

Package ‘SEQTaRget’

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Type Package

Title Sequential Trial Emulation

Version 1.3.0

Description Implementation of sequential trial emulation for the analysis of observational databases. The 'SEQTaRget' software accommodates time-varying treatments and confounders, as well as binary and failure time outcomes. 'SEQTaRget' allows to compare both static and dynamic strategies, can be used to estimate observational analogs of intention-to-treat and per-protocol effects, and can adjust for potential selection bias induced by losses-to-follow-up. (Paper to come).

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Depends R (>= 4.1)

URL <https://causalinference.github.io/SEQTaRget/>

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compevent	<i>Function to return competing event models from a SEquential object</i>
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Description

Function to return competing event models from a SEquential object

Usage

```
compevent(object)
```

Arguments

object SEQoutput object

Value

list of fastglm objects

covariates	<i>Retrieves Outcome, Numerator, and Denominator Covariates</i>
------------	---

Description

Retrieves Outcome, Numerator, and Denominator Covariates

Usage

```
covariates(object)
```

Arguments

object object of class SEQoutput

Value

list of SEQuential covariates

denominator	<i>Retrieves Denominator Models from SEQuential object</i>
-------------	--

Description

Retrieves Denominator Models from SEQuential object

Usage

```
denominator(object)
```

Arguments

object object of class SEQoutput

Value

List of both numerator models

diagnostics	<i>Function to return diagnostic tables from a SEquential object</i>
-------------	--

Description

Function to return diagnostic tables from a SEquential object

Usage

```
diagnostics(object)
```

Arguments

object SEQoutput object

Value

list of diagnostic tables

hazard_ratio	<i>Function to return hazard ratios from a SEquential object</i>
--------------	--

Description

Function to return hazard ratios from a SEquential object

Usage

```
hazard_ratio(object)
```

Arguments

object SEQoutput object

Value

list of hazard ratios

km_curve	<i>Function to print kaplan-meier curves</i>
----------	--

Description

Function to print kaplan-meier curves

Usage

```
km_curve(  
  object,  
  plot.type = "survival",  
  plot.title,  
  plot.subtitle,  
  plot.labels,  
  plot.colors  
)
```

Arguments

object	SEQoutput object to plot
plot.type	character: type of plot to print
plot.title	character: defines the title of the plot
plot.subtitle	character: plot subtitle
plot.labels	length 2 character: plot labels
plot.colors	length 2 character: plot colors

Value

ggplot object of plot plot.type

km_data	<i>Function to return survival data from a SEquential object</i>
---------	--

Description

Function to return survival data from a SEquential object

Usage

```
km_data(object)
```

Arguments

object	SEQoutput object
--------	------------------

Value

list of dataframes of survival values

numerator

Retrieves Numerator Models from SEquential object

Description

Retrieves Numerator Models from SEquential object

Usage

numerator(object)

Arguments

object object of class SEQoutput

Value

List of both numerator models

outcome

Retrieves Outcome Models from SEquential object

Description

Retrieves Outcome Models from SEquential object

Usage

outcome(object)

Arguments

object object of class SEQoutput

Value

List of all outcome models

risk_comparison *Function to return risk information from a SEquential object*

Description

Function to return risk information from a SEquential object

Usage

```
risk_comparison(object)
```

Arguments

object SEQoutput object

Value

a data frame of risk information at end of followup (risk ratios, risk differences and confidence intervals, if bootstrapped)

risk_data *Function to return risk information from a SEquential object*

Description

Function to return risk information from a SEquential object

Usage

```
risk_data(object)
```

Arguments

object SEQoutput object

Value

a data table of risk information at every followup

 SEQdata.LTFU

Simulated Lost-to-followup example data for SEquential

Description

Simulated Lost-to-followup example data for SEquential

Usage

SEQdata.LTFU

Format

A dataframe with 4,139 rows and 13 columns:

ID Integer: Unique ID emulating individual patients

time Integer: Time of observation, always begins at 0, max time of 59; however, if lost-to-followup, time is truncated at a random point

eligible Binary: eligibility criteria for timepoints

outcome Binary: If an outcome is observed at this time point

tx_init Binary: If treatment is observed at this time point

sex Binary: Sex of the emulated patient

N Numeric: Normal random variable from $N(10,5)$

L Numeric: 4% continuously increase from $U(0, 1)$

P Numeric: 2% continuously decrease from $U(9, 10)$

excusedOne Binary: Once one, always one variable emulating an excuse for treatment switch

excusedZero Binary: Once zero, always zero variable emulating an excuse for treatment switch

