, 85, 101, 115
set_labels, 96	time_intervals, <i>41</i> , 117, <i>121</i>
set_labels(), 45	tparams, 39, 67, 118
sim_costs(sim_ev), 97	tparams_def, 35
sim_ev, 97	tparams_mean, <i>104</i> , <i>112</i> , <i>113</i> , 119
sim_qalys(sim_ev), 97	tparams_transprobs, 5, 20, 42, 113, 114
sim_stateprobs(), 103	120, 123, 124
sim_stateprobs.survival, 101	tparams_transprobs(), 6, 39, 123, 125
sim_stateprobs.survival(), 99, 115, 116	tpmatrix, 7, 114, 120-122, 123
stateprobs, 9, 15, 16, 21, 50, 51, 57, 79, 80,	tpmatrix(), 39, 122, 125
98, 99, 101, 103	tpmatrix_id, <i>114</i> , <i>121</i> , 125
stateval_tbl, 32, 68, 106	tpmatrix_id(), <i>122</i>
stateval_tbl(), <i>33</i> , <i>119</i>	tpmatrix_names, 126
StateVals, 15, 17, 24, 32, 33, 50–52, 79, 81,	tpmatrix_names(), 5, 7, 123
98, 104, 107, 119	transformed parameter, 119
StateVals\$new(), 32	try(), 29
stats::Exponential, 72	3 (7)
stats::GammaDist, 73	<pre>uniform_rng (rng_distributions), 93</pre>
stats::Lognormal, 73	
stats::quantile(), 110	
stats::rbeta(), 94	
stats::rgamma(), 94	
stats::rlnorm(), 95	
stats::rnorm(), 95	
stats::runif(), 95	
stats::Weibull, 72	
summarize_ce(), 16, 52, 80, 100	
summary.ce, 108	
summary.eval_rng, 110	
summary.params, 111	
<pre>summary.params_lm (summary.params), 111</pre>	
<pre>summary.params_mlogit(summary.params),</pre>	
111	
$summary.params_mlogit(), 69$	
summary.params_mlogit_list	
(summary.params), 111	
<pre>summary.params_mlogit_list(), 71</pre>	
<pre>summary.params_surv (summary.params),</pre>	
111	