Package ‘psborrow’

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Title Bayesian Dynamic Borrowing with Propensity Score

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Description A tool which aims to help evaluate the effect of external borrowing using an integrated approach described in Lewis et al., (2019) <doi:10.1080/19466315.2018.1497533> that combines propensity score and Bayesian dynamic borrowing methods.

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`.clinClass-class`  
*S4 Class for specifying parameters for enrollment time, drop-out pattern and analysis start time*

Description

S4 Class for specifying parameters for enrollment time, drop-out pattern and analysis start time

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`.covClass-class`  
*S4 Class for setting up covariates*

Description

S4 Class for setting up covariates
.eventClass-class

S4 Class for setting parameters for time-to-events

Description

S4 Class for setting parameters for time-to-events

.priorClass-class

S4 Class for specifying prior distributions and predictors for MCMC methods

Description

S4 Class for specifying prior distributions and predictors for MCMC methods

apply_mcmc

Fit Dynamic Borrowing MCMC Model

Description

Fit a dynamic borrowing Weibull survival model to the given dataset and extract the posterior samples using MCMC. See the user guide for more information on the model formulation. See run_mcmc() for more information on the available parameters for tuning the MCMC sampling process.

Usage

apply_mcmc(dt, formula_cov, ...)

extract_samples(object)

## S3 method for class 'apply_mcmc'
summary(object, ...)

Arguments

dt
A data.frame containing data required for modelling. See details

formula_cov
A one sided formula specifying which non-treatment covariates should be included into the model. See details

...
Additional arguments passed onto run_mcmc(). Only exception being the path argument which is not supported by this function

object
A apply_mcmc object created by apply_mcmc()
Details

apply_mcmc():
The dt data.frame must contain 1 row per subject with the following variables:

- **time** - A continuous non-zero number specifying the time that the subject had an event at
- **cnsr** - A column of 0/1's where 1 indicates that the event was censored/right truncated
- **ext** - A column of 0/1's where 1 indicates that the subject was part of the external control
- **trt** - A column of 0/1's where 1 indicates that the subject was receiving the experimental treatment

The dt data.frame may also contain any additional covariates to be used in the Weibull model as specified by formula_cov. In order to fit a valid model formula_cov must contain the intercept term. The formula will be automatically adjusted to include the treatment term and as such should not be included here, if you want to include a treatment interaction term this should be done by using ~ trt:covariate and NOT via ~ trt*covariate.

extract_samples():
This function can be used to extract the samples generated by apply_mcmc()

summary():
This function provides summary statistics about the samples generated by apply_mcmc()

Extracted Samples:
The extracted samples can be roughly defined as follows (see the user guide for full details):

- **HR_cc_hc** - The hazard ratio between the concurrent control arm and the historical control arm. This can be be thought of as the ratio of the scale parameter between the baseline trial distribution and the baseline external control distribution. This is equivalent to \( \exp(\alpha[1] - \alpha[2]) \)
- **HR_trt_cc** - The hazard ratio between the treatment arm and the concurrent control arm. This is equivalent to \( \exp(\beta_{trt}) \)
- **alpha[1]** - The shape parameter for the trial’s baseline distribution
- **alpha[2]** - The shape parameter for the historical control’s baseline distribution
- **beta_trt** - The log-hazard ratio for the treatment effect. This is equivalent to \( \log(HR_{trt_cc}) \)
- **beta_<var>** - The log-hazard ratio for any other covariate provided to the model via formula_cov
- **r0** - The scale parameter for the baseline distribution of both the trial and the historical control
- **tau/sigma** - The precision/variance for alpha[1] i.e. controls how much information is borrowed from the historical control arm

---

**c,.covClass-method**

**Concatenate multiple .covClass classes**

**Description**

Concatenate multiple .covClass classes
## c,.priorClass-method

### Usage

```r
## S4 method for signature '.covClass'
c(x, ...)
```

### Arguments

- `x` 
  A `.covClasss` class with covariate information generated in `set_cov`
- `...` 
  Other `.covClasss` classes with covariate information generated in `set_cov`

### Value

A vector of `.covClasss` classes

### Examples

```r
# combine two sets of covariates
covset1 = set_cov(n_cat = 2, n_cont = 0, mu_int = 0, mu_ext = 0, var = 1)
covset2 = set_cov(n_cat = 0, n_cont = 1, mu_int = 62, mu_ext = 65, var = 11)
cov_list = c(covset1, covset2)
```

