

Package ‘eventPred’

September 17, 2024

Title Event Prediction

Version 0.2.6

Date 2024-09-17

Description

Predicts enrollment and events at the design or analysis stage using specified enrollment and time-to-event models through simulations.

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Encoding UTF-8

RoxygenNote 7.3.1

Imports 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), purrr (>= 1.0.2), flexsurv (>= 2.2.2), erify (>= 0.4.0), stats (>= 3.5.0), shiny (>= 1.7.1)

Suggests knitr, rmarkdown, testthat (>= 3.0.0)

Depends R (>= 3.5.0)

VignetteBuilder knitr

LazyData true

URL <https://github.com/kaifenglu/eventPred>

BugReports <https://github.com/kaifenglu/eventPred/issues>

NeedsCompilation no

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Repository CRAN

Date/Publication 2024-09-17 14:00:06 UTC

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eventPred-package	<i>Event Prediction</i>
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Description

Predicts enrollment and events at the design stage using assumed enrollment and treatment-specific time-to-event models, or at the analysis stage using blinded or unblinded data and specified enrollment and time-to-event models through simulations.

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. The eventPred package provides enrollment and event prediction capabilities using assumed enrollment and treatment-specific time-to-event models at the design stage, using blinded or unblinded data and specified enrollment and time-to-event models at the analysis stage.

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 eventPred 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 eventPred package also offers several time-to-event models, including exponential, Weibull, log-logistic, log-normal, piecewise exponential, model averaging of Weibull and log-normal, and spline. For time to dropout, the same set of model 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 eventPred 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 eventPred 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 eventPred 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 are 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 θ 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 `w1`, is considered fixed.
 - Spline: θ 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 eventPred 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.

Author(s)

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References

- Emilia Bagiella and Daniel F. Heitjan. Predicting analysis times in randomized clinical trials. *Stat in Med.* 2001; 20:2055-2063.
- Gui-shuang Ying and Daniel F. Heitjan. Weibull prediction of event times in clinical trials. *Pharm Stat.* 2008; 7:107-120.
- Xiaoxi Zhang and Qi Long. Stochastic modeling and prediction for accrual in clinical trials. *Stat in Med.* 2010; 29:649-658.
- Patrick Royston and Mahesh K. B. Parmar. Flexible parametric proportional-hazards and proportional-odds models for censored survival data, with application to prognostic modelling and estimation of treatment effects. *Stat in Med.* 2002; 21:2175-2197.

finalData	<i>Final enrollment and event data after achieving the target number of events</i>
-----------	--

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	<i>Fit time-to-dropout model</i>
------------	----------------------------------

Description

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

Usage

```
fitDropout(
  df,
  dropout_model = "exponential",
  piecewiseDropoutTime = 0,
  k_dropout = 0,
  scale_dropout = "hazard",
  showplot = TRUE,
  by_treatment = FALSE,
  covariates = NULL
)
```

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", "piecewise exponential", "model averaging", or "spline". 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 "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.
k_dropout	The number of inner knots of the spline. The default k_dropout=0 gives a Weibull, log-logistic or log-normal model, if scale_dropout 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_dropout	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.
showplot	A Boolean variable to control whether or not to show the fitted time-to-dropout survival curve. By default, it is set to TRUE.

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.
covariates	The names of baseline covariates from the input data frame to include in the dropout model, e.g., c("age", "sex"). Factor variables need to be declared in the input data frame.

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 Akaike Information Criterion, `aic`, and Bayesian Information Criterion, `bic`.

If the piecewise exponential model is used, the location of knots used in the model, `piecewiseDropoutTime`, 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 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.

Author(s)

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References

Patrick Royston and Mahesh K. B. Parmar. Flexible parametric proportional-hazards and proportional-odds models for censored survival data, with application to prognostic modelling and estimation of treatment effects. *Stat in Med.* 2002; 21:2175-2197.

Examples

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

fitEnrollment

Fit enrollment model

Description

Fits a specified enrollment model to the enrollment data.