LTFU Binary: Flag for losing a simulated ID to followup, if 1 there are no more records of the ID afterwards

 SEQdata.multitreatment

Simulated multitreatment example data for SEquential multinomial models

Description

Simulated multitreatment example data for SEquential multinomial models

Usage

SEQdata.multitreatment

Format

A dataframe with 5,976 rows and 11 columns:

ID Integer: Unique ID emulating individual patients

time Integer: Time of observation, always begins at 0, max time of 59; however, if lost-to-followup, time is truncated at a random point

eligible Binary: eligibility criteria for timepoints

outcome Binary: If an outcome is observed at this time point

tx_init Integer: Which treatment is observed at this time point

sex Binary: Sex of the emulated patient

N Numeric: Normal random variable from $N(10,5)$

L Numeric: 4% continuously increase from $U(0, 1)$

P Numeric: 2% continuously decrease from $U(9, 10)$

excusedOne Binary: Once one, always one variable emulating an excuse for treatment switch

excusedZero Binary: Once zero, always zero variable emulating an excuse for treatment switch

SEQestimate

Estimate the (very rough) time to run SEQUential analysis on current machine

Description

Estimate the (very rough) time to run SEQUential analysis on current machine

Usage

```
SEQestimate(
  data,
  id.col,
  time.col,
  eligible.col,
  treatment.col,
  outcome.col,
  time_varying.cols = list(),
  fixed.cols = list(),
  method,
  options,
  verbose = TRUE
)
```

Arguments

<code>data</code>	data.frame or data.table, if not already expanded with SEQexpand, will preform expansion according to arguments passed to either params or . . .
<code>id.col</code>	String: column name of the id column
<code>time.col</code>	String: column name of the time column
<code>eligible.col</code>	String: column name of the eligibility column
<code>treatment.col</code>	String: column name of the treatment column
<code>outcome.col</code>	String: column name of the outcome column
<code>time_varying.cols</code>	List: column names for time varying columns
<code>fixed.cols</code>	List: column names for fixed columns
<code>method</code>	String: method of analysis to preform
<code>options</code>	List: optional list of parameters from SEQopts
<code>verbose</code>	Logical: if TRUE, cats progress to console

Value

A list of (very rough) estimates for the time required for SEquential containing:

- `modelTime` estimated time used when running models
- `expansionTime` estimated time used when expanding data
- `totalTime` sum of model and expansion time

SEQopts

Parameter Builder for SEquential Model and Estimates

Description

Parameter Builder for SEquential Model and Estimates

Usage

```
SEQopts(
  bootstrap = FALSE,
  bootstrap.nboot = 100,
  bootstrap.sample = 0.8,
  bootstrap.CI = 0.95,
  bootstrap.CI_method = "se",
  cense = NA,
  cense.denominator = NA,
  cense.eligible = NA,
  cense.numerator = NA,
  compevent = NA,
```

```
covariates = NA,
data.return = FALSE,
denominator = NA,
deviation = FALSE,
deviation.col = NA,
deviation.conditions = c(NA, NA),
deviation.excused = FALSE,
deviation.excused_cols = c(NA, NA),
excused = FALSE,
excused.cols = c(NA, NA),
fastglm.method = 2L,
followup.class = FALSE,
followup.include = TRUE,
followup.max = Inf,
followup.min = -Inf,
followup.spline = FALSE,
hazard = FALSE,
indicator.baseline = "_bas",
indicator.squared = "_sq",
km.curves = FALSE,
multinomial = FALSE,
ncores = availableCores() - 1,
nthreads = getDTthreads(),
numerator = NA,
parallel = FALSE,
plot.colors = c("#F8766D", "#00BFC4", "#555555"),
plot.labels = NA,
plot.subtitle = NA,
plot.title = NA,
plot.type = "survival",
seed = NULL,
selection.first_trial = FALSE,
selection.prob = 0.8,
selection.random = FALSE,
subgroup = NA,
survival.max = Inf,
treat.level = c(0, 1),
trial.include = TRUE,
weight.eligible_cols = c(),
weight.lower = -Inf,
weight.lag_condition = TRUE,
weight.p99 = FALSE,
weight.preexpansion = TRUE,
weight.upper = Inf,
weighted = FALSE
)
```