---

## c,.priorClass-method

### Description

Concatenate multiple `.priorClasss` class

### Usage

```r
## S4 method for signature '.priorClass'
c(x, ...)
```

### Arguments

- `x` 
  A `.priorClasss` class with prior distribution information generated in `set_prior`
- `...` 
  A `.priorClasss` class with prior distribution information generated in `set_prior`

### Value

A vector of `.priorClasss` classes
fix_col_names

Fix Column Names

Description
Utility function to make the mcmc column names more human friendly

Usage
fix_col_names(x, column_names)

Arguments
x                  a mcmc results object created by add_mcmc()
column_names       The names to change the beta columns to

get_summary

Generate summary statistics of a simulation scenario

Description
Generate summary statistics of a simulation scenario

Usage
get_summary(dt)

Arguments
dt                a data.frame containing summary statistics for the posterior samples from each simulation

Value
a data.frame containing the mean and sd of posterior HR between treatment and control arm, the posterior mean and sd of HR between internal control and external control arm, reject rate, variance, bias and mse of the simulation set
is_psborrow_dev

Check if user is in psborrow development environment

Description
Simple function which leverages the DESCRIPTION file to check if the user is in a development environment for psborrow.

Usage
is_psborrow_dev()

Value
TRUE/FALSE flag (TRUE = in development environment)

match_cov

Description
Match

Usage
match_cov(dt, match)

Arguments
dt a list of matrix
match A vector of covariates name to match on

Value
a list of matrix containing matched cohort information

Examples
# match internal and external trial data using different covariates
smp = set_n(ssC = 140, ssE = 275, ssExt = 100)
covset1 = set_cov(n_cat = 2, n_cont = 0, mu_int = 0, mu_ext = 0, var = 1)
covset2 = set_cov(n_cat = 0, n_cont = 1, mu_int = 62, mu_ext = 65, var = 11)
cObj = c(covset1, covset2)
sample_cov <- simu_cov(ssObj = smp, covObj = cObj, HR = 1, driftHR = 1.2, nsim = 2)

# match on covariates 1 and 2
match_cov(dt = sample_cov, match = c("cov1", "cov2"))

# match on all 3 covariates
match_cov(dt = sample_cov, match = c("cov1", "cov2", "cov3"))

---

**plot_bias**

**Plot bias**

**Description**

Plot bias for each prior distribution according to selected simulation parameters

**Usage**

plot_bias(dt, HR = 1, driftHR = 1, pred = "none")

**Arguments**

- **dt**: a data.frame containing summary statistics for the posterior samples from each simulation generated with get_summary.
- **HR**: pre-specified HR between treatment and control arm in the internal trial for which the bias should be plotted. Must be within unique(dt$HR).
- **driftHR**: pre-specified HR between external control arm and internal control arm for which the bias should be plotted. Must be within unique(dt$driftHR).
- **pred**: predictors to use when fitting exponential distribution in MCMC for which the bias should be plotted. Must be within unique(dt$pred).

**Value**

a bar plot of class ggplot containing the bias for each prior distribution.

---

**plot_hr**

**Plot mean posterior hazard ratio between treatment and control**

**Description**

Plot mean posterior hazard ratio between treatment and control

**Usage**

plot_hr(dt, HR = 0.67, driftHR = 1, pred = "none")
**plot_mse**

**Arguments**

- **dt**: a data.frame containing summary statistics for the posterior samples from each simulation generated with `get_summary`.
- **HR**: pre-specified HR between treatment and control arm in the internal trial for which the mean posterior hazard ratio should be plotted. Must be within `unique(dt$HR)`.
- **driftHR**: pre-specified HR between external control arm and internal control arm for which the mean posterior hazard ratio should be plotted. Must be within `unique(dt$driftHR)`.
- **pred**: predictors to use when fitting exponential distribution in MCMC for which the mean posterior hazard ratio should be plotted. Must be within `unique(dt$pred)`.

**Value**

A plot of class `ggplot` containing the mean posterior hazard ratio for each prior distribution.

---

**plot_mse**

*Plot mean squared error (MSE)*

**Description**

Plot mean squared error (MSE) for each prior distribution according to selected simulation parameters.