Usage

```
fitEnrollment(
  df,
  enroll_model = "b-spline",
  nknots = 0,
  accrualTime = 0,
  showplot = TRUE
)
```

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.
showplot	A Boolean variable to control whether or not to show the fitted enrollment curve. By default, it is set to TRUE.

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.

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, vtheta, the Akaike Information Criterion, aic, and the Bayesian Information Criterion, bic, 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.

Author(s)

Kaifeng Lu, <kaifenglu@gmail.com>

References

Xiaoxi Zhang and Qi Long. Stochastic modeling and prediction for accrual in clinical trials. Stat in Med. 2010; 29:649-658.

Examples

```
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

```
fitEvent(
  df,
  event_model = "model averaging",
  piecewiseSurvivalTime = 0,
  k = 0,
  scale = "hazard",
  showplot = TRUE,
  by_treatment = FALSE,
  covariates = NULL
)
```

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", or "spline". 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". |
| 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. |
| 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. |

getPrediction	<i>Enrollment and event prediction</i>
---------------	--

Description

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

Usage

```
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 = "model averaging",  
  piecewiseSurvivalTime = 0,  
  k = 0,  
  scale = "hazard",  
  event_prior = NULL,  
  dropout_model = "exponential",  
  piecewiseDropoutTime = 0,  
  k_dropout = 0,  
  scale_dropout = "hazard",  
  dropout_prior = NULL,  
  fixedFollowup = FALSE,  
  followupTime = 365,  
  pilevel = 0.9,  
  nyears = 4,  
  nreps = 500,  
  showEnrollment = TRUE,  
  showEvent = TRUE,  
  showDropout = FALSE,  
  showOngoing = FALSE,  
  showssummary = TRUE,  
  showplot = TRUE,  
  by_treatment = FALSE,  
  ngroups = 1,  
  alloc = NULL,  
  treatment_label = NULL,  
  covariates_event = NULL,  
  event_prior_with_covariates = NULL,
```

```

    covariates_dropout = NULL,
    dropout_prior_with_covariates = NULL,
    fix_parameter = FALSE
)

```

Arguments

df	The subject-level enrollment and event data, including <code>trialsdt</code> , <code>usubjid</code> , <code>randdt</code> , and <code>cutoffdt</code> for enrollment prediction, and, additionally, <code>time</code> , <code>event</code> , and <code>dropout</code> for event prediction. The data should also include <code>treatment</code> coded as 1, 2, and so on, and <code>treatment_description</code> for enrollment and event prediction by treatment. By default, it is set to <code>NULL</code> 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", 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.
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., <code>c(0, 30)</code> breaks the time axis into 2 accrual intervals: <code>[0, 30)</code> and <code>[30, Inf)</code> . 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", or "spline". The model averaging uses the $\exp(-bic/2)$ weighting and combines Weibull and log-normal models. By default, it is set to "model averaging".
piecewiseSurvivalTime	A vector that specifies the time intervals for the piecewise exponential survival distribution. Must start with 0, e.g., <code>c(0, 60)</code> breaks the time axis into 2 event intervals: <code>[0, 60)</code> and <code>[60, Inf)</code> . 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 <code>k=0</code> gives a Weibull, log-logistic or log-normal model, if <code>scale</code> 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", $-\text{qnorm}(S(t))$ 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: "none", "exponential", "Weibull", "log-logistic", "log-normal", "piecewise exponential", "model averaging", or "spline". The model averaging uses the $\exp(-bic/2)$ weighting and combines Weibull and log-normal models. 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.
k_dropout	The number of inner knots of the spline dropout model of Royston and Parmar (2002). The default k_dropout=0 gives a Weibull, log-logistic or log-normal model, if scale_dropout 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_dropout	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.
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.
showsummary	A Boolean variable to control whether or not to show the prediction summary. By default, it is set to TRUE.
showplot	A Boolean variable to control whether or not to show the plots. By default, it is set to TRUE.
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.

<code>alloc</code>	The treatment allocation in a randomization block. By default, it is set to NULL, which yields equal allocation among the treatment groups.
<code>treatment_label</code>	The treatment labels for treatments in a randomization block for design stage prediction. It is replaced with the <code>treatment_description</code> in the observed data if <code>df</code> is not NULL.
<code>covariates_event</code>	The names of baseline covariates from the input data frame to include in the event model, e.g., <code>c("age", "sex")</code> . Factor variables need to be declared in the input data frame.
<code>event_prior_with_covariates</code>	The prior of event model parameters in the presence of covariates.
<code>covariates_dropout</code>	The names of baseline covariates from the input data frame to include in the dropout model, e.g., <code>c("age", "sex")</code> . Factor variables need to be declared in the input data frame.
<code>dropout_prior_with_covariates</code>	The prior of dropout model parameters in the presence of covariates.
<code>fix_parameter</code>	Whether to fix parameters at the maximum likelihood estimates when generating new data for prediction. Defaults to FALSE, in which case, parameters will be drawn from their approximate posterior distribution.

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, or piecewise poisson), `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 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` (`dropout_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), `theta` and `vtheta` to indicate the parameter values and the covariance matrix. For the piecewise exponential event (dropout) model, the list should also include `piecewiseSurvivalTime` (`piecewiseDropoutTime`) to indicate the location of knots. It should be noted that the model averaging and spline options are not appropriate for use as prior.

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. 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.

Author(s)

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Examples

