Package ‘EventPredInCure’

January 12, 2024

Title  Event Prediction Including Cured Population
Version  1.0
Date  2023-12-19
Description  Predicts enrollment and events assumed enrollment and treatment-specific time-to-
event models, and calculates test statistics for time-to-event data with cured population
based on the simulation. Methods for prediction event in the existence of cured population
License  GPL (>= 2)
Encoding  UTF-8
RoxygenNote  7.2.3
Imports  perm (>= 1.0.0.2), msm (>= 1.7.0), MLEcens (>= 0.1.7), KMsurv
(>= 0.1.5), dplyr (>= 1.1.0), rlang (>= 1.0.6), plotly (>= 4.10.1), survival (>= 2.41-3), splines (>= 3.5.0), Matrix (>= 1.2-14), mvtnorm (>= 1.1-3), rstpm2 (>= 1.6.1), numDeriv (>= 2016.8-1.1), tmvtnsim (>= 0.1.3), erify (>= 0.4.0), stats (>= 3.5.0), utils (>= 4.1.2), lubridate (>= 1.9.2), flexsurv (>= 2.2.2), MASS (>= 7.3.54)
Depends  R (>= 3.5.0)
LazyData  true
NeedsCompilation  no
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Repository  CRAN
Date/Publication  2024-01-12 10:00:05 UTC

R topics documented:

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Event Prediction Including Cured Population

Description

Predicts enrollment and events using assumed enrollment and/or treatment-specific time-to-event models in the existence of the cured population. Calculate test statistics based on the simulated data sets from the assumed enrollment and/or treatment-specific time-to-event models in the existence of the cured population.
Details

Accurately predicting the date at which a target number of subjects or events will be achieved is critical for the planning, monitoring, and execution of clinical trials in the existence of the cured population. The EventPredInCure package provides enrollment and event prediction capabilities using assumed enrollment and treatment-specific time-to-event models and calculate test statistics based on the simulated data sets from the assumed enrollment and/or treatment-specific time-to-event models in the existence of the cured population.

At the design stage, enrollment is often specified using a piecewise Poisson process with a constant enrollment rate during each specified time interval. At the analysis stage, before enrollment completion, the EventPredInCure package considers several models, including the homogeneous Poisson model, the time-decay model with an enrollment rate function $\lambda(t) = \mu/\delta \times (1 - \exp(-\delta t))$, the B-spline model with the daily enrollment rate $\lambda(t) = \exp(B(t) \times \theta)$, and the piecewise Poisson model. If prior information exists on the model parameters, it can be combined with the likelihood to yield the posterior distribution.

The EventPredInCure package offers several time-to-event models without cured-population, including exponential, Weibull, log-logistic, log-normal, piecewise exponential, model averaging of Weibull and log-normal, and spline. The models including exponential, Weibull, log-logistic, log-normal, piecewise exponential are extended to account cured-population. In the design stage, the models including exponential, Weibull, log-logistic, log-normal, piecewise exponential are also extended for delayed treatment effect setting (only for generating simulated data sets in the design stage). For time to dropout, the same set of model without cured-population and delayed treatment effect options are considered. If enrollment is complete, ongoing subjects who have not had the event of interest or dropped out of the study before the data cut contribute additional events in the future. Their event times are generated from the conditional distribution given that they have survived at the data cut. For new subjects that need to be enrolled, their enrollment time and event time can be generated from the specified enrollment and time-to-event models with parameters drawn from the posterior distribution. Time-to-dropout can be generated in a similar fashion.

The EventPredInCure package displays the Akaike Information Criterion (AIC), the Bayesian Information Criterion (BIC) and a fitted curve overlaid with observed data to help users select the most appropriate model for enrollment and event prediction. Prediction intervals in the prediction plot can be used to measure prediction uncertainty, and the simulated enrollment and event data can be used for further data exploration.

The most useful function in the EventPredInCure package is getPrediction, which combines model fitting, data simulation, and a summary of simulation results. Other functions perform individual tasks and can be used to select an appropriate prediction model.

The EventPredInCure package implements a model parameterization that enhances the asymptotic normality of parameter estimates. Specifically, the package utilizes the following parameterization to achieve this goal:

- Enrollment models
  - Poisson: $\theta = \log(\text{rate})$
  - Time-decay: $\theta = c(\log(\mu), \log(\delta))$
  - B-spline: no reparametrization is needed. The knots as considered fixed.
  - Piecewise Poisson: $\theta = \log(\text{rates})$. The left endpoints of time intervals, denoted as accrualTime, are considered fixed.

- Event or dropout models
- Exponential: \( \theta = \log(\text{rate}) \)
- Weibull: \( \theta = c(\log(\text{scale}), -\log(\text{shape})) \)
- Log-logistic: \( \theta = c(\log(\text{scale}), -\log(\text{shape})) \)
- Log-normal: \( \theta = c(\text{meanlog}, \log(\text{sdlog})) \)
- Piecewise exponential: \( \theta = \log(\text{rates}) \). The left endpoints of time intervals, denoted as piecewiseSurvivalTime for event model and piecewiseDropoutTime for dropout model, are considered fixed.
- Model averaging: \( \theta = c(\log(\text{weibull}\text{scale}), -\log(\text{weibull}\text{shape}), \text{lnorm}\text{meanlog}, \log(\text{lnorm}\text{sdlog})) \). The covariance matrix for \( \theta \) is structured as a block diagonal matrix, with the upper-left block corresponding to the Weibull component and the lower-right block corresponding to the log-normal component. In other words, the covariance matrix is partitioned into two distinct blocks, with no off-diagonal elements connecting the two components. The weight assigned to the Weibull component, denoted as \( w_1 \), is considered fixed.
- Spline: \( \theta \) corresponds to the coefficients of basis vectors. The knots and scale are considered fixed. The scale can be hazard, odds, or normal, corresponding to extensions of Weibull, log-logistic, and log-normal distributions, respectively.

The EventPredInCure package uses days as its primary time unit. If you need to convert enrollment or event rates per month to rates per day, simply divide by 30.4375.