**Usage**

```r
plot_mse(dt, HR = 1, driftHR = 1, pred = "none")
```

**Arguments**

- **dt**: a data.frame containing summary statistics for the posterior samples from each simulation generated with `get_summary`.
- **HR**: pre-specified HR between treatment and control arm in the internal trial for which the MSE should be plotted. Must be within `unique(dt$HR)`.
- **driftHR**: pre-specified HR between external control arm and internal control arm for which the MSE should be plotted. Must be within `unique(dt$driftHR)`.
- **pred**: predictors to use when fitting exponential distribution in MCMC for which the MSE should be plotted. Must be within `unique(dt$pred)`.

**Value**

A bar plot of class `ggplot` containing the MSE for each prior distribution.
plot_power

**Plot power**

**Description**

Plot power for each prior distribution according to selected simulation parameters

**Usage**

```r
plot_power(dt, HR = 0.67, driftHR = 1, pred = "none")
```

**Arguments**

- `dt`: a `data.frame` containing summary statistics for the posterior samples from each simulation generated with `get_summary()`.
- `HR`: pre-specified HR between treatment and control arm in the internal trial for which the power should be plotted. Must be within `unique(dt$HR)`.
- `driftHR`: pre-specified HR between external control arm and internal control arm for which the power should be plotted. Must be within `unique(dt$driftHR)`.
- `pred`: predictors to use when fitting exponential distribution in MCMC for which the power should be plotted. Must be within `unique(dt$pred)`.

**Value**

A bar plot of class `ggplot` containing the power for each prior distribution.

---

plot_type1error

**Plot type 1 error**

**Description**

Plot type 1 error for each prior distribution according to selected simulation parameters

**Usage**

```r
plot_type1error(dt, driftHR = 1, pred = "none")
```

**Arguments**

- `dt`: a `data.frame` containing summary statistics for the posterior samples from each simulation generated with `get_summary()` must contain simulations for HR = 1.0.
- `driftHR`: the driftHR between the external and internal control arms for which the type 1 error should be plotted. Must be within `unique(dt$driftHR)`.
- `pred`: the predictors used when fitting the exponential distribution in MCMC for which the type 1 error should be plotted. Must be within `unique(dt$pred)`.
**ps_message**

**Value**

A bar plot of class `ggplot` containing type 1 error proportions for each prior distribution.

---

**Conditional Message**

**Description**

Simple wrapper function around `message()` that will suppress printing messages if the option `psborrow.quiet` is set to TRUE i.e.

```r
options("psborrow.quiet" = TRUE)
```

**Usage**

```r
ps_message(...)
```

**Arguments**

```r
...
```

Values passed onto `message()`

---

**rej_est**

**Generate summary statistics for the MCMC chains**

**Description**

Generate summary statistics for the MCMC chains

**Usage**

```r
rej_est(samples)
```

**Arguments**

```r
samples
```

An object of class `mcmc.list`

**Value**

A vector containing the mean, median, sd, reject rate for the MCMC chains
run_mcmc

Description

Run MCMC for multiple scenarios with provided data

Usage

run_mcmc(dt, priorObj, n.chains, n.adapt, n.burn, n.iter, seed, path)

Arguments

dt a list of matrix containing simulated time-to-events information
priorObj an object of class .priorClass generated in set_prior
n.chains number of parallel chains for the model
n.adapt number of iterations for adaptation
n.burn number of iterations discarded as burn-in
n.iter number of iterations to monitor
seed the seed of random number generator. Default is the first element of .Random.seed
path file name for saving the output including folder path

Value

a data.frame containing summary statistics of the posterior distribution for each simulation

Examples

# examples in vignette

run_mcmc_p

Description

Run MCMC for multiple scenarios with provided data with parallel processing
set_clin

Usage

run_mcmc_p(
  dt,
  priorObj,
  n.chains,
  n.adapt,
  n.burn,
  n.iter,
  seed,
  path,
  n.cores = 2
)

Arguments

dt  a list of matrix containing simulated time-to-events information
priorObj  an object of class .priorClass generated in set_prior
n.chains  number of parallel chains for the model
n.adapt  number of iterations for adaptation
n.burn  number of iterations discarded as burn-in
n.iter  number of iterations to monitor
seed  the seed of random number generator. Default is the first element of .Random.seed
path  file name for saving the output including folder path
n.cores  number of processes to parallelize over (default = 2)