```
# Event prediction after enrollment completion

pred <- getPrediction(
  df = interimData2, to_predict = "event only",
  target_d = 200,
  event_model = "weibull",
  dropout_model = "exponential",
  pilevel = 0.90, nreps = 100)
```

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

```
interimData1
```

Format

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

interimData2	<i>Interim enrollment and event data after enrollment completion</i>
--------------	--

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.

predictEnrollment	<i>Predict enrollment</i>
-------------------	---------------------------

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

```

predictEnrollment(
  df = NULL,
  target_n,
  enroll_fit,
  lags = 30,
  pilevel = 0.9,
  nyears = 4,
  nreps = 500,
  showssummary = TRUE,
  showplot = TRUE,
  by_treatment = FALSE,
  ngroups = 1,
  alloc = NULL,
  treatment_label = NULL,
  fix_parameter = FALSE
)

```

Arguments

<code>df</code>	The subject-level enrollment data, including <code>trialsdt</code> , <code>randdt</code> and <code>cutoffdt</code> . The data should also include <code>treatment</code> coded as 1, 2, and so on, and <code>treatment_description</code> for prediction by treatment group. By default, it is set to <code>NULL</code> for enrollment prediction at the design stage.
<code>target_n</code>	The target number of subjects to enroll in the study.
<code>enroll_fit</code>	The pre-fitted enrollment model used to generate predictions.
<code>lags</code>	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.
<code>pilevel</code>	The prediction interval level. By default, it is set to 0.90.
<code>nyears</code>	The number of years after the data cut for prediction. By default, it is set to 4.
<code>nreps</code>	The number of replications for simulation. By default, it is set to 500.
<code>showssummary</code>	A Boolean variable to control whether or not to show the prediction summary. By default, it is set to <code>TRUE</code> .
<code>showplot</code>	A Boolean variable to control whether or not to show the prediction plot. By default, it is set to <code>TRUE</code> .
<code>by_treatment</code>	A Boolean variable to control whether or not to predict enrollment by treatment group. By default, it is set to <code>FALSE</code> .
<code>ngroups</code>	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 <code>df</code> is not <code>NULL</code> .
<code>alloc</code>	The treatment allocation in a randomization block. By default, it is set to <code>NULL</code> , which yields equal allocation among the treatment groups.
<code>treatment_label</code>	The treatment labels for treatments in a randomization block for design stage prediction. It is replaced with the <code>treatment_description</code> in the observed data if <code>df</code> is not <code>NULL</code> .

`fix_parameter` Whether to fix parameters at the maximum likelihood estimates when generating new data for prediction. Defaults to FALSE, in which case, parameters will be drawn from their approximate posterior distributions.

Details

The `enroll_fit` variable can be used for enrollment prediction at the design stage. 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.

Author(s)

Kaifeng Lu, <kaifenglu@gmail.com>

References

Xiaoxi Zhang and Qi Long. Stochastic modeling and prediction for accrual in clinical trials. *Stat in Med.* 2010; 29:649-658.

Examples

