Package 'WARDEN'

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Title Workflows for Health Technology Assessments in R using Discrete
EveNts

Version 1.2.2

Description Toolkit to support and perform discrete event simulations without
resource constraints in the context of health technology assessments (HTA).
The package focuses on cost-effectiveness modelling and aims to be submission-ready
to relevant HTA bodies in alignment with 'NICE TSD 15'
https://www.sheffield.ac.uk/nice-dsu/tsds/patient-level-simulation>.
More details an examples can be found in the package website https://jsanchezalv.github.io/WARDEN/>.

License GPL (>= 3)

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URL https://jsanchezalv.github.io/WARDEN/

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Author Javier Sanchez Alvarez [aut, cre], Gabriel Lemyre [ctb], Valerie Aponte Ribero [ctb]

Maintainer Javier Sanchez Alvarez <javiersanchezeco@gmail.com>

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2 Contents

Contents

dd_item	. 3
dd_item2	
dd_reactevt	. 5
dd_tte	. 6
st_as_list	. 7
eac_des	. 8
ond_dirichlet	9
ond_mvn	10
reate_indicators	. 11
isc_cycle	. 12
isc_cycle_v	. 13
isc_instant	. 14
isc_instant_v	. 15
isc_ongoing	15
isc_ongoing_v	
raw_tte	
vpi_des	
xtract_elements_from_list	
xtract_from_reactions	
xtract_psa_result	
 .ck_adj	
 nodify_event	
nodify_item	
nodify_item_seq	
ew_event	
cond_gompertz	
 ick_psa	
ick_val_v	
beta_mse	
cond_exp	
cond_gamma	
cond_gompertz	
cond_llogis	
cond_lnorm	
cond_norm	
cond_weibull	
gamma_mse	
andom stream	
beta_mse	
cond_gompertz	
cond_gompertz_lu	
dirichlet	
dirichlet_prob	
eplicate_profiles	
gamma_mse	
poisgamma	

add_item 3

	run_sim	1 4
	run_sim_parallel	49
	sens_iterator	53
	summary_results_det	54
	summary_results_sens	55
	summary_results_sim	56
	tte.df	57
Index		58

add_item

Define parameters that may be used in model calculations (list)

Description

Define parameters that may be used in model calculations (list)

Usage

```
add_item(.data = NULL, ...)
```

Arguments

.data Existing data

... Items to define for the simulation

Details

The functions to add/modify events/inputs use lists. Whenever several inputs/events are added or modified, it's recommended to group them within one function, as it reduces the computation cost. So rather than use two add_item with a list of one element, it's better to group them into a single add_item with a list of two elements.

Whenever a function is directly implemented which must be evaluated later and that has no object name attached (e.g., pick_val_v), it should be implemented after a first add_item() (empty or with content) to avoid confusing the .data argument, or wrapping the function within substitute()

Value

A list of items

```
library(magrittr)
add_item(fl.idfs = 0)
add_item(util_idfs = if(psa_bool){rnorm(1,0.8,0.2)} else{0.8}, util.mbc = 0.6, cost_idfs = 2500)
common_inputs <- add_item() %>%
add_item(pick_val_v(
   base = l_statics[["base"]],
```

4 add_item2

```
psa = pick_psa(
    l_statics[["function"]],
    l_statics[["n"]],
    l_statics[["b"]]),
    sens = l_statics[[sens_name_used]],
    psa_ind = psa_bool,
    sens_ind = sensitivity_bool,
    indicator = indicators_statics,
    names_out = l_statics[["parameter_name"]]
)
)
```

add_item2

Define parameters that may be used in model calculations (uses expressions)

Description

Define parameters that may be used in model calculations (uses expressions)

Usage

```
add_item2(.data = NULL, input)
```

Arguments

.data Existing data

input Items to define for the simulation as an expression (i.e., using)

Details

The functions to add/modify events/inputs use lists. If chaining together add_item2, it will just append the expressions together in the order established.

If using pick_val_v, note it should be used with the deploy_env = TRUE argument so that add_item2 process it correctly.

Value

A substituted expression to be evaluated by engine

add_reactevt 5

Examples

```
library(magrittr)
add_item2(input = {fl.idfs <- 0})</pre>
add_item2(input = {
util_idfs <- if(psa_bool)\{rnorm(1,0.8,0.2)\} else\{0.8\}
util.mbc <- 0.6
cost_idfs <- 2500})
common_inputs <- add_item2(input = {</pre>
pick_val_v(
 base
            = l_statics[["base"]],
 psa
            = pick_psa(
   l_statics[["function"]],
   l_statics[["n"]],
   l_statics[["a"]],
   l_statics[["b"]]
 ),
            = l_statics[[sens_name_used]],
 sens
 psa_ind = psa_bool,
 sens_ind = sensitivity_bool,
 indicator = indicators_statics,
 names_out = l_statics[["parameter_name"]],
 deploy_env = TRUE #Note this option must be active if using it at add_item2
)
}
)
```

add_reactevt

Define the modifications to other events, costs, utilities, or other items affected by the occurrence of the event

Description

Define the modifications to other events, costs, utilities, or other items affected by the occurrence of the event

Usage

```
add_reactevt(.data = NULL, name_evt, input)
```

Arguments

. data Existing data for event reactions

name_evt Name of the event for which reactions are defined.

input Expressions that define what happens at the event, using functions as defined in

the Details section

6 add_tte

Details

There are a series of objects that can be used in this context to help define the event reactions.

The following functions may be used to define event reactions within this add_reactevt() function: modify_item() | Adds & Modifies items/flags/variables for future events (does not consider sequential) modify_item_seq() | Adds & Modifies items/flags/variables for future events in a sequential manner new_event() | Adds events to the vector of events for that patient modify_event() | Modifies existing events by changing their time

Apart from the items defined with add_item(), we can also use standard variables that are always defined within the simulation: curtime | Current event time (numeric) prevtime | Time of the previous event (numeric) cur_evtlist | Named vector of events that is yet to happen for that patient (named numeric vector) evt | Current event being processed (character) i | Patient being iterated (character) simulation | Simulation being iterated (numeric)

The model will run until curtime is set to Inf, so the event that terminates the model should modify curtime and set it to Inf.

The user can use extract_from_reactions function on the output to obtain a data.frame with all the relationships defined in the reactions in the model.

Value

A named list with the event name, and inside it the substituted expression saved for later evaluation

Examples

```
add_reactevt(name_evt = "start",input = {})
add_reactevt(name_evt = "idfs",input = {modify_item(list("fl.idfs"= 0))})
```

 add_tte

Define events and the initial event time

Description

Define events and the initial event time

Usage

```
add_tte(.data = NULL, arm, evts, other_inp = NULL, input)
```

Arguments

.data	Existing data for initial event times
arm	The intervention for which the events and initial event times are defined
evts	A vector of the names of the events
other_inp	A vector of other input variables that should be saved during the simulation
input	The definition of initial event times for the events listed in the evts argument

ast_as_list 7

Details

Events need to be separately defined for each intervention.

For each event that is defined in this list, the user needs to add a reaction to the event using the add_reactevt() function which will determine what calculations will happen at an event.

Value

A list of initial events and event times

Examples

```
add_tte(arm="int",evts = c("start","ttot","idfs","os"),
input={
  start <- 0
  idfs <- draw_tte(1,'lnorm',coef1=2, coef2=0.5)
  ttot <- min(draw_tte(1,'lnorm',coef1=1, coef2=4),idfs)
  os <- draw_tte(1,'lnorm',coef1=0.8, coef2=0.2)
})</pre>
```

ast_as_list

Transform a substituted expression to its Abstract Syntax Tree (AST) as a list

Description

Transform a substituted expression to its Abstract Syntax Tree (AST) as a list

Usage

```
ast_as_list(ee)
```

Arguments

ee

Substituted expression

Value

Nested list with the Abstract Syntax Tree (AST)

```
expr <- substitute({
    a <- sum(5+7)
    modify_item(list(afsa=ifelse(TRUE, "asda", NULL)))
    modify_item_seq(list(</pre>
```

8 ceac_des

```
o_other_q_gold1 = if(gold == 1) { utility } else { 0 },
  o_other_q_gold2 = if(gold == 2) { utility } else { 0 },
  o_other_q_gold3 = if(gold == 3) { utility } else { 0 },
  o_other_q_gold4 = if(gold == 4) { utility } else { 0 },
  o_other_q_on_dup = if(on_dup) { utility } else { 0 }
))
if(a==1){
  modify_item(list(a=list(6+b)))
  modify_event(list(e_exn = curtime + 14 / days_in_year + qexp(rnd_exn, r_exn)))
  modify_event(list(e_exn = curtime + 14 / days_in_year + qexp(rnd_exn, r_exn)))
  if(a>6){
   modify_item(list(a=8))
}
if (sel_resp_incl == 1 & on_dup == 1) {
  modify_event(list(e_response = curtime, z = 6))
}
})
out <- ast_as_list(expr)</pre>
```

ceac_des

Calculate the cost-effectiveness acceptability curve (CEAC) for a DES model with a PSA result

Description

Calculate the cost-effectiveness acceptability curve (CEAC) for a DES model with a PSA result