References


\[ \text{b4pst} \]

Function to calculate survival time and censor variables before and post a time lag (delay treatment effect time)

**Description**

calculate survival time and censor variables before and post a time lag.
Usage

b4pst(os, osc, lag)

Arguments

os  a vector to denote the observed times
osc  a vector to denote censor variables
lag  a scalar to denote the time lag

Value

A list including the following variables:

- b4os: overall survival time before the time lag
- b4osc: censor variable before the time lag
- pstos: overall survival time post the time lag
- pstosc: censor variable post the time lag

Examples

n <- 500
event <- runif(n,1,5)
osc<-1*(event<=4)
os <- pmin(event,4)
b4pst(os,osc,3.5)

Chen_2016_event_time  Function to generate event time in the existence of cured population

Description

generate event time under the delay-treatment effect and cured population setting

Usage

Chen_2016_event_time(u, hr, distribution, p, lag, a, b, mu, sd)

Arguments

u  a scalar with between 0 and 1
hr  hazard ratio if this subject in the corresponding arm vs control arm
distribution  the distribution for the control arm, valid values of inputs include: exponential, weibull, log-normal, log-logistic
p  the proportion of cured population in the control arm
lag delayed treatment effect time after treatment initialization, when the hr between treatment arm and control =1 until lag time

a the shape parameter in the Weibull or the log-logistic distribution

b the scale parameter in the exponential, Weibull or the log-logistic distribution

mu the mean in the log-normal distribution

sd the standard deviation in the log-normal distribution

**Value**

the event time

**References**


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**Chen_2016_event_time_abovetime0**

*Function to generate event time based on Chen 2016 method for ongoing subject*

**Description**

generate event time under the delay-treatment effect and cured population setting given T>time0

**Usage**

Chen_2016_event_time_abovetime0(u, distribution, p, time0, a, b, mu, sd)

**Arguments**

u a scalar with between 0 and 1
distribution the distribution for the control arm, valid values of inputs include: exponential, weibull, log-normal, log-logistic

p the proportion of cured population in the control arm
time0 the observed ongoing survival time

a the shape parameter in the Weibull or the log-logistic distribution

b the scale parameter in the exponential, Weibull or the log-logistic distribution

mu the mean in the log-normal distribution

sd the standard deviation in the log-normal distribution

**Value**

the event time
Function to generate event time with piecewise exponential distribution for ongoing subject in the existence of cured population

Description

generate event time under the delay-treatment effect and cured population setting

Usage

Chen_2016_event_time_piecewise_exp_abovetime0(
  u,
  p,
  time0 = 0,
  piecewiseSurvivalTime = 0,
  piecewisehazard
)

Arguments

u a scalar with between 0 and 1, which is the conditional survival probability at the event time.
p the proportion of cured population in the control arm
time0 the observed ongoing survival time

piecewiseSurvivalTime

A vector that specifies the time intervals for the piecewise exponential survival distribution. Must start with 0, e.g., c(0, 60) breaks the time axis into 2 event intervals: [0, 60) and [60, Inf). By default, it is set to 0.

piecewisehazard

A vector that specifies the hazard rate in intervals for the piecewise exponential survival distribution.

Value

the event time

References

Fleming-Harrington weighted log-rank tests

Description
Calculating the Fleming-Harrington weighted log-rank tests

Usage
FH_test(survival, delta, trt, rho, gamma, test = c("Futility"))

Arguments
- survival: Time to event or censoring.
- delta: Event indicators.
- trt: Treatment assignment indicator with 1 denoting the treated group, and 0 denoting the placebo group.
- rho: First power parameter for the Fleming-Harrington weight which weights on the early departures: \( S(t^-)^\rho(1 - S(t^-))^\gamma \).
- gamma: Second power parameter for the Fleming-Harrington weight which weighs on the late departures: \( S(t^-)^\rho(1 - S(t^-))^\gamma \).
- test: A character denotes the test type, include "Superiority", "Futility", "Two-sided"

Value
A list 3 different components
- O1: Observed number of weighted events (with a multiplication of corresponding weights) in the treatment arm.
- E1: Expected number of weighted events (with a multiplication of corresponding weights) in the treatment arm.
- Z: Weighted log-rank test statistic.
- pvalue: Weighted log-rank test statistic pvalue

Examples
n <- 500
event <- runif(n,1,5)
osc<-1*(event<=4)
os <- pmin(event,4)
trt<-c(rep(0,n/2),rep(1,n/2))
FH_test(os,osc,trt,rho=1,gamma=0)
finalData

Description
A data frame with 300 rows and 7 columns:

- trialsdt: The trial start date
- usubjid: The unique subject ID
- randdt: The randomization date
- treatment: The treatment group number
- treatment_description: Description of the treatment group
- time: The day of event or censoring since randomization
- event: The event indicator: 1 for event, 0 for non-event
- dropout: The dropout indicator: 1 for dropout, 0 for non-dropout
- cutoffdt: The cutoff date

For ongoing subjects, both event and dropout are equal to 0.

Usage
finalData

Format
An object of class tbl_df (inherits from tbl.data.frame) with 300 rows and 9 columns.

fitDropout

Description
Fits a specified time-to-dropout model to the dropout data.

Usage
fitDropout(
  df,
  dropout_model = "exponential",
  piecewiseDropoutTime = 0,
  by_treatment = FALSE,
  criterion = "both"
)
fitDropout

Arguments

- **df**: The subject-level dropout data, including time and dropout. The data should also include treatment coded as 1, 2, and so on, and treatment_description for fitting the dropout model by treatment.
- **dropout_model**: The dropout model used to analyze the dropout data which can be set to one of the following options: "exponential", "Weibull", "log-logistic", "log-normal", or "piecewise exponential". By default, it is set to "exponential".
- **piecewiseDropoutTime**: A vector that specifies the time intervals for the piecewise exponential dropout distribution. Must start with 0, e.g., c(0, 60) breaks the time axis into 2 event intervals: [0, 60) and [60, Inf). By default, it is set to 0.
- **by_treatment**: A Boolean variable to control whether or not to fit the time-to-dropout data by treatment group. By default, it is set to FALSE.
- **criterion**: A character variable to denote the criterion in model selection to shown in the figure, which can be set to one of the following options: "aic","bic" or "both". By default, it is set to both.

Value

A list of results from the model fit including key information such as the dropout model, model, the estimated model parameters, theta, the covariance matrix, vtheta, as well as the Bayesian Information Criterion, bic, and Akaike Information Criterion, aic.

If the piecewise exponential model is used, the location of knots used in the model, piecewiseDropoutTime, will be included in the list of results.

When fitting the dropout model by treatment, the outcome is presented as a list of lists, where each list element corresponds to a specific treatment group.

The fitted time-to-dropout survival curve is also returned.

References


Examples

```r
dropout_fit <- fitDropout(df = interimData2,
                          dropout_model = "exponential")
```
**fitEnrollment**

*Fit enrollment model*

---

**Description**

Fits a specified enrollment model to the enrollment data.

