Package 'contTimeCausal'

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Description Implements the semiparametric efficient estimators of continuous-time causal models for time-varying treatments and confounders in the presence of dependent censoring (including structural failure time model and Cox proportional hazards marginal structural model). S. Yang, K. Pieper, and F. Cools (2019) <doi:10.1111/biom.12845>.

License GPL (>= 2)

LazyData TRUE

Depends dplyr, survival

Imports zoo, stats, methods

VignetteBuilder knitr

Suggests rmarkdown, knitr

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Collate 'zooStep.R' 'IPCWStep.R' 'VStep.R' 'VStep2.R' 'verifyInputs.R' 'ctCoxMSM.R' 'ctSFTM.R' 'ctcData.R' 'print.ctc.R'

NeedsCompilation no

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R topics documented:

`ctcData` *Toy Dataset For Illustration*

Description

This data set is provided for the purposes of illustrating the use of the software. It includes a one-dimensional baseline covariate and a one-dimensional time-dependent covariate.

Usage

```
data(ctcData)
```

Format

ctcData is a data.frame containing data for 1,000 participants. The data.frame contains 9 columns:

id An integer participant identifier.

start The left side of the time interval for time-dependent covariate xt.

stop The right side of the time interval for time-dependent covariate xt.

xt A continuous time-dependent covariate.

x A continuous baseline covariate.

deltaU A binary indicator of the clinical event. If the clinical event occurred, takes value 1; otherwise 0.

deltaV A binary indicator of treatment discontinuation. If treatment discontinuation was optional, takes value 1. If treatment discontinuation was due to the clinical event, censoring, or a treatment-terminating event, takes value 0.

U The time to the clinical event or censoring.

V The time to optimal treatment discontinuation, the clinical event, censoring, or a treatment-terminating event.

`ctCoxMSM` *Continuous-time Cox Marginal Structural Model*

Description

The function estimates the effect of treatment regime (in terms of time to treatment discontinuation) for a survival outcome under a Cox proportional hazards model with time-varying confounding in the presence of dependent censoring. Studying the effect of time to treatment initiation is applicable by redefining "treatment discontinuation" in the current description to "treatment initiation".

Usage

```
ctCoxMSM(data, base = NULL, td = NULL)
```

Arguments

`data`	A data.frame object. A data.frame containing all observed data. At a minimum, this data.frame must contain columns with headers "id", "U", "V", "deltaU", and "deltaV". If time-dependent covariates are included, additional columns include "stop" and "start". See Details for further information
`base`	A character or integer vector or NULL. The columns of data to be included in the time-independent component of the model. If NULL, time-independent covariates are excluded from the Cox model for treatment discontinuation.
`td`	A character or integer vector or NULL. The columns of data to be included in the time-dependent component of the model. If NULL, time-dependent covariates are excluded from the Cox model for treatment discontinuation.

Details

The Cox marginal structural model (MSM) assumes that the potential failure time $T^{\overline{a}}$ under the treatment $\overline{a}$ follows a proportional hazards model with $\psi * a_u$. We assume that the participant continuously received treatment until time V. The observed failure time can be censored assuming the censoring time is independent of the failure time given the treatment and covariate history (the so-called ignorable censoring). The function allows for multi-dimensional baseline covariates and/or multi-dimensional time-dependent covariates. Variance estimates can be implemented by delete-one-group jackknifing and recalling ctCoxMSM.

If only time-independent covariates are included, the data.frame must contain the following columns:

id: A unique participant identifier.

U: The time to the clinical event or censoring.

deltaU: The clinical event indicator (1 if U is the event time; 0 otherwise).

V: The time to optional treatment discontinuation, a clinical event, censoring, or a treatment-terminating event.

deltaV: The indicator of optional treatment discontinuation (1 if treatment discontinuation was optional; 0 if treatment discontinuation was due to a clinical event, censoring or a treatment-terminating event).

If time-dependent covariates are to be included, the data.frame must be a time-dependent dataset as described by package survival. Specifically, the time-dependent data must be specified for an interval (lower,upper] and the data must include the following additional columns:

start: The lower boundary of the time interval to which the data pertain.

stop: The upper boundary of the time interval to which the data pertain.

Value

An S3 object of class ctc. Object contains element 'psi', the estimate of the Cox MSM parameter(s) and 'coxPH', the Cox regression for V.

References

Yang, S., A. A. Tsiatis, and M. Blazing (2018). Modeling survival distribution as a function of time to treatment discontinuation: A dynamic treatment regime approach, Biometrics, 74, 900–909.