Usage

```
ceac_des(wtp, results, interventions = NULL, sensitivity_used = 1)
```

cond_dirichlet 9

Arguments

wtp Vector of length >=1 with the willingness to pay

results The list object returned by run_sim()

interventions A character vector with the names of the interventions to be used for the analysis

sensitivity_used

Integer signaling which sensitivity analysis to use

Value

A data frame with the CEAC results

Examples

```
res <- list(list(list(sensitivity_name = "", arm_list = c("int", "noint"), total_lys = c(int = 9.04687362556945, noint = 9.04687362556945), total_qalys = c(int = 6.20743830697466, noint = 6.18115138126336), total_costs = c(int = 49921.6357486899, noint = 41225.2544659378), total_lys_undisc = c(int = 10.8986618377039, noint = 10.8986618377039), total_qalys_undisc = c(int = 7.50117621700097, noint = 7.47414569286751), total_costs_undisc = c(int = 59831.3573929783, noint = 49293.1025437205), c_default = c(int = 49921.6357486899, noint = 41225.2544659378), c_default_undisc = c(int = 59831.3573929783, noint = 49293.1025437205), q_default = c(int = 6.20743830697466, noint = 6.18115138126336), q_default_undisc = c(int = 7.50117621700097, noint = 7.47414569286751), merged_df = list(simulation = 1L, sensitivity = 1L))))

ceac_des(seq(from=10000, to=5000000, by=100000), res)
```

cond_dirichlet

Calculate conditional dirichlet values

Description

Calculate conditional dirichlet values

Usage

```
cond_dirichlet(alpha, i, xi, full_output = FALSE)
```

Arguments

alpha	mean vector
i	index of the known parameter (1-based index)
xi	known value of the i-th parameter (should be >0)
full_output	boolean indicating whether to return the full list of parameters

10 cond_mvn

Details

Function to compute conditional dirichlet values

Value

List of length 2, one with new mu and other with covariance parameters

Examples

```
alpha <- c(2, 3, 4) i <- 2 # Index of the known parameter xi <- 0.5 # Known value of the second parameter # Compute the conditional alpha parameters with full output cond_dirichlet(alpha, i, xi, full_output = TRUE)
```

cond_mvn

Calculate conditional multivariate normal values

Description

Calculate conditional multivariate normal values

Usage

```
cond_mvn(mu, Sigma, i, xi, full_output = FALSE)
```

Arguments

mu	mean vector
Sigma	covariance matrix
i	index of the known parameter (1-based index)
xi	known value of the i-th parameter
full_output	boolean indicating whether to return the full list of parameters

Details

Function to compute conditional multivariate normal values

Value

List of length 2, one with new mu and other with covariance parameters

create_indicators 11

Examples

create_indicators

Creates a vector of indicators (0 and 1) for sensitivity/DSA analysis

Description

Creates a vector of indicators (0 and 1) for sensitivity/DSA analysis

Usage

```
create_indicators(sens, n_sensitivity, elem, n_elem_before = 0)
```

Arguments

sens current analysis iterator

 $n_sensitivity \quad total \ number \ of \ analyses \ to \ be \ run$

elem vector of 0s and 1s of elements to iterate through (1 = parameter is to be included

in scenario/DSA)

n_elem_before Sum of 1s (# of parameters to be included in scenario/DSA) that go before elem

Details

n_elem_before is to be used when several indicators want to be used (e.g., for patient level and common level inputs) while facilitating readibility of the code

Value

Numeric vector composed of 0 and 1, where value 1 will be used by pick_val_v to pick the corresponding index in its sens argument

```
create_indicators(10,20,c(1,1,1,1))
create_indicators(7,20,c(1,0,0,1,1,1,0,0,1,1),2)
```

12 disc_cycle

disc_cycle

Cycle discounting

Description

Cycle discounting

Usage

```
disc_cycle(
  lcldr = 0.035,
  lclprvtime = 0,
  cyclelength,
  lclcurtime,
  lclval,
  starttime = 0
)
```

Arguments

1cldr The discount rate

1clprvtime The time of the previous event in the simulation

cyclelength The cycle length

1clcurtime The time of the current event in the simulation

1clval The value to be discounted

starttime The start time for accrual of cycle costs (if not 0)

Details

Note this function counts both extremes of the interval, so the example below would consider 25 cycles, while disc_cycle_v leave the right interval open

Value

Double based on cycle discounting

```
disc_cycle(lcldr=0.035, lclprvtime=0, cyclelength=1/12, lclcurtime=2, lclval=500, starttime=0)
```

disc_cycle_v 13

disc_cycle_v	C
--------------	---

Cycle discounting for vectors

Description

Cycle discounting for vectors

Usage

```
disc_cycle_v(
   lcldr = 0.035,
   lclprvtime = 0,
   cyclelength,
   lclcurtime,
   lclval,
   starttime = 0,
   max_cycles = NULL
)
```

Arguments

lcldr The discount rate

lclprvtime The time of the previous event in the simulation

cyclelength The cycle length

lclcurtime The time of the current event in the simulation

lclval The value to be discounted

starttime The start time for accrual of cycle costs (if not 0)

max_cycles The maximum number of cycles

Details

This function per cycle discounting, i.e., considers that the cost/qaly is accrued per cycles, and performs it automatically without needing to create new events. It can accommodate changes in cycle length/value/starttime (e.g., in the case of induction and maintenance doses) within the same item.

Value

Double vector based on cycle discounting

14 disc_instant

Examples

```
disc_cycle_v(lcldr=0.03, lclprvtime=0, cyclelength=1/12, lclcurtime=2, lclval=500,starttime=0)
disc_cycle_v(
lcldr=0.000001,
lclprvtime=0,
cyclelength=1/12,
lclcurtime=2,
lclval=500,
starttime=0,
max\_cycles = 4)
#Here we have a change in cycle length, max number of cylces and starttime at time 2
#(e.g., induction to maintenance)
#In the model, one would do this by redifining cycle_l, max_cycles and starttime
#of the corresponding item at a given event time.
disc_cycle_v(lcldr=0,
lclprvtime=c(0,1,2,2.5),
cyclelength=c(1/12, 1/12,1/2,1/2),
lclcurtime=c(1,2,2.5,4), lclval=c(500,500,500,500),
 starttime=c(0,0,2,2), max_cycles = c(24,24,2,2)
```

disc_instant

Calculate instantaneous discounted costs or galys

Description

Calculate instantaneous discounted costs or qalys

Usage

```
disc_instant(lcldr = 0.035, lclcurtime, lclval)
```

Arguments

1cldr The discount rate

1clcurtime The time of the current event in the simulation

1clval The value to be discounted

Value

Double based on discrete time discounting

```
disc_instant(lcldr=0.035, lclcurtime=3, lclval=2500)
```

disc_instant_v 15

disc_instant_v	Calculate instantaneous discounted costs or qalys for vectors	

Description

Calculate instantaneous discounted costs or qalys for vectors

Usage

```
disc_instant_v(lcldr = 0.035, lclcurtime, lclval)
```

Arguments

1cldr The discount rate

1clcurtime The time of the current event in the simulation

1clval The value to be discounted

Value

Double based on discrete time discounting

Examples

```
disc_instant_v(lcldr=0.035, lclcurtime=3, lclval=2500)
```

disc_ongoing	Calculate discounted costs and qalys between events	
disc_ongoing	Calculate discounted costs and qalys between events	

Description

Calculate discounted costs and qalys between events

Usage

```
disc_ongoing(lcldr = 0.035, lclprvtime, lclcurtime, lclval)
```

Arguments

1cldr The discount rate

1clprvtime The time of the previous event in the simulation
1clcurtime The time of the current event in the simulation

lclval The value to be discounted

16 disc_ongoing_v

Value

Double based on continuous time discounting

Examples

```
disc_ongoing(lcldr=0.035,lclprvtime=0.5, lclcurtime=3, lclval=2500)
```

disc_ongoing_v

Calculate discounted costs and qalys between events for vectors

Description

Calculate discounted costs and qalys between events for vectors

Usage

```
disc_ongoing_v(lcldr = 0.035, lclprvtime, lclcurtime, lclval)
```

Arguments

1cldr The discount rate

lclprvtime The time of the previous event in the simulation lclcurtime The time of the current event in the simulation

1clval The value to be discounted

Value

Double based on continuous time discounting

```
disc_ongoing_v(lcldr=0.035,lclprvtime=0.5, lclcurtime=3, lclval=2500)
```

draw_tte 17

draw_tte	Draw a time to event from a list of parametric survival functions

Description

Draw a time to event from a list of parametric survival functions

Usage

```
draw_tte(
  n_chosen,
  dist,
  coef1 = NULL,
  coef2 = NULL,
  coef3 = NULL,
  ...,
  beta_tx = 1,
  seed = NULL
)
```

Arguments

n_chosen	The number of observations to be drawn
dist	The distribution; takes values 'lnorm', 'norm', 'mvnorm', 'weibullPH', 'weibull', 'llogis', 'gompertz', 'gengar
coef1	First coefficient of the distribution, defined as in the coef() output on a flex-survreg object (rate in "rpoisgamma")
coef2	Second coefficient of the distribution, defined as in the coef() output on a flex-survreg object (theta in "rpoisgamma")
coef3	Third coefficient of the distribution, defined as in the coef() output on a flex-survreg object (not used in "rpoisgamma")
• • •	Additional arguments to be used by the specific distribution (e.g., return_ind_rate if dist = "poisgamma")
beta_tx	Parameter in natural scale applied in addition to the scale/rate coefficient -e.g., a HR if used in an exponential- (not used in "rpoisgamma" nor "beta")
seed	An integer which will be used to set the seed for this draw.