**Usage**

```r
fitEnrollment(
  df,
  enroll_model = "b-spline",
  nknots = 0,
  accrualTime = 0,
  criterion = "both"
)
```

**Arguments**

- **df**: The subject-level enrollment data, including `trialsdt`, `randdt` and `cutoffdt`.
- **enroll_model**: The enrollment model which can be specified as "Poisson", "Time-decay", "B-spline", or "Piecewise Poisson". By default, it is set to "B-spline".
- **nknots**: The number of inner knots for the B-spline enrollment model. By default, it is set to 0.
- **accrualTime**: The accrual time intervals for the piecewise Poisson model. Must start with 0, e.g., `c(0, 30)` breaks the time axis into 2 accrual intervals: `[0, 30)` and `[30, Inf)`. By default, it is set to 0.
- **criterion**: A character variable to denote the criterion in model selection to shown in the figure, which can be set to one of the following options: "aic", "bic" or "both". By default, it is set to "both".

**Details**

For the time-decay model, the mean function is \( \mu(t) = \frac{\mu}{\delta} (t - 1) \delta (1 - \exp(-\delta t)) \) and the rate function is \( \lambda(t) = \frac{\mu}{\delta} (1 - \exp(-\delta t)) \). For the B-spline model, the daily enrollment rate is approximated as \( \lambda(t) = \exp(B(t) \theta) \), where \( B(t) \) represents the B-spline basis functions.

**Value**

A list of results from the model fit including key information such as the enrollment model, model, the estimated model parameters, \( \theta \), the covariance matrix, \( \Sigma_{\theta} \), and the Bayesian Information Criterion, `bic`, and Akaike Information Criterion, `aic`, as well as the design matrix \( x \) for the B-spline enrollment model, and `accrualTime` for the piecewise Poisson enrollment model.

The fitted enrollment curve is also returned.
References


Examples

```r
enroll_fit <- fitEnrollment(df = interimData1, enroll_model = "b-spline",
                           nknots = 1)
```

---

**fitEvent**  
*Fit time-to-event model*

Description

Fits a specified time-to-event model to the event data.

Usage

```r
fitEvent(  
df,  
  event_model = "model averaging",  
  piecewiseSurvivalTime = 0,  
  k = 0,  
  scale = "hazard",  
  by_treatment = FALSE,  
  criterion = "both"  
)
```

Arguments

- `df`: The subject-level event data, including time and event. The data should also include treatment coded as 1, 2, and so on, and treatment_description for fitting the event model by treatment.
- `event_model`: The event model used to analyze the event data which can be set to one of the following options: "exponential", "Weibull", "log-logistic", "log-normal", "piecewise exponential", "model averaging", "spline", "exponential with cured population", "weibull with cured population", "log-normal with cured population", "log-logistic with cured population" or "piecewise exponential with cured population". The model averaging uses the exp(-bic/2) weighting and combines Weibull and log-normal models. The spline model of Royston and Parmar (2002) assumes that a transformation of the survival function is modeled as a natural cubic spline function of log time. By default, it is set to "model averaging".
fitEvent

piecewiseSurvivalTime
A vector that specifies the time intervals for the piecewise exponential survival distribution or piecewise exponential with cured population. Must start with 0, e.g., c(0, 60) breaks the time axis into 2 event intervals: [0, 60) and [60, Inf). By default, it is set to 0.

k
The number of inner knots of the spline. The default k=0 gives a Weibull, log-logistic or log-normal model, if scale is "hazard", "odds", or "normal", respectively. The knots are chosen as equally-spaced quantiles of the log uncensored survival times. The boundary knots are chosen as the minimum and maximum log uncensored survival times.

scale
If "hazard", the log cumulative hazard is modeled as a spline function. If "odds", the log cumulative odds is modeled as a spline function. If "normal", -qnorm(S(t)) is modeled as a spline function.

by_treatment
A Boolean variable to control whether or not to fit the time-to-event data by treatment group. By default, it is set to FALSE.

criterion
A character variable to denote the criterion in model selection to shown in the figure, which can be set to one of the following options: "aic", "bic" or "both". By default, it is set to both.

Value
A list of results from the model fit including key information such as the event model, model, the estimated model parameters, theta, the covariance matrix, vtheta, as well as the Bayesian Information Criterion, bic, and Akaike Information Criterion, aic.

If the piecewise exponential model is used, the location of knots used in the model, piecewiseSurvivalTime, will be included in the list of results.

If the model averaging option is chosen, the weight assigned to the Weibull component is indicated by the w1 variable.

If the spline option is chosen, the knots and scale will be included in the list of results.

When fitting the event model by treatment, the outcome is presented as a list of lists, where each list element corresponds to a specific treatment group.

The fitted time-to-event survival curve is also returned.

References


Examples

event_fit <- fitEvent(df = interimData2,
                      event_model = "piecewise exponential",
                      piecewiseSurvivalTime = c(0, 180))
getPrediction

Enrollment and event prediction

Description

Performs enrollment and event prediction by utilizing observed data and specified enrollment and event models.

