

Package ‘SEQTaRget’

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Type Package

Title Sequential Trial Emulation

Version 1.4.2

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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Contents

compevent	2
covariates	3
denominator	3
diagnostics	4
hazard_ratio	4
km_curve	5
km_data	5
numerator	6
outcome	6
risk_comparison	7
risk_data	7
SEQdata	8
SEQdata.LTFU	8
SEQdata.multitreatment	9
SEQestimate	10
SEQopts	11
SEQoutput-class	16
SEQquential	16
SEQ_data	18
show,SEQoutput-method	18
Index	20

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

Description

Function to return competing event models from a SEquential object

Usage

```
compevent(object)
```

Arguments

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

Value

A fastglm object, or a named list of fastglm objects when subgroups are specified

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 denominator 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

A named vector of hazard ratios, or a named list of vectors when subgroups are specified

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; one of: "survival" (default), "risk", "inc"
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

A data frame of survival values, or a named list of data frames when subgroups are specified

numerator	<i>Retrieves Numerator Models from SEquential object</i>
-----------	--

Description

Retrieves Numerator Models from SEquential object

Usage

numerator(object)

Arguments

object object of class SEQoutput

Value

List of both numerator models

outcome	<i>Retrieves Outcome Models from SEquential object</i>
---------	--

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 the end of followup

SEQdata

Simulated observational example data for SEquential()

Description

Simulated observational example data for [SEquential\(\)](#)

Usage

SEQdata

Format

A data frame with 12,180 rows and 11 columns:

ID Integer: Unique ID emulating individual patients

time Integer: Time of observation, always begins at 0, max time of 59. Should be continuous

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 one, always one variable emulating an excuse for treatment switch

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 54,687 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 one, always one 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

eligible_cense Binary: emulates columns which are eligible to entering into censoring models (e.g. if you want to limit columns for the LTFU model)

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 one, always one variable emulating an excuse for treatment switch

SEQestimate	<i>Estimate the (very rough) time to run SEQuential analysis on current machine</i>
-------------	---

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 <code>SEQexpand()</code> , will perform expansion according to arguments passed to either <code>params</code> or <code>...</code>
<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

fixed.cols	List: column names for fixed columns
method	String: method of analysis to perform
options	List: optional list of parameters from SEQopts()
verbose	Logical: if TRUE, cats progress to console, default is TRUE

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),
  expand.only = FALSE,
  fastglm.method = 2L,
  glm.package = "fastglm",
```