See Also

ctSFTM

Examples

```
data(ctcData)

# sample data to reduce computation time of example
smp <- ctcData$id %in% sample(1:1000, 150, FALSE)
ctcData <- ctcData[smp,]

# analysis with both time-dependent and time-independent components
res <- ctCoxMSM(data = ctcData, base = "x", td = "xt")

# analysis with only the time-independent component
res <- ctCoxMSM(data = ctcData, base = "x")

# analysis with only the time-dependent component
res <- ctCoxMSM(data = ctcData, td = "xt")
```

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ctSFTM *Continuous-time Structural Failure Time Model*

Description

The function estimates the regime (in terms of time to treatment initiation) of treatment effect for a survival outcome under a Structural Failure Time Model (SFTM) with time-varying confounding in the presence of dependent censoring. Studying the effect of time to treatment discontinuation is applicable by redefining "treatment initiation" in the current description to "treatment discontinuation".

Usage

```
ctSFTM(data, base = NULL, td = NULL)
```

Arguments

data	A data.frame object. A data.frame containing all observed data. At a minimum, this data.frame must contain columns with headers "id", "U", "V", "deltaU", and "deltaV". If time-dependent covariates are included, additional columns include "stop" and "start". See Details for further information
base	A character or integer vector or NULL. The columns of data to be included in the time-independent component of the model. If NULL, time-independent covariates are excluded from the Cox model for treatment discontinuation.
td	A character or integer vector or NULL. The columns of data to be included in the time-dependent component of the model. If NULL, time-dependent covariates are excluded from the Cox model for treatment discontinuation.

Details

The SFTM assumes that the potential failure time U had the individual never received treatment and the observed failure time T follow

$$U \sim \int_0^T e^{\psi A_u} du,$$

where ~ means "has the same distribution as", and A_u is the treatment indicator at time u. We assume that the individual continuously received treatment until time V. The observed failure time can be censored assuming the censoring time is independent of the failure time given the treatment and covariate history (the so-called ignorable censoring). The current function allows for multi-dimensional baseline covariates and/or multi-dimensional time-dependent covariate. Variance estimates should be implemented by delete-one-group jackknifing and recalling ctSFTM.

If only time-independent covariates are included, the data.frame must contain the following columns:

id: A unique participant identifier.

U: The time to the clinical event or censoring.

deltaU: The clinical event indicator (1 if U is the event time; 0 otherwise.

V: The time to optional treatment discontinuation, a clinical event, censoring, or a treatment-terminating event.

deltaV: The indicator of optional treatment discontinuation (1 if treatment discontinuation was optional; 0 if treatment discontinuation was due to a clinical event, censoring or a treatment-terminating event.

If time-dependent covariates are to be included, the data.frame must be a time-dependent dataset as described by package survival. Specifically, the time-dependent data must be specified for an interval (lower,upper] and the data must include the following additional columns:

start: The lower boundary of the time interval to which the data pertain.

stop: The upper boundary of the time interval to which the data pertain.

Value

An S3 object of class ctc. Object contains element 'psi', the estimate of the SFTM parameter(s) and 'coxPH', the Cox regression for V.

References

Yang, S., K. Pieper, and F. Cools. (2019) Semiparametric estimation of structural failure time model in continuous-time processes. Biometrika, 107(1), 123-136.

See Also

ctCoxMSM

Examples

```
 data(ctcData)

# sample data to reduce computation time of example
smp <- ctcData$id %in% sample(1:1000, 200, FALSE)
ctcData <- ctcData[smp,]

# analysis with both time-dependent and time-independent components
res <- ctSFTM(data = ctcData, base = "x", td = "xt")

# analysis with only the time-independent component
res <- ctSFTM(data = ctcData, base = "x")

# analysis with only the time-dependent component
res <- ctSFTM(data = ctcData, td = "xt")
```

`print` *Print the Primary Results*

Description

Print the primary results of a ctCoxMSM() or ctSFTM() analysis.

Usage

```
## S3 method for class 'ctc'
print(x, ...)
```

Arguments

`x`	An S3 object of class ctc. The value object returned by a call to ctCoxMSM() or ctSFTM().
`...`	ignored

Value

No return value, called to display key results.

Examples

```
data(ctcData)

# sample data to reduce computation time of example
smp <- ctcData$id %in% sample(1:1000, 150, FALSE)
ctcData <- ctcData[smp,]
```

```
# analysis with both time-dependent and time-independent components
res <- ctCoxMSM(data = ctcData, base = "x", td = "xt")

print(x = res)

# analysis with both time-dependent and time-independent components
res <- ctSFTM(data = ctcData, base = "x", td = "xt")

print(x = res)
```

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