Usage

```r
getPrediction(
  df = NULL,
  to_predict = "enrollment and event",
  target_n = NA,
  target_d = NA,
  enroll_model = "b-spline",
  nknots = 0,
  lags = 30,
  accrualTime = 0,
  enroll_prior = NULL,
  event_model = "exponential",
  piecewiseSurvivalTime = 0,
  k = 0,
  scale = "hazard",
  event_prior = NULL,
  dropout_model = "exponential",
  piecewiseDropoutTime = 0,
  dropout_prior = NULL,
  fixedFollowup = FALSE,
  followupTime = 365,
  pilevel = 0.9,
  nyears = 4,
  nreps = 500,
  showEnrollment = TRUE,
  showEvent = TRUE,
  showDropout = FALSE,
  showOngoing = FALSE,
  by_treatment = FALSE,
  ngroups = 1,
  alloc = NULL,
  treatment_label = NULL,
  criterion = "both",
  seed.num = NULL
)`
getPrediction

Arguments

df
The subject-level enrollment and event data, including trialsdt, usubjid, randdt, and cutoffdt for enrollment prediction, and, additionally, time, event, and dropout for event prediction. The data should also include treatment coded as 1, 2, and so on, and treatment_description for enrollment and event prediction by treatment. By default, it is set to NULL for enrollment and event prediction at the design stage.

to_predict
Specifies what to predict: "enrollment only", "event only", or "enrollment and event". By default, it is set to "enrollment and event".

target_n
The target number of subjects to enroll in the study.

target_d
The target number of events to reach in the study.
enroll_model
The enrollment model which can be specified as "Poisson", "Time-decay", "B-spline", "Piecewise Poisson" or "Piecewise Uniform". By default, it is set to "B-spline".

nknots
The number of inner knots for the B-spline enrollment model. By default, it is set to 0.

lags
The day lags to compute the average enrollment rate to carry forward for the B-spline enrollment model. By default, it is set to 30.

accrualTime
The accrual time intervals for the piecewise Poisson model. Must start with 0, e.g., c(0, 30) breaks the time axis into 2 accrual intervals: [0, 30) and [30, Inf). By default, it is set to 0.
enroll_prior
The prior of enrollment model parameters.

event_model
The event model used to analyze the event data which can be set to one of the following options: "exponential", "Weibull", "log-logistic", "log-normal", "piecewise exponential", "model averaging", "exponential with cured population", "weibull with cured population", "log-normal with cured population", "log-logistic with cured population", or "piecewise exponential with cured population". For the design stage analysis, there are additional options: "exponential with cured population and delayed treatment", "weibull with cured population and delayed treatment", "log-normal with cured population and delayed treatment", "log-logistic with cured population and delayed treatment". The model averaging uses the \( \exp(-bic/2) \) weighting and combines Weibull and log-normal models. By default, it is set to "exponential".

piecewiseSurvivalTime
A vector that specifies the time intervals for the piecewise exponential survival distribution, or piecewise exponential with cured population. Must start with 0, e.g., c(0, 60) breaks the time axis into 2 event intervals: [0, 60) and [60, Inf). By default, it is set to 0.

k
The number of inner knots of the spline event model of Royston and Parmar (2002). The default k=0 gives a Weibull, log-logistic or log-normal model, if scale is "hazard", "odds", or "normal", respectively. The knots are chosen as equally-spaced quantiles of the log uncensored survival times. The boundary knots are chosen as the minimum and maximum log uncensored survival times.

scale
If "hazard", the log cumulative hazard is modeled as a spline function. If "odds", the log cumulative odds is modeled as a spline function. If "normal", -qnorm(S(t)) is modeled as a spline function.
event_prior  The prior of event model parameters.
dropout_model  The dropout model used to analyze the dropout data which can be set to one of the following options: "exponential", "Weibull", "log-logistic", "log-normal", or "piecewise exponential". By default, it is set to "exponential".

piecewiseDropoutTime  A vector that specifies the time intervals for the piecewise exponential dropout distribution. Must start with 0, e.g., c(0, 60) breaks the time axis into 2 event intervals: [0, 60) and [60, Inf). By default, it is set to 0.
dropout_prior  The prior of dropout model parameters.
fixedFollowup  A Boolean variable indicating whether a fixed follow-up design is used. By default, it is set to FALSE for a variable follow-up design.
followupTime  The follow-up time for a fixed follow-up design, in days. By default, it is set to 365.
pilevel  The prediction interval level. By default, it is set to 0.90.
nyears  The number of years after the data cut for prediction. By default, it is set to 4.
nreps  The number of replications for simulation. By default, it is set to 500.
showEnrollment  A Boolean variable to control whether or not to show the number of enrolled subjects. By default, it is set to TRUE.
showEvent  A Boolean variable to control whether or not to show the number of events. By default, it is set to TRUE.
showDropout  A Boolean variable to control whether or not to show the number of dropouts. By default, it is set to FALSE.
showOngoing  A Boolean variable to control whether or not to show the number of ongoing subjects. By default, it is set to FALSE.
by_treatment  A Boolean variable to control whether or not to predict by treatment group. By default, it is set to FALSE.
ngroups  The number of treatment groups for enrollment prediction at the design stage. By default, it is set to 1. It is replaced with the actual number of treatment groups in the observed data if df is not NULL.
alloc  The treatment allocation in a randomization block. By default, it is set to NULL, which yields equal allocation among the treatment groups.
treatment_label  The treatment labels for treatments in a randomization block for design stage prediction.
criterion  A character variable to denote the criterion in model selection to shown in the figure, which can be set to one of the following options: "aic", "bic" or "both". By default, it is set to both.
seed.num  The number of the random seed. The default is NULL.

Details

For the time-decay model, the mean function is \(\mu(t) = \mu / \delta * (t - 1 / \delta * (1 - \exp(-\delta * t)))\) and the rate function is \(\lambda(t) = \mu / \delta * (1 - \exp(-\delta * t))\). For the B-spline model, the
daily enrollment rate is approximated as $\lambda(t) = \exp(B(t) + \theta)$, where $B(t)$ represents the B-spline basis functions.

The `enroll_prior` variable should be a list that includes `model` to specify the enrollment model (poisson, time-decay, piecewise poisson, or piecewise uniform), `theta` and `vtheta` to indicate the parameter values and the covariance matrix. One can use a very small value of `vtheta` to fix the parameter values. For the piecewise Poisson enrollment or piecewise uniform rate model, the list should also include `accrualTime`. It should be noted that the B-spline model is not appropriate for use as prior.

For event prediction by treatment with prior information, the `event_prior` variable should be a list with one element per treatment. For each treatment, the element should include `model` to specify the event (dropout) model (exponential, weibull, log-logistic, log-normal, or piecewise exponential, weibull with cured population, exponential with cured population, log-normal with cured population, log-logistic with cured population, piecewise exponential with cured population, exponential with cured population and delayed treatment, weibull with cured population and delayed treatment, log-normal with cured population and delayed treatment, log-logistic with cured population and delayed treatment), `theta` and `vtheta` to indicate the parameter values and the covariance matrix. For the piecewise exponential or piecewise exponential with cured population or piecewise exponential with cured population and delayed treatment event model, the list should also include `piecewiseSurvivalTime` to indicate the location of knots. It should be noted that the model averaging and spline options are not appropriate for use as prior.

The `dropout_prior` should be a list with one element per treatment. For each treatment, the element should include `w` to specify the weight of the treatment in a randomization block, `model` to specify the dropout model (exponential, weibull, log-logistic, log-normal, or piecewise exponential), `theta` and `vtheta` to indicate the parameter values and the covariance matrix. For the piecewise exponential dropout model, the list should also include `piecewiseDropoutTime` to indicate the location of knots.

If the event prediction is not by treatment while the prior information is given by treatment, then each element of `event_prior` (dropout_prior) should also include `w` to specify the weight of the treatment in a randomization block. This method can only be used in the event prior with exponential, weibull, log-logistic, log-normal, or piecewise exponential.

If the prediction is not by treatment and the prior is given for the overall study, then `event_prior` (dropout_prior) is a flat list with `model`, `theta`, and `vtheta`. For the piecewise exponential event (dropout) model, it should also include `piecewiseSurvivalTime` (piecewiseDropoutTime) to indicate the location of knots.

For analysis-stage enrollment and event prediction, the `enroll_prior`, `event_prior`, and `dropout_prior` are either set to `NULL` to use the observed data only, or specify the prior distribution of model parameters to be combined with observed data likelihood for enhanced modeling flexibility.

**Value**

A list that includes the fits of observed data models, as well as simulated enrollment data for new subjects and simulated event data for ongoing and new subjects.

**Examples**