Value

da data.frame containing summary statistics of the posterior distribution for each simulation

Examples

  # similar to run_mcmc

____________________________________________________________________________
set_clin
Specify parameters for enrollment time, drop-out pattern and analysis start time

____________________________________________________________________________

Description

This function allows user to specify the enrollment and drop-out rate, and the type of clinical cut-off Date. Both enrollment times and drop-out times follow piece-wise exponential distribution.
**set_clin**

**Usage**

```r
set_clin(gamma, e_itv, CCOD, CCOD_t, etaC, etaE, d_itv)
```

**Arguments**

- `gamma`: A vector of rate of enrollment per unit of time
- `e_itv`: A vector of duration of time periods for recruitment with rates specified in `gamma`. Note that the length of `e_itv` should be same length as `gamma` or 1 less.
- `CCOD`: Type of analysis start time. Analysis starts at `CCOD_t` months after the first or last patient’s enrollment if `CCOD = "fixed-first"` or `CCOD = "fixed-last"` respectively. Analysis starts when `CCOD_t` events have been observed if `CCOD = "event"`
- `CCOD_t`: Time difference between analysis start and first patient’s enrollment if `CCOD = "fixed-first"`. Time difference between analysis start and last patient’s enrollment if `CCOD = "fixed-last"`. Number of events observed when analysis starts if `CCOD = "event"`. Patients enrolled after the analysis start time are excluded from the analysis
- `etaC`: A vector for dropout rate per unit time for control arm
- `etaE`: A vector for dropout rate per unit time for experimental arm. If left `NULL`, it uses the same dropout rate as `eta`.
- `d_itv`: A vector of duration of time periods for dropping out the study with rates specified in `etaC` and `etaE`. Note that the length of `d_itv` should be same length as `etaC` or 1 less.

**Value**

A `.clinClass` class containing information on enrollment time, drop-out pattern and analysis start time

**Examples**

```r
# set the operational parameter values for the trial
# analysis starts at 64 time units after first patient in
set_clin(gamma = 10, e_itv = 4, etaC = 0.003, CCOD = "fixed-first", CCOD_t = 64)

# analysis starts at 12 time units after last patient in
set_clin(gamma = 2, e_itv = 18, etaC = 0.005, CCOD = "fixed-last", CCOD_t = 12)
```
set_cov

**Description**

This function saves the mean, variance and covariance among covariates. For technical details, see the vignette.

**Usage**

```r
def_set_cov(n_cat, n_cont, mu_int, mu_ext, var, cov, prob_int, prob_ext)
```

**Arguments**

- `n_cat` Number of binary variable. See details
- `n_cont` Number of continuous variable
- `mu_int` Mean of covariates in the internal trial. All the covariates are simulated from a multivariate normal distribution. If left NULL, it uses default value 0 for all covariates. If provided one value, this value is used for all covariates
- `mu_ext` Mean of covariates in the external trial. If left NULL, it uses the same mean as `mu_int`
- `var` Variance of covariates. If left NULL, it uses default value 0 for all covariates. If provided one value, it uses this value for all covariates
- `cov` Covariance between each pair of covariates. Covariance needs to be provided in a certain order and users are encouraged to read the example provided in the vignette. If left NULL, it uses default value 0 for all covariates. If provided one value, it uses this value for every pair of covariates
- `prob_int` Probability of binary covariate equalling 1 in the internal trial. If left NULL, it uses default value 0.5 for all covariates. If provided one value, it uses this value for all covariates
- `prob_ext` Probability of binary covariate equalling 1 in the external trial. If left NULL, it uses the same probability as `prob_int`

**Details**

Categorical variables are created by sampling a continuous variable from the multivariate normal distribution (thus respecting the correlation to other covariates specified by `cov`) and then applying a cut point derived from the `prob_int` or `prob_ext` quantile of said distribution i.e. for a univariate variable it would be derived as:

```r
binvar <- as.numeric(rnorm(n, mu, sqrt(var)) < qnorm(prob, mu, sqrt(var)))
```

Please note that this means that the value of `mu_int` & `mu_ext` has no impact on categorical covariates and thus can be set to any value.
As an example of how this process works assume n_cat=3 and n_cont=2. First 5 variables are sampled from the multivariate normal distribution as specified by mu_int/mu_ext, var & cov. Then, the first 3 of these variables are converted to binary based on the probabilities specified by prob_int and prob_ext. This means that that the 2 continuous variables will take their mean and sd from the last 2 entries in the vectors mu_int/mu_ext and var.