Details

Other arguments relevant to each function can be called directly

Value

A vector of time to event estimates from the given parameters

18 evpi_des

Examples

```
draw_tte(n_chosen=1,dist='exp',coef1=1,beta_tx=1)
draw_tte(n_chosen=10,"poisgamma",coef1=1,coef2=1,obs_time=1,return_ind_rate=FALSE)
```

evpi_des

Calculate the Expected Value of Perfect Information (EVPI) for a DES model with a PSA result

Description

Calculate the Expected Value of Perfect Information (EVPI) for a DES model with a PSA result

Usage

```
evpi_des(wtp, results, interventions = NULL, sensitivity_used = 1)
```

Arguments

wtp Vector of length >=1 with the willingness to pay

results The list object returned by run_sim()

interventions A character vector with the names of the interventions to be used for the analysis sensitivity_used

Integer signaling which sensitivity analysis to use

Value

A data frame with the EVPI results

```
res <- list(list(list(sensitivity_name = "", arm_list = c("int", "noint"), total_lys = c(int = 9.04687362556945, noint = 9.04687362556945), total_qalys = c(int = 6.20743830697466, noint = 6.18115138126336), total_costs = c(int = 49921.6357486899, noint = 41225.2544659378), total_lys_undisc = c(int = 10.8986618377039, noint = 10.8986618377039), total_qalys_undisc = c(int = 7.50117621700097, noint = 7.47414569286751), total_costs_undisc = c(int = 59831.3573929783, noint = 49293.1025437205), c_default = c(int = 49921.6357486899, noint = 41225.2544659378), c_default_undisc = c(int = 59831.3573929783, noint = 49293.1025437205), q_default = c(int = 6.20743830697466, noint = 6.18115138126336), q_default_undisc = c(int = 7.50117621700097, noint = 7.47414569286751), merged_df = list(simulation = 1L, sensitivity = 1L))))
evpi_des(seq(from=10000, to=500000, by=10000), res)
```

```
extract_elements_from_list
```

Extracts items and events by looking into assignments, modify_item, modify_item_seq, modify_event and new_event

Description

Extracts items and events by looking into assignments, modify_item, modify_item_seq, modify_event and new_event

Usage

```
extract_elements_from_list(node, conditional_flag = FALSE)
```

Arguments

```
node Relevant node within the nested AST list conditional_flag
```

Boolean whether the statement is contained within a conditional statement

Value

A data.frame with the relevant item/event, the event where it's assigned, and whether it's contained within a conditional statement

```
expr <- substitute({
    a <- sum(5+7)
    modify_item(list(afsa=ifelse(TRUE, "asda", NULL)))
modify_item_seq(list(
    o_other_q_gold1 = if(gold == 1) { utility } else { 0 },
    o_other_q_gold2 = if(gold == 2) { utility } else { 0 },
    o_other_q_gold3 = if(gold == 3) { utility } else { 0 },
    o_other_q_gold4 = if(gold == 4) { utility } else { 0 },
    o_other_q_on_dup = if(on_dup) { utility } else { 0 }
))
if(a==1){
    modify_item(list(a=list(6+b)))</pre>
```

20 extract_from_reactions

```
modify_event(list(e_exn = curtime + 14 / days_in_year + qexp(rnd_exn, r_exn)))
else{
    modify_event(list(e_exn = curtime + 14 / days_in_year + qexp(rnd_exn, r_exn)))
    if(a>6){
        modify_item(list(a=8))
    }
}

if (sel_resp_incl == 1 & on_dup == 1) {
    modify_event(list(e_response = curtime, z = 6))
}

out <- ast_as_list(expr)

results <- extract_elements_from_list(out)</pre>
```

extract_from_reactions

Extract all items and events and their interactions from the event reactions list

Description

Extract all items and events and their interactions from the event reactions list

Usage

```
extract_from_reactions(reactions)
```

Arguments

reactions

list generated through add_reactevt

Value

A data.frame with the relevant item/event, the event where it's assigned, and whether it's contained within a conditional statement

extract_psa_result 21

Examples

```
evt_react_list2 <-
   add_reactevt(name_evt = "sick",
        input = {modify_item(list(a=1+5/3))}
        assign("W", 5 + 3 / 6 )
        x[5] <- 18
        for(i in 1:5){
            assign(paste0("x_",i),5+3)
        }
        if(j == TRUE){
            y[["w"]] <- 612-31+3
        }#'
        q_default <- 0
        c_default <- 0
        curtime <- Inf
        d <- c <- k <- 67
        })

extract_from_reactions(evt_react_list2)</pre>
```

extract_psa_result

Extract PSA results from a treatment

Description

Extract PSA results from a treatment

Usage

```
extract_psa_result(x, element)
```

Arguments

x The output_sim data frame from the list object returned by run_sim()
element Variable for which PSA results are being extracted (single string)

Value

A dataframe with PSA results from the specified intervention

```
res <- list(list(list(sensitivity_name = "", arm_list = c("int", "noint"
), total_lys = c(int = 9.04687362556945, noint = 9.04687362556945
), total_qalys = c(int = 6.20743830697466, noint = 6.18115138126336
), total_costs = c(int = 49921.6357486899, noint = 41225.2544659378
), total_lys_undisc = c(int = 10.8986618377039, noint = 10.8986618377039</pre>
```

22 luck_adj

```
), total_qalys_undisc = c(int = 7.50117621700097, noint = 7.47414569286751
), total_costs_undisc = c(int = 59831.3573929783, noint = 49293.1025437205
), c_default = c(int = 49921.6357486899, noint = 41225.2544659378
), c_default_undisc = c(int = 59831.3573929783, noint = 49293.1025437205
), q_default = c(int = 6.20743830697466, noint = 6.18115138126336
), q_default_undisc = c(int = 7.50117621700097, noint = 7.47414569286751
), merged_df = list(simulation = 1L, sensitivity = 1L))))

extract_psa_result(res[[1]],"total_costs")
```

luck_adj

Perform luck adjustment

Description

Perform luck adjustment

Usage

```
luck_adj(prevsurv, cursurv, luck, condq = TRUE)
```

Arguments

prevsurv Value of the previous survival cursurv Value of the current survival

luck Luck used to be adjusted (number between 0 and 1) condq Conditional quantile approach or standard approach

Details

This function performs the luck adjustment automatically for the user, returning the adjusted luck number. Luck is interpreted in the same fashion as is standard in R (higher luck, higher time to event).

Note that if TTE is predicted using a conditional quantile function (e.g., conditional gompertz, conditional quantile weibull...) prevsurv and cursurv are the unconditional survival using the "previous" parametrization but at the previous time for presurv and at the current time for cursurv. For other distributions, presurv is the survival up to current time using the previous parametrization, and cursurv is the survival up to current time using the current parametrization.

Note that the advantage of the conditional quantile function is that it does not need the new parametrization to update the luck, which makes this approach computationally more efficient. This function can also work with vectors, which could allow to update multiple lucks in a single approach, and it can preserve names

Value

Adjusted luck number between 0 and 1

modify_event 23

```
luck_adj(prevsurv = 0.8,
 cursurv = 0.7,
luck = 0.5,
 condq = TRUE)
luck_adj(prevsurv = c(1,0.8,0.7),
 cursurv = c(0.7, 0.6, 0.5),
 luck = setNames(c(0.5,0.6,0.7),c("A","B","C")),
 condq = TRUE)
luck_adj(prevsurv = 0.8,
 cursurv = 0.7,
 luck = 0.5,
 condq = FALSE) #different results
#Unconditional approach, timepoint of change is 25,
# parameter goes from 0.02 at time 10 to 0.025 to 0.015 at time 25,
# starting luck is 0.37
new_luck <- luck_adj(prevsurv = 1 - pweibull(q=10,3,1/0.02),</pre>
 cursurv = 1 - pweibull(q=10,3,1/0.025),
 luck = 0.37,
 condq = FALSE) #time 10 change
new_luck <- luck_adj(prevsurv = 1 - pweibull(q=25,3,1/0.025),</pre>
 cursurv = 1 - pweibull(q=25,3,1/0.015),
 luck = new_luck,
 condq = FALSE) #time 25 change
qweibull(new_luck, 3, 1/0.015) #final TTE
#Conditional quantile approach
new_luck <- luck_adj(prevsurv = 1-pweibull(q=0,3,1/0.02),</pre>
                      cursurv = 1- pweibull(q=10,3,1/0.02),
                      luck = 0.37,
                   condq = TRUE) #time 10 change, previous time is 0 so prevsurv will be 1
new_luck <- luck_adj(prevsurv = 1-pweibull(q=10,3,1/0.025),</pre>
                      cursurv = 1- pweibull(q=25, 3, 1/0.025),
                      luck = new_luck,
                       condq = TRUE) #time 25 change
qcond_weibull(rnd = new_luck,
                      shape = 3,
                      scale = 1/0.015,
                      lower_bound = 25) + 25 #final TTE
```

24 modify_item

Description

Modify the time of existing events

Usage

```
modify_event(evt, create_if_null = TRUE)
```

Arguments

evt

A list of events and their times

create_if_null A boolean. If TRUE, it will create non-existing events with the chosen time to event. If FALSE, it will ignore those.

Details

The functions to add/modify events/inputs use lists. Whenever several inputs/events are added or modified, it's recommended to group them within one function, as it reduces the computation cost. So rather than use two modify_event with a list of one element, it's better to group them into a single modify_event with a list of two elements.

This function does not evaluate sequentially.

This function is intended to be used only within the add_reactevt function in its input parameter and should not be run elsewhere or it will return an error.

Value

No return value, modifies/adds event to cur_evtlist and integrates it with the main list for storage

Examples

```
add_reactevt(name_evt = "idfs",input = {modify_event(list("os"=5))})
```

modify_item

Modify the value of existing items

Description

Modify the value of existing items

Usage

```
modify_item(list_item)
```

Arguments

list_item

A list of items and their values or expressions

modify_item_seq 25

Details

The functions to add/modify events/inputs use lists. Whenever several inputs/events are added or modified, it's recommended to group them within one function, as it reduces the computation cost. So rather than use two modify_item with a list of one element, it's better to group them into a single modify_item with a list of two elements.

Note that modify_item nor modify_item_seq can work on subelements (e.g., modify_item(list(obj\$item = 5)) will not work as intended, for that is better to assign directly using the expression approach, so obj\$item <- 5).

Costs and utilities can be modified by using the construction type_name_category, where type is either "qaly" or "cost", name is the name (e.g., "default") and category is the category used (e.g., "instant"), so one could pass cost_default_instant and modify the cost. This will overwrite the value defined in the corresponding cost/utility section.

This function is intended to be used only within the add_reactevt function in its input parameter and should not be run elsewhere or it will return an error.