```r
fit1 <- list(model = "piecewise uniform",
```
\begin{verbatim}
theta = -0.58,
vtheta=0, accrualTime =0)

fit2 <- list()
fit2[[1]] <- list(model = "weibull with cured population and delayed treatment",
theta = c(-2.2,0,6.5,0,1),
vtheta = matrix(0,5,5))
fit2[[2]] <- list(model = "weibull with cured population and delayed treatment",
theta = c(-2.2,0,6.5,46,0.65),
vtheta = matrix(0,5,5))

fit3 <- list()
fit3[[1]] <- list(model = "exponential",
theta = log(0.0003),
vtheta=0)
fit3[[2]] <- list(model = "exponential",
theta = log(0.0003),
vtheta=0)

getPrediction(target_n=200,target_d=60,lags=46,enroll_prior=fit1,
    event_prior=fit2,
    dropout_prior=fit3,ngroups=2)
\end{verbatim}

---

**interimData1**

*Interim enrollment and event data before enrollment completion*

### Description

A data frame with 225 rows and 9 columns:

- **trialsdt**  The trial start date
- **usubjid**  The unique subject ID
- **randdt**  The randomization date
- **treatment**  The treatment group number
- **treatment_description**  Description of the treatment group
- **time**  The day of event or censoring since randomization
- **event**  The event indicator: 1 for event, 0 for non-event
- **dropout**  The dropout indicator: 1 for dropout, 0 for non-dropout
- **cutoffdt**  The cutoff date

For ongoing subjects, both event and dropout are equal to 0.
**Usage**

`interimData2`

**Format**

An object of class `tbl_df` (inherits from `tbl.data.frame`) with 224 rows and 9 columns.

---

**interimData2**  |  *Interim enrollment and event data after enrollment completion*

**Description**

A data frame with 300 rows and 7 columns:

- **trialsdt**: The trial start date
- **usubjid**: The unique subject ID
- **randdt**: The randomization date
- **treatment**: The treatment group number
- **treatment_description**: Description of the treatment group
- **time**: The day of event or censoring since randomization
- **event**: The event indicator: 1 for event, 0 for non-event
- **dropout**: The dropout indicator: 1 for dropout, 0 for non-dropout
- **cutoffdt**: The cutoff date

For ongoing subjects, both event and dropout are equal to 0.

**Usage**

`interimData2`

**Format**

An object of class `tbl_df` (inherits from `tbl.data.frame`) with 300 rows and 9 columns.
loglik_Chen_exponential

Log-likelihood function for exponential distribution with cured population

Description

Provide log-likelihood function for exponential distribution with cured population

Usage

loglik_Chen_exponential(par, df)

Arguments

par a vector with two elements, where the first element denotes the logistic of the proportion of the cured population, and the second element denotes the log of the hazard rate.

df The subject-level event data, including time and event.

Value

The negative value of the log-likelihood function given parameter par and the dataset df

References


loglik_Chen_log_logistic

Log-likelihood function for log-logistic distribution with cured population

Description

Provide log-likelihood function for log-logistic distribution with cured population

Usage

loglik_Chen_log_logistic(par, df)
**Arguments**

par  
a vector with three elements, where the first element denotes the logistic of the proportion of the cured population, and the second element and the third element denote the log of shape and the log of the scale parameter of the log-logistic distribution.

df  
The subject-level event data, including time and event.

**Value**

The negative value of the log-likelihood function given parameter par and the dataset df

**References**

Description

Provide log-likelihood function for piecewise-exponential distribution with cured population

Usage

loglik_Chen_piecewise_exponential(par = NULL, df, piecewiseSurvivalTime)

Arguments

- **par**: a vector with m+1 elements, where the first element denotes the logistic of the proportion of the cured population, and the rest element denotes the log of the hazard rate in intervals.
- **df**: The subject-level event data, including `time` and `event`.
- **piecewiseSurvivalTime**: A vector with length m that specifies the time intervals for the piecewise exponential survival distribution. Must start with 0, e.g., c(0, 60) breaks the time axis into 2 event intervals: [0, 60) and [60, Inf). By default, it is set to 0.

Value

The negative value of the log-likelihood function given parameter `par` and the dataset `df`.

References


Description

Provide log-likelihood function for Weibull distribution with cured population

Usage

loglik_Chen_weibull(par, df)
**Arguments**

- **par**
  a vector with three elements, where the first element denotes the logistic of the proportion of the cured population, and the second element and the third element denote the log of the shape and log of the scale parameter of the Weibull distribution.

- **df**
  The subject-level event data, including time and event.

**Value**

The negative value of the log-likelihood function given parameter par and the dataset df.

**References**


### predictEnrollment

**Description**

Utilizes a pre-fitted enrollment model to generate enrollment times for new subjects and provide a prediction interval for the expected time to reach the enrollment target.

**Usage**