Value

A .covClass class containing covariate information

---

**set_event**

**Set up time-to-events**

---

**Description**

Defines the model formula and distribution to be used when simulating time-to-events. Please see the user-guide for the model formulations

**Usage**

`set_event(event, lambdaC, beta, shape, t_itv, change, keep)`

**Arguments**

- **event** Distribution of time-to-events: event = "pwexp" for piece-wise exponential distribution. event = "weibull" for Weibull distribution
- **lambdaC** Baseline hazard rate of internal control arm. Specify a vector for piece-wise hazard with duration specified in t_itv if event = "pwexp"  
- **beta** covariates' coefficients (i.e. log hazard ratios). Must be equal in length to the number of covariates created by `simu_cov()` (or less if restricted by keep) plus the number of covariates defined by change.
- **shape** the shape parameter of Weibull distribution if event = "weibull". NULL if event = "pwexp"
- **t_itv** a vector indicating interval lengths where the exponential rates provided in lambdaC apply. Note that the length of t_itv is at least 1 less than that of lambdaC and that the final value rate in lambdaC applies after time sum(t_itv). NULL if event = "weibull"
- **change** A list of additional delivered covariates to be used in simulating time-to-events. See details
- **keep** A character vector specifying which of the original covariates (i.e. those not derived via the change argument) should be included into the model to simulate time-to-events. If left unspecified all covariates will be included.
**Details**

The change argument is used to specify additional derived covariates to be used when simulating time-to-events. For example, let’s say have 3 covariates cov1, cov2 & cov3 but that we also wish to include a new covariate that is an interaction between cov1 and cov2 as well as another covariate that is equal to the sum of cov2 and cov3; we could implement this as follows:

```r
set_event(
  event = "weibull",
  shape = 0.9,
  lambdaC = 0.0135,
  beta = c(5, 3, 1, 7, 9),
  change = list(
    c("cov1", "*", "cov2"),
    c("cov2", "+", "cov3")
  )
)
```

Note that in the above example 5 values have been specified to beta, 3 for the original three covariates and 2 for the two additional derived covariates included via change. Variables derived via change are automatically included in the model regardless of whether they are listed in `keep` or not. Likewise, these covariates are derived separately and not via a standard R formula, that is to say including an interaction term does not automatically include the individual fixed effects.

**Value**

- `.eventClass` class containing time-to-events information
- A matrix containing simulated time-to-events information

**Examples**

# time-to-event follows a Weibull distribution
set_event(event = "weibull", shape = 0.9, lambdaC = 0.0135)

# time-to-event follows a piece-wise exponential distribution
set_event(event = "pwexp", t_itv = 1, lambdaC = c(0.1, 0.02))

---

**Description**

This function conducts validity check and generates a matrix with two binary variables indicating

1. if the observation belongs to the external trial
2. if the observation belongs to the treatment arm.
set_n(ssC, ssE, ssExt)

Arguments

ssC Number of observations in the internal control arm. Default is 100
ssE Number of observations in the internal experiment arm. Default is the same number of observations as ssC
ssExt Number of observations in the external control arm. Default is the same number of observations as ssC

Value

A matrix containing external trial indicator and treatment indicator

set_prior Specify prior distributions and predictors for MCMC methods

Description

Specify prior distributions and predictors for MCMC methods

Usage

set_prior(pred, prior, r0, alpha, sigma)

Arguments

pred Predictors to include in the weibull distribution. No covariates except for treatment indicator is included if pred = NULL. Only propensity score generated using a logistic regression model on all covariates and treatment indicator are included if pred = ps. All covariates and treatment indicator are included if pred = all
prior Prior distribution for the precision parameter that controls the degree of borrowing. Half-cauchy distribution if prior = "cauchy". No external data is included in the data if prior = "no_ext". External control arm is assumed to have the same baseline hazards as internal control arm if prior = "full_ext". Other options include "gamma" and "unif"
r0 Initial values for the shape of the weibull distribution for time-to-events
alpha Initial values for log of baseline hazard rate for external and internal control arms. Length of alpha should be 1 if prior = "full_ext" or prior = "no_ext", and equal to 2 otherwise
sigma Initial values for precision parameter if prior = "cauchy". If left NULL, default value 0.03 is used
Value

a .priorClass class containing survival data and prior information

Examples

# hierarchical Bayesian model with precision parameter follows a half-cauchy distribution
set_prior(pred = "none", prior = "cauchy", r0 = 1, alpha = c(0, 0), sigma = 0.03)