Arguments

<code>bootstrap</code>	Logical: defines if SEQUential should run bootstrapping, default is FALSE
<code>bootstrap.nboot</code>	Integer: number of bootstraps
<code>bootstrap.sample</code>	Numeric: percentage of data to use when bootstrapping, should in [0, 1], default is 0.8
<code>bootstrap.CI</code>	Numeric: defines the confidence interval after bootstrapping, default is 0.95 (95% CI)
<code>bootstrap.CI.method</code>	Character: selects which way to calculate bootstraps confidence intervals ("se", "percentile")
<code>cense</code>	String: column name for additional censoring variable, e.g. loss-to-follow-up
<code>cense.denominator</code>	String: censoring denominator covariates to the right hand side of a formula object
<code>cense.eligible</code>	String: column name for indicator column defining which rows to use for censoring model
<code>cense.numerator</code>	String: censoring numerator covariates to the right hand side of a formula object
<code>compevent</code>	String: column name for competing event indicator
<code>covariates</code>	String: covariates to the right hand side of a formula object
<code>data.return</code>	Logical: whether to return the expanded dataframe with weighting information
<code>denominator</code>	String: denominator covariates to the right hand side of a to formula object
<code>deviation</code>	Logical: create switch based on deviation from column <code>deviation.col</code>
<code>deviation.col</code>	Character: column name for deviation
<code>deviation.conditions</code>	Character list: RHS evaluations of the same length as <code>treat.levels</code>
<code>deviation.excused</code>	Logical: whether deviations should be excused by <code>deviation.excused_cols</code>
<code>deviation.excused_cols</code>	Character list: excused columns for deviation switches
<code>excused</code>	Logical: in the case of censoring, whether there is an excused condition
<code>excused.cols</code>	List: list of column names for treatment switch excuses - should be the same length, and ordered the same as <code>treat.level</code>
<code>fastglm.method</code>	Integer: decomposition method for fastglm (1-QR, 2-Cholesky, 3-LDLT, 4-QR.FPIV)
<code>followup.class</code>	Logical: treat followup as a class, e.g. expands every time to it's own indicator column
<code>followup.include</code>	Logical: whether or not to include 'followup' and 'followup_squared' in the outcome model

followup.max	Numeric: maximum time to expand about, default is Inf (no maximum)
followup.min	Numeric: minimum time to expand about, default is -Inf (no minimum)
followup.spline	Logical: treat followup as a cubic spline
hazard	Logical: hazard error calculation instead of survival estimation
indicator.baseline	String: identifier for baseline variables in covariates, numerator, denominator - intended as an override
indicator.squared	String: identifier for squared variables in covariates, numerator, denominator - intended as an override
km.curves	Logical: Kaplan-Meier survival curve creation and data return
multinomial	Logical: whether to expect multilevel treatment values
ncores	Integer: number of cores to use in parallel processing, default is one less than system max
nthreads	Integer: number of threads to use for data.table processing
numerator	String: numerator covariates to the right hand side of a formula object
parallel	Logical: define if the SEQUential process is run in parallel, default is FALSE
plot.colors	Character: Colors for output plot if km.curves = TRUE, defaulted to ggplot2 defaults
plot.labels	Character: Color labels for output plot if km.curves = TRUE in order e.g. c("risk.0", "risk.1")
plot.subtitle	Character: Subtitle for output plot if km.curves = TRUE
plot.title	Character: Title for output plot if km.curves = TRUE
plot.type	Character: Type of plot to create if km.curves = TRUE, available options are 'survival', 'risk', and 'inc' (in the case of censoring)
seed	Integer: starting seed
selection.first_trial	Logical: selects only the first eligible trial in the expanded dataset
selection.prob	Numeric: percent of total IDs to select for selection.random, should be bound [0, 1]
selection.random	Logical: randomly selects IDs with replacement to run analysis
subgroup	Character: Column name to stratify outcome models on
survival.max	Numeric: maximum time for survival curves, default is Inf (no maximum)
treat.level	List: treatment levels to compare
trial.include	Logical: whether or not to include 'trial' and 'trial_squared' in the outcome model
weight.eligible_cols	List: list of column names for indicator columns defining which weights are eligible for weight models - in order of treat.level