```r
predictEnrollment(
  df = NULL,
  target_n,
  enroll_fit,
  lags = 1,
  pilevel = 0.9,
  nyears = 4,
  nreps = 500,
  by_treatment = FALSE,
  ngroups = 1,
  alloc = NULL,
  treatment_label = NULL,
  seed.num = NULL
)
```

**Arguments**

- **df**
  The subject-level enrollment data, including trialsdt, randdt and cutoffdt. The data should also include treatment coded as 1, 2, and so on, and treatment_description for prediction by treatment group. By default, it is set to NULL for enrollment prediction at the design stage.
predictEnrollment

target_n  The target number of subjects to enroll in the study.
enroll_fit The pre-fitted enrollment model used to generate predictions.
lags  The day lags to compute the average enrollment rate to carry forward for the B-spline enrollment model. By default, it is set to 1.
pilevel  The prediction interval level. By default, it is set to 0.90.
nyears  The number of years after the data cut for prediction. By default, it is set to 4.
nreps  The number of replications for simulation. By default, it is set to 500.
by_treatment  A Boolean variable to control whether or not to predict enrollment by treatment group. By default, it is set to FALSE.
ngroups  The number of treatment groups for enrollment prediction at the design stage. By default, it is set to 1. It is replaced with the actual number of treatment groups in the observed data if df is not NULL.
alloc  The treatment allocation in a randomization block. By default, it is set to NULL, which yields equal allocation among the treatment groups.
treatment_label  The treatment labels for treatments in a randomization block for design stage prediction.
seed.num  The number of the random seed. The default is NULL.

Details

The enroll_fit variable can be used for enrollment prediction at the design stage. A piecewise uniform can be parameterized through the time intervals, accrualTime, which is treated as fixed, and the enrollment rates in the intervals, accrualrate, the number of patients in each intervals. A piecewise Poisson model can be parameterized through the time intervals, accrualTime, which is treated as fixed, and the enrollment rates in the intervals, accrualIntensity, the log of which is used as the model parameter. For the homogeneous Poisson, time-decay, and piecewise Poisson models, enroll_fit is used to specify the prior distribution of model parameters, with a very small variance being used to fix the parameter values. It should be noted that the B-spline model is not appropriate for use during the design stage.

During the enrollment stage, enroll_fit is the enrollment model fit based on the observed data. The fitted enrollment model is used to generate enrollment times for new subjects.

Value

A list of prediction results, which includes important information such as the median, lower and upper percentiles for the estimated time to reach the target number of subjects, as well as simulated enrollment data for new subjects. The data for the prediction plot is also included within the list.

References

Examples

# Enrollment prediction at the design stage
fit1 <- list(model = "piecewise uniform",
             theta = -0.58,
             vtheta=0, accrualTime =0)

predictEnrollment(df = NULL, target_n=200, enroll_fit = fit1,lags=46,
                  pilevel=0.9, nyears=4, nreps=100,by_treatment=TRUE,
                  ngroups=2, alloc=c(1,1), treatment_label=c('a','b'))

predictEvent

Predict event time for ongoing subjects with or without cured population.

Description

Utilizes pre-fitted time-to-event and time-to-dropout models to generate event and dropout times for ongoing subjects and new subjects. It also provides a prediction interval for the expected time to reach the target number of events.

Usage

predictEvent(
  df = NULL,
  target_d,
  newSubjects = NULL,
  event_fit,
  dropout_fit = NULL,
  fixedFollowup = FALSE,
  followupTime = 365,
  pilevel = 0.9,
  nyears = 4,
  nreps = 500,
  showEnrollment = TRUE,
  showEvent = TRUE,
  showDropout = FALSE,
  showOngoing = FALSE,
  by_treatment = FALSE,
  seed.num = NULL
)

Arguments

df The subject-level enrollment and event data, including randdt, cutofftdt, time, event, and dropout. By default, it is set to NULL for event prediction at the design stage.
predictEvent

- **target_d**: The target number of events to reach in the study.
- **newSubjects**: The enrollment data for new subjects including `draw` and `arrivalTime`. By default, it is set to NULL, indicating the completion of subject enrollment.
- **event_fit**: The pre-fitted event model used to generate predictions.
- **dropout_fit**: The pre-fitted dropout model used to generate predictions. By default, it is set to NULL, indicating no dropout.
- **fixedFollowup**: A Boolean variable indicating whether a fixed follow-up design is used. By default, it is set to FALSE for a variable follow-up design.
- **followupTime**: The follow-up time for a fixed follow-up design, in days. By default, it is set to 365.
- **pilevel**: The prediction interval level. By default, it is set to 0.90.
- **nyears**: The number of years after the data cut for prediction. By default, it is set to 4.
- **nreps**: The number of replications for simulation. By default, it is set to 500. If `newSubjects` is not NULL, the number of draws in `newSubjects` should be `nreps`.
- **showEnrollment**: A Boolean variable to control whether or not to show the number of enrolled subjects. By default, it is set to TRUE.
- **showEvent**: A Boolean variable to control whether or not to show the number of events. By default, it is set to TRUE.
- **showDropout**: A Boolean variable to control whether or not to show the number of dropouts. By default, it is set to FALSE.
- **showOngoing**: A Boolean variable to control whether or not to show the number of ongoing subjects. By default, it is set to FALSE.
- **by_treatment**: A Boolean variable to control whether or not to predict event by treatment group. By default, it is set to FALSE.
- **seed.num**: The number of the random seed. The default is NULL.

**Details**

To ensure successful event prediction at the design stage, it is important to provide the `newSubjects` data set.

To specify the event model used during the design-stage event prediction, the `event_fit` be a list with one element per treatment. For each treatment, the element should include `w` to specify the weight of the treatment in a randomization block, `model` to specify the event model (exponential, weibull, log-logistic, log-normal, or piecewise exponential, weibull with cured population, exponential with cured population, log-normal with cured population, log-logistic with cured population, piecewise exponential with cured population, exponential with cured population and delayed treatment, weibull with cured population and delayed treatment, log-normal with cured population and delayed treatment, log-logistic with cured population and delayed treatment), `theta` and `vtheta` to indicate the parameter values and the covariance matrix. For the piecewise exponential or piecewise exponential with cured population or piecewise exponential with cured population and delayed treatment event model, the list should also include `piecewiseSurvivalTime` to indicate the location of knots. It should be noted that the model averaging and spline options are not appropriate for use as prior.
To specify the dropout model used during the design stage event prediction, the dropout_fit should be a list with one element per treatment. For each treatment, the element should include w to specify the weight of the treatment in a randomization block, model to specify the dropout model (exponential, weibull, log-logistic, log-normal, or piecewise exponential), theta and vtheta to indicate the parameter values and the covariance matrix. For the piecewise exponential dropout model, the list should also include piecewiseDropoutTime to indicate the location of knots.

Following the commencement of the trial, we obtain the event model fit and the dropout model fit based on the observed data, denoted as event_fit and dropout_fit, respectively. These fitted models are subsequently utilized to generate event and dropout times for both ongoing and new subjects in the trial.

Value

A list of prediction results which includes important information such as the median, lower and upper percentiles for the estimated day and date to reach the target number of events, as well as simulated event data for both ongoing and new subjects. The data for the prediction plot is also included within this list.

References


Examples

```r
fit1 <- list(model = "piecewise uniform",
             theta = -0.58,
             vtheta = 0,
             accrualTime = 0)
fit2 <- list()
fitt[[1]] <- list(model = "weibull with cured population and delayed treatment",
                 theta = c(-2.2, 0, 6.5, 0, 1),
                 vtheta = matrix(0, 5, 5))
fitt[[2]] <- list(model = "weibull with cured population and delayed treatment",
                 theta = c(-2.2, 0, 6.5, 46, 0.65),
                 vtheta = matrix(0, 5, 5))

enroll_pred <- predictEnrollment(df = NULL, target_n = 200, enroll_fit = fit1, lags = 46,
                                  plevel = 0.9, nyears = 4, nreps = 100, by_treatment = TRUE,
                                  ngroups = 2, alloc = c(1, 1), treatment_label = c("a", "b"))

event_pred <- predictEvent(df = NULL, target_d = 60,
                            newSubjects = enroll_pred$newSubjects,
                            event_fit = fit2, dropout_fit = NULL,
                            plevel = 0.9,
                            ...)
SP_Chen_exponential

Survival probability function of the exponential distribution with cured population

Description

Calculate survival probability of the exponential distribution with cured population

Usage

SP_Chen_exponential(par, t)
Arguments
par  a vector with two elements, where the first element denotes the logistic of the proportion of the cured population, and the second element denotes the log of the hazard rate.
t  a vector with non-negative elements.