Value

No return value, modifies/adds item to the environment and integrates it with the main list for storage

Examples

```
add_reactevt(name_evt = "idfs",input = {modify_item(list("cost.it"=5))})
```

modify_item_seq

Modify the value of existing items

Description

Modify the value of existing items

Usage

```
modify_item_seq(...)
```

Arguments

A list of items and their values or expressions. Will be evaluated sequentially (so one could have list(a = 1, b = a + 2))

26 new_event

Details

The functions to add/modify events/inputs use lists. Whenever several inputs/events are added or modified, it's recommended to group them within one function, as it reduces the computation cost. So rather than use two modify_item with a list of one element, it's better to group them into a single modify_item with a list of two elements.

Note that modify_item nor modify_item_seq can work on subelements (e.g., modify_item_seq(list(obj\$item = 5)) will not work as intended, for that is better to assign directly using the expression approach, so obj\$item <- 5).

Costs and utilities can be modified by using the construction type_name_category, where type is either "qaly" or "cost", name is the name (e.g., "default") and category is the category used (e.g., "instant"), so one could pass cost_default_instant and modify the cost. This will overwrite the value defined in the corresponding cost/utility section.

The function is different from modify_item in that this function evaluates sequentially the arguments within the list passed. This implies a slower performance relative to modify_item, but it can be more cleaner and convenient in certain instances.

This function is intended to be used only within the add_reactevt function in its input parameter and should not be run elsewhere or it will return an error.

Value

No return value, modifies/adds items sequentially and deploys to the environment and with the main list for storage

Examples

```
add_reactevt(name_evt = "idfs",input = {
  modify_item_seq(list(cost.idfs = 500, cost.tx = cost.idfs + 4000))
  })
```

new_event

Generate new events to be added to existing vector of events

Description

Generate new events to be added to existing vector of events

Usage

```
new_event(evt)
```

Arguments

evt

Event name and event time

pcond_gompertz 27

Details

The functions to add/modify events/inputs use lists. Whenever several inputs/events are added or modified, it's recommended to group them within one function, as it reduces the computation cost. So rather than use two new_event with a list of one element, it's better to group them into a single new_event with a list of two elements.

This function is intended to be used only within the add_reactevt function in its input parameter and should not be run elsewhere or it will return an error.

Value

No return value, adds event to cur_evtlist and integrates it with the main list for storage

Examples

```
add_reactevt(name_evt = "idfs",input = {new_event(list("ae"=5))})
```

pcond_gompertz Survival Probaility function for conditional Gompertz distribution (lower bound only)	on for conditional Gompertz distribution
--	--

Description

Survival Probaility function for conditional Gompertz distribution (lower bound only)

Usage

```
pcond_gompertz(time = 1, shape, rate, lower_bound = 0)
```

Arguments

time	Vector of times
shape	The shape parameter of the Gompertz distribution, defined as in the $coef()$ output on a flexsurvreg object
rate	The rate parameter of the Gompertz distribution, defined as in the coef() output on a flexsurvreg object
lower_bound	The lower bound of the conditional distribution

Value

Estimate(s) from the conditional Gompertz distribution based on given parameters

```
pcond_gompertz(time=1,shape=0.05,rate=0.01,lower_bound = 50)
```

28 pick_psa

pick_psa	Helper function to create a list with random draws or whenever a series of functions needs to be called. Can be implemented within pick_val_v.
	p16K_141_1.

Description

Helper function to create a list with random draws or whenever a series of functions needs to be called. Can be implemented within pick_val_v.

Usage

```
pick_psa(f, ...)
```

Arguments

f A string or vector of strings with the function to be called, e.g., "rnorm"
... parameters to be passed to the function (e.g., if "rnorm", arguments n, mean, sd)

Details

This function can be used to pick values for the PSA within pick_val_v.

The function will ignore NA items within the respective parameter (see example below). If an element in f is NA (e.g., a non PSA input) then it will return NA as its value This feature is convenient when mixing distributions with different number of arguments, e.g., rnorm and rgengamma.

While it's slightly lower than individually calling each function, it makes the code easier to read and more transparent

Value

List with length equal to f of parameters called

```
params <- list(
param=list("a","b"),
dist=list("rlnorm","rnorm"),
n=list(4,1),
a=list(c(1,2,3,4),1),
b=list(c(0.5,0.5,0.5,0.5),0.5),
dsa_min=list(c(1,2,3,4),2),
dsa_max=list(c(1,2,3,4),3))
pick_psa(params[["dist"]],params[["n"]],params[["a"]],params[["b"]])
#It works with functions that require different number of parameters params <- list(
    param=list("a","b","c"),</pre>
```

pick_val_v 29

```
dist=list("rlnorm", "rnorm", "rgengamma"),
 n=list(4,1,1),
 a=list(c(1,2,3,4),1,0),
 b=list(c(0.5,0.5,0.5,0.5),0.5,1),
 c=list(NA,NA,0.2),
 dsa_min=list(c(1,2,3,4),2,1),
 dsa_max=list(c(1,2,3,4),3,3)
pick_psa(params[["dist"]],params[["n"]],params[["a"]],params[["b"]],params[["c"]])
#Can be combined with multiple type of functions and distributions if parameters are well located
params <- list(</pre>
param=list("a","b","c","d"),
dist=list("rlnorm","rnorm","rgengamma","draw_tte"),
n=list(4,1,1,1),
a=list(c(1,2,3,4),1,0,"norm"),
b=list(c(0.5,0.5,0.5,0.5),0.5,1,1),
c=list(NA,NA,0.2,0.5),
c=list(NA,NA,NA,NA), #NA arguments will be ignored
dsa_min=list(c(1,2,3,4),2,1,0),
dsa_max=list(c(1,2,3,4),3,3,2)
)
```

Description

pick_val_v

Select which values should be applied in the corresponding loop for several values (vector or list).

several values (vector or list).

Select which values should be applied in the corresponding loop for

Usage

```
pick_val_v(
  base,
  psa,
  sens,
  psa_ind = psa_bool,
  sens_ind = sens_bool,
  indicator,
  indicator_psa = NULL,
  names_out = NULL,
  indicator_sens_binary = TRUE,
  sens_iterator = NULL,
  distributions = NULL,
  covariances = NULL,
  deploy_env = FALSE
)
```

pick_val_v

Arguments

	base	Value if no PSA/DSA/Scenario
	psa	Value if PSA
	sens	Value if DSA/Scenario
	psa_ind	Boolean whether PSA is active
	sens_ind	Boolean whether Scenario/DSA is active
	indicator	Indicator which checks whether the specific parameter/parameters is/are active in the DSA or Scenario loop
	indicator_psa	Indicator which checks whether the specific parameter/parameters is/are active in the PSA loop. If NULL, it's assumed to be a vector of 1s of length equal to length(indicator)
	names_out	Names to give the output list
indicator_sens_binary		
		Boolean, TRUE if parameters will be varied fully, FALSE if some elements of the parameters may be changed but not all
	sens_iterator	Current iterator number of the DSA/scenario being run, e.g., 5 if it corresponds to the 5th DSA parameter being changed
	distributions	List with length equal to length of base where the distributions are stored
	covariances	List with length equal to length of base where the variance/covariances are stored (only relevant if multivariate normal are being used)
	deploy_env	Boolean, if TRUE will deploy all objects in the environment where the function is called for. Must be active if using add_item2 (and FALSE if using add_item)

Details

This function can be used with vectors or lists, but will always return a list. Lists should be used when correlated variables are introduced to make sure the selector knows how to choose among those This function allows to choose between using an approach where only the full parameters are varied, and an approach where subelements of the parameters can be changed

Value

List used for the inputs

qbeta_mse 31

```
pick_val_v(base = list(2,3,c(1,2)),
             psa =sapply(1:3,
                          function(x) eval(call(
                            c("rnorm", "rnorm", "mvrnorm")[[x]],
                            c(2,3,list(c(1,2)))[[x]],
                            c(0.1,0.1,list(matrix(c(1,0.1,0.1,1),2,2)))[[x]]
                          ))),
             sens = list(4,5,c(1.3,2.3)),
             psa_ind = FALSE,
             sens_ind = TRUE,
             indicator=list(1,2,c(3,4)),
             names_out=c("util","util2","correlated_vector") ,
             indicator_sens_binary = FALSE,
             sens_iterator = 4,
             distributions = list("rnorm", "rnorm", "mvrnorm"),
             covariances = list(0.1, 0.1, matrix(c(1, 0.1, 0.1, 1), 2, 2))
)
```

qbeta_mse

Draw from a beta distribution based on mean and se (quantile)

Description

Draw from a beta distribution based on mean and se (quantile)

Usage

```
qbeta_mse(q, mean_v, se)
```

Arguments

q Quantiles to be used

mean_v A vector of the mean values

se A vector of the standard errors of the means

Value

A single estimate from the beta distribution based on given parameters

```
qbeta_mse(q=0.5,mean_v=0.8,se=0.2)
```

32 qcond_gamma

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Conditional quantile function for exponential distribution

Description

Conditional quantile function for exponential distribution

Usage

```
qcond_{exp}(rnd = 0.5, rate)
```

Arguments

rnd Vector of quantiles rate The rate parameter

Note taht the conditional quantile for an exponential is independent of time due

to constant hazard

Value

Estimate(s) from the conditional exponential distribution based on given parameters

Examples

```
qcond_exp(rnd = 0.5, rate = 3)
```

qcond_gamma

Conditional quantile function for gamma distribution

Description

Conditional quantile function for gamma distribution

Usage

```
qcond_gamma(rnd = 0.5, rate, shape, lower_bound = 0, s_obs)
```

Arguments

rnd Vector of quantiles
rate The rate parameter
shape The shape parameter

lower_bound The lower bound to be used (current time)

s_obs is the survival observed up to lower_bound time, normally defined from time 0

as 1 - pgamma(q = lower_bound, rate, shape) but may be different if parametriza-

tion has changed previously

qcond_gompertz 33

Value

Estimate(s) from the conditional gamma distribution based on given parameters

Examples

```
qcond_gamma(rnd = 0.5, rate = 1.06178, shape = 0.01108,lower_bound = 1, s_obs=0.8)
```

qcond_gompertz	Quantile function for conditional Gompertz distribution (lower bound only)
----------------	--