<code>weight.lower</code>	Numeric: weights truncated at lower end at this weight
<code>weight.lag_condition</code>	Logical: whether weights should be conditioned on treatment lag value
<code>weight.p99</code>	Logical: forces weight truncation at 1st and 99th percentile weights, will override provided <code>weight.upper</code> and <code>weight.lower</code>
<code>weight.preexpansion</code>	Logical: whether weighting should be done on pre-expanded data
<code>weight.upper</code>	Numeric: weights truncated at upper end at this weight
<code>weighted</code>	Logical: whether or not to preform weighted analysis, default is FALSE

Value

An object of class 'SEQopts'

SEQoutput-class	<i>An S4 class used to hold the outputs for the SEQuential process</i>
-----------------	--

Description

An S4 class used to hold the outputs for the SEQuential process

Slots

`params` SEQparams object
`outcome` outcome covariates
`numerator` numerator covariates
`denominator` denominator covariates
`outcome.model` list of length `bootstrap.nboot` containing outcome coefficients
`hazard` hazard ratio
`survival.curve` ggplot object for the survival curves
`survival.data` data.table of survival data
`risk.difference` risk difference calculated from survival data
`risk.ratio` risk ratio calculated from survival data
`time` time in minutes used for the SEQuential process
`weight.statistics` information from the weighting process, containing weight coefficients and weight statistics
`info` list of outcome and switch information (if applicable)
`ce.model` list of competing event models if `compevent` is specified, NA otherwise

Description

‘SEquential’ is an all-in-one API to SEquential analysis, returning a SEQoutput object of results. More specific examples can be found on pages at <https://causalinference.github.io/SEQTaRget/>

Usage

```
SEquential(  
  data,  
  id.col,  
  time.col,  
  eligible.col,  
  treatment.col,  
  outcome.col,  
  time_varying.cols = list(),  
  fixed.cols = list(),  
  method,  
  options,  
  verbose = TRUE  
)
```

Arguments

<code>data</code>	data.frame or data.table, will preform expansion according to arguments passed to options
<code>id.col</code>	String: column name of the id column
<code>time.col</code>	String: column name of the time column
<code>eligible.col</code>	String: column name of the eligibility column
<code>treatment.col</code>	String: column name of the treatment column
<code>outcome.col</code>	String: column name of the outcome column
<code>time_varying.cols</code>	List: column names for time varying columns
<code>fixed.cols</code>	List: column names for fixed columns
<code>method</code>	String: method of analysis to preform
<code>options</code>	List: optional list of parameters from SEQopts
<code>verbose</code>	Logical: if TRUE, cats progress to console

Details

Implementation of sequential trial emulation for the analysis of observational databases. The SE-Sequential software accommodates time-varying treatments and confounders, as well as binary and failure time outcomes. SEQ allows to compare both static and dynamic strategies, can be used to estimate observational analogs of intention-to-treat and per-protocol effects, and can adjust for potential selection bias induced by losses-to-follow-up.

Value

An S4 object of class SEQoutput

Examples

```
data <- SEQdata
model <- SEquential(data, id.col = "ID",
                    time.col = "time",
                    eligible.col = "eligible",
                    treatment.col = "tx_init",
                    outcome.col = "outcome",
                    time_varying.cols = c("N", "L", "P"),
                    fixed.cols = "sex",
                    method = "ITT",
                    options = SEQopts())
```

SEQ_data

Function to return the internal data from a SEquential object

Description

Function to return the internal data from a SEquential object

Usage

```
SEQ_data(object)
```

Arguments

object SEQoutput object

Value

data.table

show, SEQoutput-method *Show method for S4 object - SEQoutput.*

Description

Show method for S4 object - SEQoutput.

Usage

```
## S4 method for signature 'SEQoutput'  
show(object)
```

Arguments

object A SEQoutput object - usually generated from SEQuential

Value

No return value, sends information about SEQoutput to the console

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