Value
Survival probability of the exponential distribution with cured population given parameters par at times t.

References

Description
Calculate survival probability of the log-logistic distribution with cured population

Usage
SP_Chen_log_logistic(par, t)

Arguments
par  a vector with three elements, where the first element denotes the logistic of the proportion of the cured population, and the second element and the third element denote the log of shape and the log of the scale parameter of the log-logistic distribution.
t  a vector with non-negative elements.

Value
Survival probability of the log-logistic distribution with cured population given parameters par at times t.

References
**SP_Chen_log_normal**  
*Survival probability function of the log-normal distribution with cured population*

**Description**

Calculate survival probability of the log-normal distribution with cured population

**Usage**

```r
SP_Chen_log_normal(par, t)
```

**Arguments**

- `par`  
  a vector with three elements, where the first element denotes the logistic of the proportion of the cured population, and the second element and the third element denote the mean and the log of standard deviation parameter of the log-normal distribution.

- `t`  
  a vector with non-negative elements.

**Value**

Survival probability of the log-normal distribution with cured population given parameters `par` at times `t`.

**References**


---

**SP_Chen_piecewise_exponential**  
*Survival probability function of the piecewise exponential distribution with cured population*

**Description**

Calculate survival probability of the piecewise exponential distribution with cured population

**Usage**

```r
SP_Chen_piecewise_exponential(par, t, piecewiseSurvivalTime)
```
Arguments

par: a vector with m+1 elements, where the first element denotes the logistic of the proportion of the cured population, and the rest element denotes the log of the hazard rate in intervals.

t: a vector with non-negative elements.

piecewiseSurvivalTime

A vector that specifies the time intervals for the piecewise exponential survival distribution. Must start with 0, e.g., c(0, 60) breaks the time axis into 2 event intervals: [0, 60) and [60, Inf). By default, it is set to 0.

Value

Survival probability of the piecewise-exponential distribution with cured population given parameters par at times t.

References


---

SP_Chen_weibull

Survival probability function of the Weibull distribution with cured population

Description

Calculate survival probability of the Weibull distribution with cured population

Usage

SP_Chen_weibull(par, t)

Arguments

par: a vector with three elements, where the first element denotes the logistic of the proportion of the cured population, and the second element and the third element denote the log of the shape and log of the scale parameter of the Weibull distribution.

t: a vector with non-negative elements.

Value

Survival probability of the Weibull distribution with cured population given parameters par at times t.
References


summarizeObserved

summarizeObserved

Summarize observed data

Description

Provides an overview of the observed data, including the trial start date, data cutoff date, enrollment duration, number of subjects enrolled, number of events and dropouts, number of subjects at risk, cumulative enrollment and event data, daily enrollment rates, and Kaplan-Meier plots for time to event and time to dropout.

Usage

summarizeObserved(
  df,
  to_predict = "event only",
  showplot = TRUE,
  by_treatment = FALSE
)

Arguments

df The subject-level data, including trialsdt, usubjid, randdt, and cutoffdt for enrollment prediction, as well as time, event and dropout for event prediction, and treatment coded as 1, 2, and so on, and treatment_description for prediction by treatment group.
to_predict Specifies what to predict: "enrollment only", "event only", or "enrollment and event". By default, it is set to "event only".
showplot A Boolean variable to control whether or not to show the observed data plots. By default, it is set to TRUE.
by_treatment A Boolean variable to control whether or not to summarize observed data by treatment group. By default, it is set to FALSE.

Value

A list that includes a range of summary statistics, data sets, and plots depending on the value of to_predict.

Examples

observed1 <- summarizeObserved(df = interimData1,
                                 to_predict = "enrollment and event")
test_plot

Function to plot KM plot for time-to-event data in simulation

Description
Plot KM plot for each arm at one realization

Usage
```
test_plot(test0, plot.index = 1)
```

Arguments
- **test0**: an object obtained from `test_procedure`
- **plot.index**: the index of simulation

Value
A KM plot for events in each arm

Examples
```
fit1 <- list(model = "piecewise uniform",
             theta = -0.58,
             vtheta=0, accrualTime =0)
fit2<-list()
fit2[[1]] <- list(model = "weibull with cured population and delayed treatment",
                 theta = c(0.5,0,6.5,0,1),
                 vtheta = matrix(0,5,5))
fit2[[2]] <- list(model = "weibull with cured population and delayed treatment",
                 theta = c(0.5,0,6.5,46,0.65),
                 vtheta = matrix(0,5,5))
fit3<-list()
fit3[[1]] <- list(model = "weibull with cured population and delayed treatment",
                 theta = c(0.5,0,6.5,0,1),
                 vtheta = matrix(0,5,5))
fit3[[2]] <- list(model = "weibull with cured population and delayed treatment",
                 theta = c(0.5,0,6.5,0,1),
                 vtheta = matrix(0,5,5))
fit4 <- list(model = "exponential",
             theta =log(0.0003),
             vtheta=0)

test1<-test_procedure(pilevel=0.9,nyears=4,enroll_fit=fit1,
dropout_fit=fit4,enroll_prior=fit1,event_prior_h0=fit3,
event_prior_ha=fit2,dropout_prior=NULL,
target_n=200,target_IA_d=40,
target_d=60,ialpha=0.016,falpha=0.0450,
```
test_procedure

**Description**

Provides summary and test statistics based on simulation.