Description

Quantile function for conditional Gompertz distribution (lower bound only)

Usage

```
qcond_gompertz(rnd = 0.5, shape, rate, lower_bound = 0)
```

Arguments

rnd	Vector of quantiles
shape	The shape parameter of the Gompertz distribution, defined as in the coef() output on a flexsurvreg object
rate	The rate parameter of the Gompertz distribution, defined as in the coef() output on a flexsurvreg object
lower_bound	The lower bound of the conditional distribution

Value

Estimate(s) from the conditional Gompertz distribution based on given parameters

```
qcond_gompertz(rnd=0.5,shape=0.05,rate=0.01,lower_bound = 50)
```

34 qcond_lnorm

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Conditional quantile function for loglogistic distribution

Description

Conditional quantile function for loglogistic distribution

Usage

```
qcond_llogis(rnd = 0.5, shape, scale, lower_bound = 0)
```

Arguments

rnd Vector of quantiles shape The shape parameter scale The scale parameter

lower_bound The lower bound to be used (current time)

Value

Estimate(s) from the conditional loglogistic distribution based on given parameters

Examples

```
qcond_llogis(rnd = 0.5, shape = 1, scale = 1, lower_bound = 1)
```

qcond_lnorm

Conditional quantile function for lognormal distribution

Description

Conditional quantile function for lognormal distribution

Usage

```
qcond_lnorm(rnd = 0.5, meanlog, sdlog, lower_bound = 0, s_obs)
```

Arguments

rnd Vector of quantiles
meanlog The meanlog parameter
sdlog The sdlog parameter

lower_bound The lower bound to be used (current time)

s_obs is the survival observed up to lower_bound time, normally defined from time

0 as 1 - plnorm(q = lower_bound, meanlog, sdlog) but may be different if

parametrization has changed previously

qcond_norm 35

Value

Estimate(s) from the conditional lognormal distribution based on given parameters

Examples

```
qcond_lnorm(rnd = 0.5, meanlog = 1,sdlog = 1,lower_bound = 1, s_obs=0.8)
```

qcond_norm

Conditional quantile function for normal distribution

Description

Conditional quantile function for normal distribution

Usage

```
qcond_norm(rnd = 0.5, mean, sd, lower_bound = 0, s_obs)
```

Arguments

rnd Vector of quantiles

mean The mean parameter

sd The sd parameter

lower_bound The lower bound to be used (current time)

s_obs is the survival observed up to lower_bound time, normally defined from time 0

as 1 - pnorm(q = lower_bound, mean, sd) but may be different if parametrization

has changed previously

Value

Estimate(s) from the conditional normal distribution based on given parameters

```
qcond_norm(rnd = 0.5, mean = 1,sd = 1,lower_bound = 1, s_obs=0.8)
```

36 qgamma_mse

qcond_weibull	Conditional quantile function for weibull distribution
---------------	--

Description

Conditional quantile function for weibull distribution

Usage

```
qcond_weibull(rnd = 0.5, shape, scale, lower_bound = 0)
```

Arguments

rnd Vector of quantiles

shape The shape parameter as in R stats package weibull scale The scale parameter as in R stats package weibull lower_bound The lower bound to be used (current time)

Value

Estimate(s) from the conditional weibull distribution based on given parameters

Examples

```
gcond_weibull(rnd = 0.5, shape = 3, scale = 66.66, lower_bound = 50)
```

qgamma_mse Use qu

Use quantiles from a gamma distribution based on mean and se

Description

Use quantiles from a gamma distribution based on mean and se

Usage

```
qgamma_mse(q = 1, mean_v, se, seed = NULL)
```

Arguments

q Quantile to draw

mean_v A vector of the mean values

se A vector of the standard errors of the means

seed An integer which will be used to set the seed for this draw.

random_stream 37

Value

A single estimate from the gamma distribution based on given parameters

Examples

```
qgamma_mse(q=0.5, mean_v=0.8, se=0.2)
```

random_stream

Creates an environment (similar to R6 class) of random uniform numbers to be drawn from

Description

Creates an environment (similar to R6 class) of random uniform numbers to be drawn from

Usage

```
random_stream(stream_size = 100)
```

Arguments

stream_size Length of the vector of random uniform values to initialize

Details

This function creates an environment object that behaves similar to an R6 class but offers more speed vs. an R6 class.

The object is always initialized (see example below) to a specific vector of random uniform values. The user can then call the object with obj\$draw_number(n), where n is an integer, and will return the first n elements of the created vector of uniform values. It will automatically remove those indexes from the vector, so the next time the user calls obj\$draw_n() it will already consider the next index.

The user can also access the latest elements drawn by accessing obj\$random_n (useful for when performing a luck adjustment), the current stream still to be drawn using obj\$stream and the original size (when created) using obj\$stream_size.

If performing luck adjustment, the user can always modify the random value by using obj\$random_n <- luck_adj(...) (only valid if used with the expression approach, not with modify_item)

Value

Self (environment) behaving similar to R6 class

38 rcond_gompertz

Examples

```
stream_1 <- random_stream(1000)
number_1 <- stream_1$draw_n() #extract 1st index from the vector created
identical(number_1,stream_1$random_n) #same value
number_2 <- stream_1$draw_n() #gets 1st index (considers previous)
identical(number_2,stream_1$random_n) #same value</pre>
```

rbeta_mse

Draw from a beta distribution based on mean and se

Description

Draw from a beta distribution based on mean and se

Usage

```
rbeta_mse(n = 1, mean_v, se, seed = NULL)
```

Arguments

n Number of draws (must be >= 1)
mean_v A vector of the mean values

se A vector of the standard errors of the means

seed An integer which will be used to set the seed for this draw.

Value

A single estimate from the beta distribution based on given parameters

Examples

```
rbeta_mse(n=1,mean_v=0.8,se=0.2)
```

 ${\tt rcond_gompertz}$

Draw from a conditional Gompertz distribution (lower bound only)

Description

Draw from a conditional Gompertz distribution (lower bound only)

Usage

```
rcond_gompertz(n = 1, shape, rate, lower_bound = 0, seed = NULL)
```

rcond_gompertz_lu 39

Arguments

n The number of observations to be drawn

shape The shape parameter of the Gompertz distribution, defined as in the coef() output

on a flexsurvreg object

rate The rate parameter of the Gompertz distribution, defined as in the coef() output

on a flexsurvreg object

lower_bound The lower bound of the conditional distribution

seed An integer which will be used to set the seed for this draw.

Value

Estimate(s) from the conditional Gompertz distribution based on given parameters

Examples

```
rcond_gompertz(1, shape=0.05, rate=0.01, lower_bound = 50)
```

rcond_gompertz_lu

Draw from a Conditional Gompertz distribution (lower and upper bound)

Description

Draw from a Conditional Gompertz distribution (lower and upper bound)

Usage

```
rcond_gompertz_lu(
    n,
    shape,
    rate,
    lower_bound = 0,
    upper_bound = Inf,
    seed = NULL
)
```

Arguments

n The number of observations to be drawn

shape The shape parameter of the Gompertz distribution, defined as in the coef() output

on a flexsurvreg object

rate The rate parameter of the Gompertz distribution, defined as in the coef() output

on a flexsurvreg object

lower_bound The lower bound of the conditional distribution upper_bound The upper bound of the conditional distribution

seed An integer which will be used to set the seed for this draw.

40 rdirichlet

Value

Estimate(s) from the Conditional Gompertz distribution based on given parameters

Examples

```
rcond_gompertz_lu(1,shape=0.05,rate=0.01,lower_bound = 50)
```

rdirichlet

Draw from a dirichlet distribution based on number of counts in transition. Adapted from brms::rdirichlet

Description

Draw from a dirichlet distribution based on number of counts in transition. Adapted from brms::rdirichlet

Usage

```
rdirichlet(n = 1, alpha, seed = NULL)
```

Arguments

Number of draws (must be ≥ 1). If n > 1, it will return a list of matrices.

alpha A matrix of alphas (transition counts)

seed An integer which will be used to set the seed for this draw.

Value

A transition matrix. If n>1, it will return a list of matrices.

```
rdirichlet(n=1,alpha= matrix(c(1251, 0, 350, 731),2,2))
rdirichlet(n=2,alpha= matrix(c(1251, 0, 350, 731),2,2))
```

rdirichlet_prob 41

-i ,	rom a dirichlet distribution based on mean transition probabild standard errors
------	---

Description

Draw from a dirichlet distribution based on mean transition probabilities and standard errors

Usage

```
rdirichlet_prob(n = 1, alpha, se, seed = NULL)
```

Arguments

Number of draws (must be >= 1). If n>1, it will return a list of matrices.
 alpha A matrix of transition probabilities
 A matrix of standard errors

seed An integer which will be used to set the seed for this draw.

Value

A transition matrix. If n>1, it will return a list of matrices.