```
# Enrollment prediction at the design stage

enroll_pred <- predictEnrollment(
  target_n = 300,
  enroll_fit = list(model = "piecewise poisson",
                    theta = log(26/9*seq(1, 9)/30.4375),
                    vtheta = diag(9)*1e-8,
                    accrualTime = seq(0, 8)*30.4375),
  pilevel = 0.90, nreps = 100)
```

predictEvent	<i>Predict event</i>
--------------	----------------------

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 = NULL,
  dropout_fit = NULL,
  fixedFollowup = FALSE,
  followupTime = 365,
  pilevel = 0.9,
  nyears = 4,
  nreps = 500,
  showEnrollment = TRUE,
  showEvent = TRUE,
  showDropout = FALSE,
  showOngoing = FALSE,
  showsummary = TRUE,
  showplot = TRUE,
  by_treatment = FALSE,
  covariates_event = NULL,
  event_fit_with_covariates = NULL,
  covariates_dropout = NULL,
  dropout_fit_with_covariates = NULL,
  fix_parameter = FALSE
)
```

Arguments

df	The subject-level enrollment and event data, including trialsdt, usubjid, randdt, cutoffdt, time, event, and dropout. The data should also include treatment coded as 1, 2, and so on, and treatment_description for by-treatment prediction. By default, it is set to NULL for event prediction at the design stage.
target_d	The target number of events to reach in the study.
newSubjects	The enrollment data for new subjects including draw and arrivalTime. The data should also include treatment for prediction by treatment. 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.
showsummary	A Boolean variable to control whether or not to show the prediction summary. By default, it is set to TRUE.
showplot	A Boolean variable to control whether or not to show the prediction plot. By default, it is set to TRUE.
by_treatment	A Boolean variable to control whether or not to predict event by treatment group. By default, it is set to FALSE.
covariates_event	The names of baseline covariates from the input data frame to include in the event model, e.g., c("age", "sex"). Factor variables need to be declared in the input data frame.
event_fit_with_covariates	The pre-fitted event model with covariates used to generate event predictions for ongoing subjects.
covariates_dropout	The names of baseline covariates from the input data frame to include in the dropout model, e.g., c("age", "sex"). Factor variables need to be declared in the input data frame.
dropout_fit_with_covariates	The pre-fitted dropout model with covariates used to generate dropout predictions for ongoing subjects.
fix_parameter	Whether to fix parameters at the maximum likelihood estimates when generating new data for prediction. Defaults to FALSE, in which case, parameters will be drawn from their approximate posterior distribution.

pwexpreg	<i>Piecewise exponential regression</i>
----------	---

Description

Obtains the maximum likelihood estimates for piecewise exponential regression.

Usage

```
pwexpreg(time, event, J, tcut, q, x)
```

Arguments

time	The survival time.
event	The event indicator.
J	The number of time intervals.
tcut	A vector that specifies the endpoints of time intervals for the baseline 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.
q	The number of columns of the covariates matrix.
x	The covariates matrix (excluding the intercept).

Value

The maximum likelihood estimates and the associated covariance matrix, AIC and BIC.

runShinyApp	<i>Run Shiny app</i>
-------------	----------------------

Description

Runs the event prediction Shiny app.

Usage

```
runShinyApp()
```

Author(s)

Kaifeng Lu, <kaifenglu@gmail.com>

summarizeObserved	<i>Summarize observed data</i>
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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 <code>trialsdt</code> , <code>usubjid</code> , <code>randdt</code> , and <code>cutoffdt</code> for enrollment prediction, as well as <code>time</code> , <code>event</code> and <code>dropout</code> for event prediction, and <code>treatment</code> coded as 1, 2, and so on, and <code>treatment_description</code> 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`.

Author(s)

Kaifeng Lu, <kaifenglu@gmail.com>

Examples

```
observed1 <- summarizeObserved(df = interimData1,  
                               to_predict = "enrollment and event")  
  
observed2 <- summarizeObserved(df = interimData2,
```

```
to_predict = "event only")
```

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