**Usage**

```r
test_procedure(
  pilevel = 0.9,
  nyears = 4,
  enroll_fit = enroll_fit,
  dropout_fit = dropout_fit,
  enroll_prior = NULL,
  event_prior_h0 = NULL,
  event_prior_ha = NULL,
  dropout_prior = NULL,
  target_n,
  target_IA_d,
  target_d,
  ialpha = 0.025,
  falpha,
  lag,
  by_fitted_enroll = FALSE,
  by_fitted_dropout = FALSE,
  treatment_label = FALSE,
  ngroups = 2,
  alloc = NULL,
  nreps = 500,
  IA_included,
  test = "Superiority",
  test_IA = "Superiority",
  Futility_boundary = 1,
  seed.num = NULL
)
```

**Arguments**

- `pilevel`: the confidence interval, the default is 0.95.
- `nyears`: the year after data cutoff or follow-up.
enroll_fit an object generated from fitEnrollment.
dropout_fit an object generated from fitDropout.
enroll_prior The prior of enrollment model parameters.
event_prior_h0 The prior of event model parameters under null hypothesis
event_prior_ha The prior of event model parameters under alternative hypothesis
dropout_prior The prior of dropout model parameters.
target_n The target number of subjects to enroll in the study.
target_IA_d number of events needed for interim analysis
target_d number of events needed for primary analysis
ialpha interim analysis alpha nominal value (only one interim allowed)
falpha primary analysis alpha nominal value
lag a scalar to denote time (days). Hazard ratio before and after this time would be calculated.
by_fitted_enroll A Boolean variable to control whether or not to predict enrollment time with fitted model. By default, it is set to FALSE.
by_fitted_dropout A Boolean variable to control whether or not to predict dropout time with fitted model. By default, it is set to FALSE.
treatment_label The treatment labels for treatments in a randomization block for design stage prediction.
ngroups The number of treatment groups for enrollment prediction at the design stage. By default, it is set to 2. It is replaced with the actual number of treatment groups in the observed data if df is not NULL.
alloc The treatment allocation in a randomization block. By default, it is set to NULL, which yields equal allocation among the treatment groups.
nreps The number of replications for simulation. By default, it is set to 500.
IA_included A Boolean variable to control whether or not to include one interim analysis. By default, it is set to FALSE.
test a character denotes the test type, includes "Superiority","Futility","Two-sided"
test_IA a character denotes the test type in interim analysis, includes "Efficacy","Futility", or "Efficacy and Futility"
Futility_boundary a positive number denotes the boundary of the Futility in the scale of hazard ratio
seed.num The number of the random seed. The default is NULL.

Value
A list with following components
• iteration0 - the number of simulations that achieved target number of events in interim analysis and primary analysis under null hypothesis.
• iteration1 - the number of simulations that achieved target number of events in interim analysis and primary analysis under alternative hypothesis.
• simu_summary - the summary table of number of simulations that achieved or do not achieve target number of events in each analysis under null hypothesis and alternative hypothesis.
• power - the alpha and powers from log-rank test and Fleming&Harrington test
• samplesize - the counts per arm and total, includes the number of patients, events at interim analysis and primary analysis, events at interim analysis before delay, events at primary analysis before delay
• hzratio - average hazard ratio at primary analysis and interim analysis
• hzrc - Frequencies of hazard ratios in specific zones
• hzratio2 - HR before and after delay
• median - Medians of survival time at interim analysis and primary analysis
• osrate - survival rate at milestones (1, 2 and 4 years)
• duration - Study duration for enrollment, interim analysis and primary analysis
• duration1 - Durations for interim analysis and primary analysis with 95% CI
• textH0 - the summary text of number of simulations that achieved or do not achieve target number of events in primary analysis under null hypothesis.
• textHA - the summary text of number of simulations that achieved or do not achieve target number of events in primary analysis under alternative hypothesis.

Examples

```r
fit1 <- list(model = "piecewise uniform",
            theta = -0.58,
            vtheta=0, accrualTime =0)
fit2<-list()
fit2[[1]] <- list(model = "weibull with cured population and delayed treatment",
                 theta = c(-2.2,0,6.5,0,1),
                 vtheta = matrix(0,5,5))
fit2[[2]] <- list(model = "weibull with cured population and delayed treatment",
                 theta = c(-2.2,0,6.5,46,0.65),
                 vtheta = matrix(0,5,5))
fit3 <-list()
fit3[[1]] <- list(model = "weibull with cured population and delayed treatment",
                 theta = c(-2.2,0,6.5,0,1),
                 vtheta = matrix(0,5,5))
fit3[[2]] <- list(model = "weibull with cured population and delayed treatment",
                 theta = c(-2.2,0,6.5,0,1),
                 vtheta = matrix(0,5,5))
fit4 <-list()
fit4[[1]] <- list(model = "exponential",
                 theta =log(0.0003),
                 vtheta=0)
```
fit4[[2]] <- list(model = "exponential",
                theta = log(0.0003),
                vtheta=0)

test1<-test_procedure(pilevel=0.9,nyears=4,enroll_fit=fit1,
                      dropout_fit=fit4,enroll_prior=fit1,event_prior_h0=fit3,
                      event_prior_ha=fit2,dropout_prior=NULL,
                      target_n=200,target_IA_d=40,target_d=60,
                      ialpha=0.016,falpha=0.0450,
                      lag=46,by_fitted_enroll=FALSE,
                      by_fitted_dropout=FALSE,treatment_label=c("Var","Var"),
                      ngroups=2,alloc=c(1,1),nreps=100, IA_included=TRUE)

---

tte Calculating log-rank test p-value, median time from each arm, hazard ratio between two arms, number of subjects and events in time-to-event outcomes.

Description

Calculate log-rank test p-value, median time from each arm, HR between arms, number of subjects and events

Usage

tte(os, osc, grp, type, test = "Futility")

Arguments

<table>
<thead>
<tr>
<th>Argument</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>os</td>
<td>Time to event variable</td>
</tr>
<tr>
<td>osc</td>
<td>Time to event censoring variable</td>
</tr>
<tr>
<td>grp</td>
<td>Treatment assignment indicator with 1 denoting the treated group, and 0 denoting the placebo group.</td>
</tr>
<tr>
<td>type</td>
<td>either &quot;all&quot; or &quot;logrank&quot; or &quot;hr&quot;</td>
</tr>
<tr>
<td>test</td>
<td>a character denotes the test type, include &quot;Superiority&quot;,&quot;Futility&quot;,&quot;Two-sided&quot;</td>
</tr>
</tbody>
</table>

Details

The control arm

Value

If type='all', return a list that includes the log-rank p-value, median time from each arm, hazard ratio between arms, and 95% confidence interval of hazard ratio, number of subjects and events; and events If type='logrank', return a list that includes the log-rank p-value, number of subjects and events; If type='hr', return a list that includes hazard ratio between arms, and 95% confidence interval of hazard ratio
Examples

```r
n <- 500
event <- runif(n, 1, 5)
osc <- 1 * (event <= 4)
os <- pmin(event, 4)
trt <- c(rep(0, n/2), rep(1, n/2))
tte(os, osc, trt, type = 'all')
```
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