Examples

```
 \begin{split} & \mathsf{rdirichlet\_prob}(\mathsf{n=1}, \mathsf{alpha=} \ \mathsf{matrix}(\mathsf{c}(0.7, 0.3, 0, 0.1, 0.7, 0.2, 0.1, 0.2, 0.7), 3, 3), \\ & \mathsf{se=} \mathsf{matrix}(\mathsf{c}(0.7, 0.3, 0, 0.1, 0.7, 0.2, 0.1, 0.2, 0.7) / 10, 3, 3)) \\ & \mathsf{rdirichlet\_prob}(\mathsf{n=2}, \mathsf{alpha=} \ \mathsf{matrix}(\mathsf{c}(0.7, 0.3, 0, 0.1, 0.7, 0.2, 0.1, 0.2, 0.7), 3, 3), \\ & \mathsf{se=} \mathsf{matrix}(\mathsf{c}(0.7, 0.3, 0, 0.1, 0.7, 0.2, 0.1, 0.2, 0.7) / 10, 3, 3)) \\ \end{split}
```

 $replicate_profiles$

Replicate profiles data.frame

Description

Replicate profiles data.frame

Usage

```
replicate_profiles(
  profiles,
  replications,
  probabilities = NULL,
  replacement = TRUE,
  seed_used = NULL
)
```

42 rgamma_mse

Arguments

profiles data.frame of profiles

replications integer, final number of observations

probabilities vector of probabilities with the same length as the number of rows of profiles.

Does not need to add up to 1 (are reweighted)

replacement Boolean whether replacement is used

seed_used Integer with the seed to be used for consistent results

Value

Resampled data.frame of profiles

Examples

```
replicate_profiles(profiles=data.frame(id=1:100,age=rnorm(100,60,5)),
replications=200,probabilities=rep(1,100))
```

rgamma_mse

Draw from a gamma distribution based on mean and se

Description

Draw from a gamma distribution based on mean and se

Usage

```
rgamma_mse(n = 1, mean_v, se, seed = NULL)
```

Arguments

n Number of draws (must be >= 1)
mean_v A vector of the mean values

se A vector of the standard errors of the means

seed An integer which will be used to set the seed for this draw.

Value

A single estimate from the gamma distribution based on given parameters

```
rgamma_mse(n=1, mean_v=0.8, se=0.2)
```

rpoisgamma 43

rpoisgamma	Draw time to event (tte) from a Poisson or Poisson-Gamma (PG) Mix-
	ture/Negative Binomial (NB) Process

Description

Draw time to event (tte) from a Poisson or Poisson-Gamma (PG) Mixture/Negative Binomial (NB) Process

Usage

```
rpoisgamma(
    n,
    rate,
    theta = NULL,
    obs_time = 1,
    t_reps,
    seed = NULL,
    return_ind_rate = FALSE,
    return_df = FALSE
)
```

Arguments

n	The number of observations to be drawn	
rate	rate of the event (in terms of events per observation-time)	
theta	Optional. When omitted, the function simulates times for a Poisson process. Represents the shape of the gamma mixture distribution. Estimated and reported as theta in negative binomial regression analyses in r.	
obs_time	period over which events are observable	
t_reps	Optional. Number of TBEs to be generated to capture events within the observation window. When omitted, the function sets t_reps to the 99.99th quantile of the Poisson (if no theta is provided) or negative binomial (if theta is provided). Thus, the risk of missing possible events in the observation window is 0.01%.	
seed	An integer which will be used to set the seed for this draw.	
return_ind_rate		
	A boolean that indicates whether an additional vector with the rate parameters used per observation is used. It will alter the structure of the results to two lists,	

return_df A boolean that indicates whether a data.table object should be returned

one storing tte with name tte, and the other with name ind_rate

Details

Function to simulate event times from a Poisson or Poisson-Gamma (PG) Mixture/Negative Binomial (NB) Process Event times are determined by sampling times between events (TBEs) from an exponential distribution, and cumulating these to derive the event times. Events occurring within the set observation time window are retained and returned. For times for a Poisson process, the provided rate is assumed constant. For a PG or NB, the individual rates are sampled from a Gamma distribution with shape = theta and scale = rate/theta.

Value

Estimate(s) from the time to event based on poisson/Poisson-Gamma (PG) Mixture/Negative Binomial (NB) distribution based on given parameters

Examples

```
rpoisgamma(1,rate=1,obs_time=1,theta=1)
```

run_sim

Run the simulation

Description

Run the simulation

Usage

```
run_sim(
  arm_list = c("int", "noint"),
  sensitivity_inputs = NULL,
  common_all_inputs = NULL,
  common_pt_inputs = NULL,
  unique_pt_inputs = NULL,
  init_event_list = NULL,
  evt_react_list = evt_react_list,
  util_ongoing_list = NULL,
  util_instant_list = NULL,
  util_cycle_list = NULL,
  cost_ongoing_list = NULL,
  cost_instant_list = NULL,
  cost_cycle_list = NULL,
  other_ongoing_list = NULL,
  other_instant_list = NULL,
  npats = 500,
  n_sim = 1,
  psa_bool = NULL,
  sensitivity_bool = FALSE,
  sensitivity_names = NULL,
```

```
n_sensitivity = 1,
input_out = NULL,
ipd = 1,
timed_freq = NULL,
debug = FALSE,
accum_backwards = FALSE,
continue_on_error = FALSE,
seed = NULL
)
```

Arguments

 $\begin{tabular}{ll} arm_list & A vector of the names of the interventions evaluated in the simulation \\ sensitivity_inputs \\ \end{tabular}$

A list of sensitivity inputs that do not change within a sensitivity in a similar fashion to common_all_inputs, etc

common_all_inputs

A list of inputs common across patients that do not change within a simulation

common_pt_inputs

A list of inputs that change across patients but are not affected by the intervention

unique_pt_inputs

A list of inputs that change across each intervention

init_event_list

A list of initial events and event times. If no initial events are given, a "Start" event at time 0 is created automatically

evt_react_list A list of event reactions
util_ongoing_list

Vector of QALY named variables that are accrued at an ongoing basis (discounted using drq)

util_instant_list

Vector of QALY named variables that are accrued instantaneously at an event (discounted using drq)

util_cycle_list

Vector of QALY named variables that are accrued in cycles (discounted using drq)

cost_ongoing_list

Vector of cost named variables that are accrued at an ongoing basis (discounted using drc)

cost_instant_list

Vector of cost named variables that are accrued instantaneously at an event (discounted using drc)

cost_cycle_list

Vector of cost named variables that are accrued in cycles (discounted using drc) other_ongoing_list

Vector of other named variables that are accrued at an ongoing basis (discounted using drq)

other_instant_list

Vector of other named variables that are accrued instantaneously at an event

(discounted using drq)

npats The number of patients to be simulated (it will simulate npats * length(arm_list))

n_sim The number of simulations to run per sensitivity

psa_bool A boolean to determine if PSA should be conducted. If n_sim > 1 and psa_bool

= FALSE, the differences between simulations will be due to sampling

sensitivity_bool

A boolean to determine if Scenarios/DSA should be conducted.

sensitivity_names

A vector of scenario/DSA names that can be used to select the right sensitivity (e.g., c("Scenario_1", "Scenario_2")). The parameter "sens_name_used" is created from it which corresponds to the one being used for each iteration.

Number of sensitivity analysis (DSA or Scenarios) to run. It will be interacted n_sensitivity

> with sensitivity_names argument if not null (n_sensitivityitivity = n_sensitivity * length(sensitivity_names)). For DSA, it should be as many parameters as there

are. For scenario, it should be 1.

input_out A vector of variables to be returned in the output data frame

Integer taking value 1 for full IPD data returned, and 2 IPD data but aggregating ipd

> events (returning last value for numeric/character/factor variables. For other objects (e.g., matrices), the IPD will still be returned as the aggregation rule is not clear). Other values mean no IPD data returned (removes non-numerical or

length>1 items)

timed_freq If NULL, it does not produce any timed outputs. Otherwise should be a number

(e.g., every 1 year)

debug If TRUE, will generate a log file

accum_backwards

If TRUE, the ongoing accumulators will count backwards (i.e., the current value is applied until the previous update). If FALSE, the current value is applied between the current event and the next time it is updated. If TRUE, user must

use modify_item and modify_item_seq or results will be incorrect.

continue_on_error

If TRUE, on error it will attempt to continue by skipping the current simulation

seed Starting seed to be used for the whole analysis. If null, it's set to 1 by default.

Details

This function is slightly different from run_sim_parallel. run_sim_parallel only runs multiplecore at the simulation level. run_sim uses only-single core. run_sim can be more efficient if using only one simulation (e.g., deterministic), while run_sim_parallel will be more efficient if the number of simulations is >1 (e.g., PSA).

Event ties are processed in the order declared within the init_event_list argument (evts argument within the first sublist of that object). To do so, the program automatically adds a sequence from to 0 to the (number of events - 1) times 1e-10 to add to the event times when selecting the event with minimum time. This time has been selected as it's relatively small yet not so small as to be ignored by which.min (see .Machine for more details)

A list of protected objects that should not be used by the user as input names or in the global environment to avoid the risk of overwriting them is as follows: c("arm", "arm_list", "categories_for_export", "cur_evtlist", "curtime", "evt", "i", "prevtime", "sens", "simulation", "sens_name_used", "list_env", "uc_lists", "npats", "ipd").

The engine uses the L'Ecuyer-CMRG for the random number generator. Note that the random seeds are set to be unique in their category (i.e., at patient level, patient-arm level, etc.)

If no drc or drq parameters are passed within sensitivity or common_all input lists, these are assigned a default value 0.03 for discounting costs, QALYs and others.

Ongoing items will look backward to the last time updated when performing the discounting and accumulation. This means that the user does not necessarily need to keep updating the value, but only add it when the value changes looking forward (e.g., o_q = utility at event 1, at event 2 utility does not change, but at event 3 it does, so we want to make sure to add o_q = utility at event 3 before updating utility. The program will automatically look back until event 1). Note that in previous versions of the package backward was the default, and now this has switched to forward.

If using accum_backwards = TRUE, then it is mandatory for the user to use modify_item and modify_item_seq in event reactions, as the standard assignment approach (e.g., a <- 5) will not calculate the right results, particularly in the presence of conditional statements.

It is important to note that the QALYs and Costs (ongoing or instant or per cycle) used should be of length 1. If they were of length > 1, the model would expand the data, so instead of having each event as a row, the event would have N rows (equal to the length of the costs/qalys to discount passed). This means more processing of the results data would be needed in order for it to provide the correct results.