# hierarchical Bayesian model with precision parameter follows a gamma distribution
set_prior(pred = "none", prior = "gamma", r0 = 1, alpha = c(0, 0))

# conventional Bayesian model to not borrow from external control arm
set_prior(pred = "none", prior = "no_ext", alpha = 0)

# conventional Bayesian model to fully borrow from external control arm
set_prior(pred = "none", prior = "full_ext", alpha = 0)

---

**simu_cov**

*Simulate covariates*

**Description**

This function generates continuous and binary covariates through simulating from a multivariate normal distribution. Outcomes are further converted to binary variables using quantiles of the normal distribution calculated from the probability provided. Then the covariates are added to the external trial and treatment arm indicators.

**Usage**

simu_cov(ssObj, covObj, driftHR, HR, nsim, seed, path)

**Arguments**

- **ssObj**: an object of class .covClass generated in set_n
- **covObj**: an object of class .covClass generated in set_cov
- **driftHR**: hazard ratio of external control and internal control arms
- **HR**: a list of hazard ratio of treatment and control arms
- **nsim**: number of simulation. Default is 5
- **seed**: the seed of R's random number generator. Default is the first element of .Random.seed
- **path**: file name for saving the output including folder path

**Value**

a list of matrix containing simulated covariates information
Examples

# simulate patient-level data with 1 continuous covariate
sample = set_n(ssC = 10, ssE = 20, ssExt = 40)
cov1 = set_cov(n_cat = 0, n_cont = 1, mu_int = 0, mu_ext = 0, var = 1)
simu_cov(ssObj = sample, covObj = cov1, HR = 0.5, driftHR = 1, nsim = 2)

# simulate patient-level data with 1 binary and 2 continuous covariate
 cov2 = set_cov(n_cat = 1, n_cont = 2, mu_int = 0, mu_ext = 0, var = 1,
                 cov = 0.3, prob_int = 0.2, prob_ext = 0.3)
simu_cov(ssObj = sample, covObj = cov2, HR = 0.5, driftHR = 1, nsim = 2)

---

## simu_time

**Simulate time-to-events for multiple scenarios**

### Description

Simulate time-to-events for multiple scenarios

### Usage

`simu_time(dt, eventObj, clinInt, clinExt, seed, path)`

### Arguments

- **dt**
  - a list of matrix generated in `simu_cov` containing simulated covariates information

- **eventObj**
  - an object of class .eventClass generated in `set_event` including event information

- **clinInt**
  - an object of class .clinClass generated in `set_clin` including internal trial information

- **clinExt**
  - an object of class .clinClass generated in `set_clin` including external trial information

- **seed**
  - the seed of R’s random number generator. Default is the first element of `.Random.seed`

- **path**
  - file name for saving the output including folder path

### Value

a list of matrix containing simulated time-to-events information
Examples

# simulate patient-level data without covariates
# simulate survival time following weibull distribution

# simulate trial indicator and set hazard ratios
sample = set_n(ssC = 10, ssE = 20, ssExt = 40)
sample_hr <- simu_cov(ssObj = sample, HR = 1, driftHR=c(1,1.2), nsim = 10)

# enrollment pattern, drop-out, analysis start time
cl_int = set_clin(gamma = 2, e_itv = 10, etaC = 0.5, CCOD = "fixed-first", CCOD_t = 64)
c_ext = c_int

# simulate time-to-event with a weibull distribution
evt1 <- set_event(event = "weibull", shape = 0.8, lambdaC = 0.01)
simu_time(dt = sample_hr, eventObj = evt1, clinInt = c_int, clinExt = c_ext)

# simulate time-to-event with an exponential distribution
evt2 <- set_event(event = "pwexp", t_itv = 1, lambdaC = c(0.1, 0.02))
simu_time(dt = sample_hr, eventObj = evt2, clinInt = c_int, clinExt = c_int)
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