```

parglm.control = NULL,
followup.class = FALSE,
followup.include = TRUE,
followup.max = Inf,
followup.min = 0,
followup.spline = FALSE,
followup.spline.df = 4L,
hazard = FALSE,
indicator.baseline = "_bas",
indicator.squared = "_sq",
km.curves = FALSE,
multinomial = FALSE,
ncores = availableCores(omit = 1L),
nthreads = getDTthreads(),
numerator = NA,
parallel = FALSE,
plot.colors = c("#F8766D", "#00BFC4", "#555555"),
plot.labels = NA,
plot.subtitle = NA,
plot.title = NA,
plot.type = "survival",
risk.times = NA,
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,
visit = NA,
visit.denominator = NA,
visit.numerator = NA,
weight.eligible_cols = c(),
weight.lower = 0,
weight.lag_condition = TRUE,
weight.p99 = FALSE,
weight.preexpansion = TRUE,
weight.upper = Inf,
weighted = FALSE
)

```

Arguments

bootstrap Logical: defines if SEQuential() should run bootstrapping, default is FALSE
bootstrap.nboot Integer: number of bootstraps, default is 100
bootstrap.sample Numeric: percentage of data to use when bootstrapping, should be 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"), default is "se"
<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, default is FALSE
<code>denominator</code>	String: denominator covariates to the right hand side of a formula object
<code>deviation</code>	Logical: create switch based on deviation from column <code>deviation.col</code> , default is FALSE
<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> , default is FALSE
<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, default is FALSE
<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>expand.only</code>	Logical: if TRUE, <code>SEQential()</code> returns the expanded <code>data.table</code> immediately after expansion and skips weighting, outcome modelling and survival/risk steps. Useful when you only need the expanded dataset (e.g. to inspect or store separately). Default is FALSE
<code>fastglm.method</code>	Integer: decomposition method for <code>fastglm</code> (0L-column-pivoted QR, 1L-unpivoted QR, 2L-LLT Cholesky, 3L-LDLT Cholesky), default is 2L
<code>glm.package</code>	Character: package to use for fitting GLMs, either "fastglm" (default) or "parglm". When "parglm" is selected the <code>nthreads</code> option controls the number of threads passed to <code>parglm::parglm.fit()</code> . For most realistic SEQTaRget workloads (expanded datasets up to approximately a few million rows) "fastglm" is faster; "parglm" may help only on substantially larger datasets where the parallel chunking outweighs its setup overhead.

<code>parglm.control</code>	A control object from <code>parglm::parglm.control()</code> to pass to <code>parglm::parglm.fit()</code> . Only used when <code>glm.package = "parglm"</code> . Defaults to <code>parglm::parglm.control(method = "FAST")</code> . If you encounter a <code>chol(): decomposition failed</code> error (e.g. with near-singular model matrices on large datasets), pass <code>parglm.control = parglm::parglm.control(method = "LAPACK")</code> to use the more numerically stable QR decomposition instead, or switch to using the <code>fastglm</code> backend.
<code>followup.class</code>	Logical: treat followup as a class, e.g. expands every time to it's own indicator column, default is FALSE
<code>followup.include</code>	Logical: whether or not to include 'followup' and 'followup_squared' in the outcome model, default is TRUE
<code>followup.max</code>	Numeric: maximum time to expand about, default is Inf (no maximum)
<code>followup.min</code>	Numeric: minimum follow-up time since trial enrollment to include, must be non-negative, default is 0
<code>followup.spline</code>	Logical: treat followup as a natural cubic spline (<code>splines::ns()</code>), default is FALSE
<code>followup.spline.df</code>	Integer: degrees of freedom passed to <code>splines::ns()</code> when <code>followup.spline = TRUE</code> . With <code>df = k</code> , <code>ns()</code> places <code>k - 1</code> interior knots at quantiles of followup. Must be <code>>= 1</code> ; <code>df = 1</code> is equivalent to a linear term and is generally not what you want. Default is 4 (3 interior knots).
<code>hazard</code>	Logical: hazard error calculation instead of survival estimation, default is FALSE
<code>indicator.baseline</code>	String: identifier for baseline variables in covariates, numerator, denominator - intended as an override
<code>indicator.squared</code>	String: identifier for squared variables in covariates, numerator, denominator - intended as an override
<code>km.curves</code>	Logical: Kaplan-Meier survival curve creation and data return, default is FALSE
<code>multinomial</code>	Logical: whether to expect multilevel treatment values, default is FALSE
<code>ncores</code>	Integer: number of cores to use in parallel processing, default is one less than system max, see <code>parallely::availableCores()</code>
<code>nthreads</code>	Integer: number of threads to use for <code>data.table</code> processing, default is <code>data.table::getDTthreads()</code>
<code>numerator</code>	String: numerator covariates to the right hand side of a formula object
<code>parallel</code>	Logical: define if the SEquential process is run in parallel, default is FALSE
<code>plot.colors</code>	Character: Colors for output plot if <code>km.curves = TRUE</code> , defaulted to <code>ggplot2</code> defaults
<code>plot.labels</code>	Character: Color labels for output plot if <code>km.curves = TRUE</code> in order e.g. <code>c("risk.0", "risk.1")</code>
<code>plot.subtitle</code>	Character: Subtitle for output plot if <code>km.curves = TRUE</code>
<code>plot.title</code>	Character: Title for output plot if <code>km.curves = TRUE</code>
<code>plot.type</code>	Character: Type of plot to create if <code>km.curves = TRUE</code> , available options are 'survival' (the default), 'risk', and 'inc' (in the case of censoring)

<code>risk.times</code>	Numeric vector: follow-up times (in the data's follow-up units) at which to report risk difference and risk ratio when <code>km.curves = TRUE</code> . Each requested time is snapped to the latest available follow-up at or before it. The final follow-up time is always included. Default NA reports only the final follow-up time.
<code>seed</code>	Integer: starting seed
<code>selection.first_trial</code>	Logical: selects only the first eligible trial in the expanded dataset, default FALSE
<code>selection.prob</code>	Numeric: percent of total IDs to select for <code>selection.random</code> , should be bound [0, 1], default is 0.8
<code>selection.random</code>	Logical: randomly selects IDs with replacement to run analysis, default FALSE
<code>subgroup</code>	Character: Column name to stratify outcome models on
<code>survival.max</code>	Numeric: maximum time for survival curves, default is Inf (no maximum)
<code>treat.level</code>	List: treatment levels to compare, default is <code>c(0, 1)</code>
<code>trial.include</code>	Logical: whether or not to include 'trial' and 'trial_squared' in the outcome model, default is TRUE
<code>visit</code>	String: column name for visit indicator variable, e.g. "visit"
<code>visit.denominator</code>	String: visit denominator covariates to the right hand side of a formula object
<code>visit.numerator</code>	String: visit numerator covariates to the right hand side of a formula object
<code>weight.eligible_cols</code>	List: list of column names for indicator columns defining which weights are eligible for weight models - in order of <code>treat.level</code>
<code>weight.lower</code>	Numeric: IPCW weights truncated at this lower bound, must be non-negative, default is 0
<code>weight.lag_condition</code>	Logical: whether weights should be conditioned on treatment lag value, default TRUE
<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, default TRUE
<code>weight.upper</code>	Numeric: weights truncated at upper end at this weight, default is Inf
<code>weighted</code>	Logical: whether or not to perform 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 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

SEquential	<i>SEquential trial emulation</i>
------------	-----------------------------------

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 perform expansion according to arguments passed through the options argument
<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 perform; should be one of "ITT", "dose-response", or "censoring"
<code>options</code>	List: optional list of parameters from SEQopts()
<code>verbose</code>	Logical: if TRUE, cats progress to console, default is TRUE

Details

Implementation of sequential trial emulation for the analysis of observational databases. The SEquential software accommodates time-varying treatments and confounders, as well as binary and failure time outcomes. SEquential 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. If `options = SEQopts(expand.only = TRUE)`, returns the expanded data.table directly, with analysis steps skipped.

Examples

```

data <- SEQdata
model <- SEQquential(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 SEQquential object

Description

Function to return the internal data from a SEQquential 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

Index

* datasets

- SEQdata, 8
- SEQdata.LTFU, 8
- SEQdata.multitreatment, 9

- compevent, 2
- covariates, 3

- data.table::getDTthreads(), 14
- denominator, 3
- diagnostics, 4

- hazard_ratio, 4

- km_curve, 5
- km_data, 5

- numerator, 6

- outcome, 6

- parallelly::availableCores(), 14
- parglm::parglm.control(), 14

- risk_comparison, 7
- risk_data, 7

- SEQ_data, 18
- SEQdata, 8
- SEQdata.LTFU, 8
- SEQdata.multitreatment, 9
- SEQestimate, 10
- SEQexpand(), 10
- SEQopts, 11
- SEQopts(), 11, 17
- SEQoutput-class, 16
- SEQential, 16
- SEQential(), 8, 9, 13, 19
- show, SEQoutput-method, 18