If the cycle lists are used, then it is expected the user will declare as well the name of the variable pasted with cycle_l and cycle_starttime (e.g., c_default_cycle_l and c_default_cycle_starttime) to ensure the discounting can be computed using cycles, with cycle_l being the cycle length, and cycle_starttime being the starting time in which the variable started counting. Optionally, max_cycles must also be added (if no maximum number of cycles, it should be set equal to NA).

debug = TRUE will export a log file with the timestamp up the error in the main working directory. Note that using this mode without modify_item or modify_item_seq may lead to inaccuracies if assignments are done in non-standard ways, as the AST may not catch all the relevant assignments (e.g., an assignment like assign(paste("x_",i),5) in a loop will not be identified, unless using modify_item(_seq)).

continue_on_error will skip the current simulation (so it won't continue for the rest of patientarms) if TRUE. Note that this will make the progress bar not correct, as a set of patients that were expected to be run is not.

Value

A list of data frames with the simulation results

```
library(magrittr)
common_all_inputs <-add_item(
util.sick = 0.8,
util.sicker = 0.5,
cost.sick = 3000,
cost.sicker = 7000,</pre>
```

```
cost.int = 1000,
coef_noint = log(0.2),
HR_int = 0.8,
drc = 0.035, #different values than what's assumed by default
drq = 0.035,
random_seed_sicker_i = sample.int(100000,5,replace = FALSE)
common_pt_inputs <- add_item(death= max(0.0000001,rnorm(n=1, mean=12, sd=3)))</pre>
unique_pt_inputs <- add_item(fl.sick = 1,</pre>
                              q_default = util.sick,
                              c_default = cost.sick + if(arm=="int"){cost.int}else{0})
init_event_list <-</pre>
add_tte(arm=c("noint","int"), evts = c("sick","sicker","death") ,input={
  sick <- 0
  sicker <- draw_tte(1,dist="exp",</pre>
  coef1=coef_noint, beta_tx = ifelse(arm=="int",HR_int,1),
    seed = random_seed_sicker_i[i])
})
evt_react_list <-
add_reactevt(name_evt = "sick",
             input = {}) %>%
  add_reactevt(name_evt = "sicker",
               input = {
                 modify_item(list(q_default = util.sicker,
                               c_default = cost.sicker + if(arm=="int"){cost.int}else{0},
                                   fl.sick = 0))
               }) %>%
  add_reactevt(name_evt = "death",
               input = {
                 modify_item(list(q_default = 0,
                                   c_{default} = 0,
                                   curtime = Inf))
               })
util_ongoing <- "q_default"
cost_ongoing <- "c_default"</pre>
run_sim(arm_list=c("int","noint"),
common_all_inputs = common_all_inputs,
common_pt_inputs = common_pt_inputs,
unique_pt_inputs = unique_pt_inputs,
init_event_list = init_event_list,
evt_react_list = evt_react_list,
util_ongoing_list = util_ongoing,
cost_ongoing_list = cost_ongoing,
npats = 2,
n_sim = 1,
```

```
psa_bool = FALSE,
ipd = 1)
```

run_sim_parallel

Run simulations in parallel mode (at the simulation level)

Description

Run simulations in parallel mode (at the simulation level)

Usage

```
run_sim_parallel(
  arm_list = c("int", "noint"),
  sensitivity_inputs = NULL,
  common_all_inputs = NULL,
  common_pt_inputs = NULL,
  unique_pt_inputs = NULL,
  init_event_list = NULL,
  evt_react_list = evt_react_list,
  util_ongoing_list = NULL,
  util_instant_list = NULL,
  util_cycle_list = NULL,
  cost_ongoing_list = NULL,
  cost_instant_list = NULL,
  cost_cycle_list = NULL,
 other_ongoing_list = NULL,
 other_instant_list = NULL,
  npats = 500,
  n_sim = 1,
 psa_bool = NULL,
  sensitivity_bool = FALSE,
  sensitivity_names = NULL,
  n_{sensitivity} = 1,
  ncores = 1,
  input_out = NULL,
  ipd = 1,
  timed_freq = NULL,
  debug = FALSE,
  accum_backwards = FALSE,
 continue_on_error = FALSE,
  seed = NULL
)
```

Arguments

arm_list A vector of the names of the interventions evaluated in the simulation sensitivity_inputs

A list of sensitivity inputs that do not change within a sensitivity in a similar fashion to common_all_inputs, etc

common_all_inputs

A list of inputs common across patients that do not change within a simulation common_pt_inputs

A list of inputs that change across patients but are not affected by the intervention

unique_pt_inputs

A list of inputs that change across each intervention

init_event_list

A list of initial events and event times. If no initial events are given, a "Start" event at time 0 is created automatically

evt_react_list A list of event reactions

util_ongoing_list

Vector of QALY named variables that are accrued at an ongoing basis (discounted using drq)

util_instant_list

Vector of QALY named variables that are accrued instantaneously at an event (discounted using drq)

util_cycle_list

Vector of QALY named variables that are accrued in cycles (discounted using drq)

cost_ongoing_list

Vector of cost named variables that are accrued at an ongoing basis (discounted using drc)

cost_instant_list

Vector of cost named variables that are accrued instantaneously at an event (discounted using drc)

cost_cycle_list

Vector of cost named variables that are accrued in cycles (discounted using drc)

other_ongoing_list

Vector of other named variables that are accrued at an ongoing basis (discounted using drq)

other_instant_list

Vector of other named variables that are accrued instantaneously at an event (discounted using drq)

npats The number of patients to be simulated (it will simulate npats * length(arm_list))

n_sim The number of simulations to run per sensitivity

psa_bool A boolean to determine if PSA should be conducted. If n_sim > 1 and psa_bool

= FALSE, the differences between simulations will be due to sampling

sensitivity_bool

A boolean to determine if Scenarios/DSA should be conducted.

sensitivity_names

A vector of scenario/DSA names that can be used to select the right sensitivity (e.g., c("Scenario_1", "Scenario_2")). The parameter "sens_name_used" is created from it which corresponds to the one being used for each iteration.

n_sensitivity

Number of sensitivity analysis (DSA or Scenarios) to run. It will be interacted with sensitivity_names argument if not null (n_sensitivityitivity = n_sensitivity * length(sensitivity_names)). For DSA, it should be as many parameters as there are. For scenario, it should be 1.

ncores The number of cores to use for parallel computing

input_out A vector of variables to be returned in the output data frame

ipd Integer taking value 0 if no IPD data returned, 1 for full IPD data returned, and

2 IPD data but aggregating events

timed_freq If NULL, it does not produce any timed outputs. Otherwise should be a number

(e.g., every 1 year)

debug If TRUE, will generate a log file

accum_backwards

If TRUE, the ongoing accumulators will count backwards (i.e., the current value is applied until the previous update). If FALSE, the current value is applied between the current event and the next time it is updated. If TRUE, user must use modify_item_and modify_item_seq or results will be incorrect.

continue_on_error

If TRUE, on error at patient stage will attempt to continue to the next simulation (only works if n_s and/or n_s ensitivity are > 1, not at the patient level)

seed Starting seed to be used for the whole analysis. If null, it's set to 1 by default.

Details

This function is slightly different from run_sim. run_sim allows to run single-core. run_sim_parallel allows to use multiple-core at the simulation level, making it more efficient for a large number of simulations relative to run_sim (e.g., for PSA).

Event ties are processed in the order declared within the init_event_list argument (evts argument within the first sublist of that object). To do so, the program automatically adds a sequence from to 0 to the (number of events - 1) times 1e-10 to add to the event times when selecting the event with minimum time. This time has been selected as it's relatively small yet not so small as to be ignored by which.min (see .Machine for more details)

A list of protected objects that should not be used by the user as input names or in the global environment to avoid the risk of overwriting them is as follows: c("arm", "arm_list", "categories_for_export", "cur_evtlist", "curtime", "evt", "i", "prevtime", "sens", "simulation", "sens_name_used", "list_env", "uc_lists", "npats", "ipd").

The engine uses the L'Ecuyer-CMRG for the random number generator. Note that if ncores > 1, then results per simulation will only be exactly replicable if using run_sim_parallel (as seeds are automatically transformed to be seven integer seeds -i.e, L'Ecuyer-CMRG seeds-) Note that the random seeds are set to be unique in their category (i.e., at patient level, patient-arm level, etc.)

If no drc or drq parameters are passed within sensitivity or common_all input lists, these are assigned a default value 0.03 for discounting costs, QALYs and others.

Ongoing items will look backward to the last time updated when performing the discounting and accumulation. This means that the user does not necessarily need to keep updating the value, but only add it when the value changes looking forward (e.g., o_q = utility at event 1, at event 2 utility does not change, but at event 3 it does, so we want to make sure to add o_q = utility at event 3 before updating utility. The program will automatically look back until event 1). Note that in previous versions of the package backward was the default, and now this has switched to forward.

If using accum_backwards = TRUE, then it is mandatory for the user to use modify_item and modify_item_seq in event reactions, as the standard assignment approach (e.g., a <- 5) will not calculate the right results, particularly in the presence of conditional statements.

If the cycle lists are used, then it is expected the user will declare as well the name of the variable pasted with cycle_l and cycle_starttime (e.g., c_default_cycle_l and c_default_cycle_starttime) to ensure the discounting can be computed using cycles, with cycle_l being the cycle length, and cycle_starttime being the starting time in which the variable started counting. Optionally, max_cycles must also be added (if no maximum number of cycles, it should be set equal to NA).

debug = TRUE will export a log file with the timestamp up the error in the main working directory. Note that using this mode without modify_item or modify_item_seq may lead to inaccuracies if assignments are done in non-standard ways, as the AST may not catch all the relevant assignments (e.g., an assignment like assign(paste("x_",i),5) in a loop will not be identified, unless using modify_item()).

If continue_on_error is set to FALSE, it will only export analysis level inputs due to the parallel engine (use single-engine for those inputs) continue_on_error will skip the current simulation (so it won't continue for the rest of patient-arms) if TRUE. Note that this will make the progress bar not correct, as a set of patients that were expected to be run is not.

Value

A list of lists with the analysis results

```
library(magrittr)
common_all_inputs <-add_item(</pre>
util.sick = 0.8,
util.sicker = 0.5,
cost.sick = 3000,
cost.sicker = 7000,
cost.int = 1000,
coef_noint = log(0.2),
HR_int = 0.8,
drc = 0.035, #different values than what's assumed by default
drq = 0.035,
random_seed_sicker_i = sample.int(100000,5,replace = FALSE)
common_pt_inputs <- add_item(death= max(0.0000001,rnorm(n=1, mean=12, sd=3)))</pre>
unique_pt_inputs <- add_item(fl.sick = 1.</pre>
                              q_default = util.sick,
                              c_default = cost.sick + if(arm=="int"){cost.int}else{0})
```

sens_iterator 53

```
init_event_list <-</pre>
add_tte(arm=c("noint","int"), evts = c("sick","sicker","death") ,input={
  sick <- 0
  sicker <- draw_tte(1,dist="exp",</pre>
  coef1=coef_noint, beta_tx = ifelse(arm=="int",HR_int,1),
   seed = random_seed_sicker_i[i])
})
evt_react_list <-
add_reactevt(name_evt = "sick",
             input = {}) %>%
  add_reactevt(name_evt = "sicker",
               input = {
                 modify_item(list(q_default = util.sicker,
                               c_default = cost.sicker + if(arm=="int"){cost.int}else{0},
                                   fl.sick = 0))
               }) %>%
  add_reactevt(name_evt = "death",
               input = {
                 modify_item(list(q_default = 0,
                                   c_{default} = 0,
                                   curtime = Inf))
               })
util_ongoing <- "q_default"
cost_ongoing <- "c_default"</pre>
run_sim_parallel(arm_list=c("int","noint"),
common_all_inputs = common_all_inputs,
common_pt_inputs = common_pt_inputs,
unique_pt_inputs = unique_pt_inputs,
init_event_list = init_event_list,
evt_react_list = evt_react_list,
util_ongoing_list = util_ongoing,
cost_ongoing_list = cost_ongoing,
npats = 2,
n_sim = 1,
psa_bool = FALSE,
ipd = 1,
ncores = 1)
```

sens_iterator

Create an iterator based on sens of the current iteration within a scenario (DSA)

54 summary_results_det

Description

Create an iterator based on sens of the current iteration within a scenario (DSA)

Usage

```
sens_iterator(sens, n_sensitivity)
```

Arguments

sens current analysis iterator
n_sensitivity total number of analyses to be run

Details

In a situation like a DSA, where two (low and high) scenarios are run, sens will go from 1 to n_sensitivity*2. However, this is not ideal as the parameter selector may depend on knowing the parameter order (i.e., 1, 2, 3...), which means resetting the counter back to 1 once sens reaches n_sensitivity (or any multiple of n_sensitivity) is needed.

Value

Integer iterator based on the number of sensitivity analyses being run and the total iterator

Examples

```
sens_iterator(5,20)
sens_iterator(25,20)
```

summary_results_det

Deterministic results for a specific treatment

Description

Deterministic results for a specific treatment

Usage

```
summary_results_det(out = results[[1]][[1]], arm = NULL, wtp = 50000)
```

Arguments

out	The final_output data frame from the list object returned by run_sim()
arm	The reference treatment for calculation of incremental outcomes
wtp	Willingness to pay to have INMB

Value

A dataframe with absolute costs, LYs, QALYs, and ICER and ICUR for each intervention

summary_results_sens 55

Examples

```
res <- list(list(list(sensitivity_name = "", arm_list = c("int", "noint"
), total_lys = c(int = 9.04687362556945, noint = 9.04687362556945
), total_qalys = c(int = 6.20743830697466, noint = 6.18115138126336
), total_costs = c(int = 49921.6357486899, noint = 41225.2544659378
), total_lys_undisc = c(int = 10.8986618377039, noint = 10.8986618377039
), total_qalys_undisc = c(int = 7.50117621700097, noint = 7.47414569286751
), total_costs_undisc = c(int = 59831.3573929783, noint = 49293.1025437205
), c_default = c(int = 49921.6357486899, noint = 41225.2544659378
), c_default_undisc = c(int = 59831.3573929783, noint = 49293.1025437205
), q_default = c(int = 6.20743830697466, noint = 6.18115138126336
), q_default_undisc = c(int = 7.50117621700097, noint = 7.47414569286751
), merged_df = list(simulation = 1L, sensitivity = 1L))))
summary_results_det(res[[1]][[1]], arm="int")</pre>
```

summary_results_sens Summary of sensitivity outputs for a treatment

Description

Summary of sensitivity outputs for a treatment

Usage

```
summary_results_sens(out = results, arm = NULL, wtp = 50000)
```

Arguments

out	The list object returned by run_sim()
arm	The reference treatment for calculation of incremental outcomes
wtp	Willingness to pay to have INMB

Value

A data frame with each sensitivity output per arm

```
res <- list(list(list(sensitivity_name = "", arm_list = c("int", "noint"
), total_lys = c(int = 9.04687362556945, noint = 9.04687362556945
), total_qalys = c(int = 6.20743830697466, noint = 6.18115138126336
), total_costs = c(int = 49921.6357486899, noint = 41225.2544659378
), total_lys_undisc = c(int = 10.8986618377039, noint = 10.8986618377039
), total_qalys_undisc = c(int = 7.50117621700097, noint = 7.47414569286751
), total_costs_undisc = c(int = 59831.3573929783, noint = 49293.1025437205</pre>
```

```
), c_default = c(int = 49921.6357486899, noint = 41225.2544659378
), c_default_undisc = c(int = 59831.3573929783, noint = 49293.1025437205
), q_default = c(int = 6.20743830697466, noint = 6.18115138126336
), q_default_undisc = c(int = 7.50117621700097, noint = 7.47414569286751
), merged_df = list(simulation = 1L, sensitivity = 1L))))
summary_results_sens(res,arm="int")
```

summary_results_sim

Summary of PSA outputs for a treatment

Description

Summary of PSA outputs for a treatment

Usage

```
summary_results_sim(out = results[[1]], arm = NULL, wtp = 50000)
```

Arguments

out	The output_sim data frame from the list object returned by run_sim()
arm	The reference treatment for calculation of incremental outcomes
wtp	Willingness to pay to have INMB

Value

A data frame with mean and 95% CI of absolute costs, LYs, QALYs, ICER and ICUR for each intervention from the PSA samples

```
res <- list(list(sensitivity_name = "", arm_list = c("int", "noint"
), total_lys = c(int = 9.04687362556945, noint = 9.04687362556945
), total_qalys = c(int = 6.20743830697466, noint = 6.18115138126336
), total_costs = c(int = 49921.6357486899, noint = 41225.2544659378
), total_lys_undisc = c(int = 10.8986618377039, noint = 10.8986618377039
), total_qalys_undisc = c(int = 7.50117621700097, noint = 7.47414569286751
), total_costs_undisc = c(int = 59831.3573929783, noint = 49293.1025437205
), c_default = c(int = 49921.6357486899, noint = 41225.2544659378
), c_default_undisc = c(int = 59831.3573929783, noint = 49293.1025437205
), q_default = c(int = 6.20743830697466, noint = 6.18115138126336
), q_default_undisc = c(int = 7.50117621700097, noint = 7.47414569286751
), merged_df = list(simulation = 1L, sensitivity = 1L))))
summary_results_sim(res[[1]],arm="int")</pre>
```

tte.df

tte.df

Example TTE IPD data

Description

An example of TTE IPD data for the example_ipd file

Usage

tte.df

Format

tte.df:

A data frame with 1000 rows and 8 columns:

USUBJID Patient ID

ARMCD, ARM Arm code and variables

PARAMCD, PARAM Parameter

AVAL, AVALCD Values of interest

CNSR Censored observation?

Source

Simulated through FlexsurvPlus package using $sim_adtte(seed = 821, rho = 0, beta_1a = log(0.6), beta_1b = log(0.6), beta_pd = log(0.2))$

Index

* datasets	qcond_gamma, 32
tte.df, 57	qcond_gompertz,33
	qcond_llogis,34
add_item, 3	qcond_lnorm, 34
add_item2, 4	qcond_norm, 35
add_reactevt, 5	qcond_weibull, 36
add_tte, 6	qgamma_mse, 36
ast_as_list,7	-
	random_stream, 37
ceac_des, 8	rbeta_mse,38
cond_dirichlet, 9	rcond_gompertz,38
cond_mvn, 10	rcond_gompertz_lu,39
create_indicators, 11	rdirichlet,40
	rdirichlet_prob,41
disc_cycle, 12	replicate_profiles,41
disc_cycle_v, 13	rgamma_mse,42
disc_instant, 14	rpoisgamma,43
disc_instant_v, 15	run_sim,44
disc_ongoing, 15	run_sim_parallel,49
disc_ongoing_v, 16	
draw_tte, 17	sens_iterator,53
	<pre>summary_results_det, 54</pre>
evpi_des, 18	<pre>summary_results_sens, 55</pre>
<pre>extract_elements_from_list, 19</pre>	<pre>summary_results_sim, 56</pre>
extract_from_reactions, 20	
extract_psa_result, 21	tte.df, <u>57</u>
luck_adj, 22	
madify avant 22	
modify_event, 23	
modify_item, 24	
<pre>modify_item_seq, 25</pre>	
new_event, 26	
new_evente, 20	
pcond_gompertz, 27	
pick_psa, 28	
pick_val_v, 29	
F	
qbeta_mse, 31	
qcond_exp, 32	