Package 'InformativeCensoring'

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Type Package

Title Multiple Imputation for Informative Censoring

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Description Multiple Imputation for Informative Censoring.
This package implements two methods. Gamma Imputation
from Jackson et al. (2014) <DOI:10.1002/sim.6274> and Risk Score Imputation
from Hsu et al. (2009) <DOI:10.1002/sim.3480>.

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Imports boot, dplyr (>= 0.4.3), parallel

Suggests knitr, testthat

VignetteBuilder knitr

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`InformativeCensoring-package`

Perform methods of multiple imputation for time to event data

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Description

Perform methods of multiple imputation for time to event data

Details

See Nonparametric comparison of two survival functions with dependent censoring via nonparametric multiple imputation. Hsu and Taylor Statistics in Medicine (2009) 28:462-475 for Hsu's method

See Relaxing the independent censoring assumption in the Cox proportional hazards model using multiple imputation. Jackson et al., Statistics in Medicine (2014) 33:4681-4694 for Jackson's method

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col.headings — *Specify the columns of the data frame required by score imputation method*

Description

Specify the columns of the data frame required by score imputation method

Usage

```
col.headings(arm, has.event, time, Id, DCO.time, to.impute,
  censor.type = NULL)
```

Arguments

arm	column name which will contain the subject's treatment group
has.event	column name which will contain whether the subject has an event (1) or not(0)
time	column name of censoring/event time
Id	column name of subject Id
DCO.time	column name of the time at which the subject would have been censored had they not had an event before data cut off
to.impute	column name of the logical column as to whether events should be imputed
censor.type	column name of the column containing the reason for censoring, 0=had event, 1=non-administrative censoring 2=administrative censoring – only subjects with 1 in this column count as having an 'event' in the Cox model for censoring (optionally used – if not used then all subjects who are censored are used)

Value

A list contain the given arguments

cox.zph — *Test Cox proportional hazards assumption*

Description

See cox.zph function in the survival package

Usage

```
cox.zph(fit, transform = "km", global = TRUE, ...)
```

Arguments

fit	the result of fitting a Cox regression model, using the coxph function.
transform	a character string specifying how the survival times should be transformed before the test is performed. Possible values are "km", "rank", "identity" or a function of one argument.
global	should a global chi-square test be done, in addition to the per-variable tests.
...	Additional arguments to cox.zph, for example index if fit is a GammaStatList object

See Also

cox.zph

ExtractSingle *Extract a single risk score/gamma imputed data set/model fit*

Description

Extract a single risk score/gamma imputed data set/model fit

Usage

```
## S3 method for class 'GammaImputedSet'
ExtractSingle(x, index)

## S3 method for class 'GammaStatList'
ExtractSingle(x, index)

ExtractSingle(x, index)

## S3 method for class 'ScoreImputedSet'
ExtractSingle(x, index)

## S3 method for class 'ScoreStatList'
ExtractSingle(x, index)
```

Arguments

x	The multiple imputed object
index	Integer, which imputed data set/model fit should be returned

Value

The individual data set/model fit

gammaImpute *Perform gamma-Imputation for a given data set*

Description

This function performs the Imputation described in Relaxing the independent censoring assumptions in the Cox proportional hazards model using multiple imputation. (2014) D. Jackson et al. Statist. Med. (33) 4681-4694

Usage

```
gammaImpute(formula, data, m, gamma, gamma.factor, bootstrap.strata = rep(1,
  nrow(data)), DCO.time, ..., parallel = c("no", "multicore", "snow")[1],
  ncpus = 1L, cl = NULL)
```

Arguments

formula	The model formula to be used when fitting the models to calculate the cumulative hazard. A formula for coxph can include strata terms but not cluster or tt and only right-censored Surv objects can be used. Note the function does not allow multiple strata to be written as strata(W1)+strata(W2), use strata(W1,W2) instead
data	A time to event data set for which event times are to be imputed
m	The number of imputations to be created
gamma	Either column name containing the value of gamma or a vector of values giving the subject specific size of the step change in the log hazard at censoring. If a subject has NA in this column then no imputation is performed for this subject (i.e. the subject's censored time remains unchanged after imputation). If a subject has already had an event then the value of gamma is ignored. If gamma.factor is also used then the subject specific gamma are all multipled by gamma.factor. At least one of gamma and gamma.factor must be included.
gamma.factor	If used, a single numeric value. If no gamma then the step change in log hazard for all subjects at censoring is given by gamma.factor. If gamma is used then for each subject, the step change in log hazard is given by gamma.factor multiplied by the subject specific gamma. At least one of gamma and gamma.factor must be included.
bootstrap.strata	The strata argument for stratified bootstrap sampling, see argument strata for the function boot::boot for further details. If argument is not used then standard sampling with replacement will be used
DCO.time	Either column name containing the subject's data cutoff time or a vector of DCO.times for the subjects or a single number to be used as the DCO.time for all subjects (if imputed events are > this DCO.time then subjects are censored at DCO.time in imputed data sets)
...	Additional parameters to be passed into the model fit function

parallel	The type of parallel operation to be used (if any).
ncpus	integer: number of processes to be used in parallel operation: typically one would chose this to be the number of available CPUs
cl	An optional parallel or snow cluster for use if parallel="snow". If not supplied, a cluster on the local machine is created for the duration of the call.

Details

See the Gamma Imputation vignette for further details

Value

A GammaImputedSet.object containing the imputed data sets

See Also

GammaImputedSet.object GammaImputedData.object

Examples

```
## Not run:
data(nwtco)
nwtco <- nwtco[1:500,]

#creating 2 imputed data sets (m=2) for speed, would normally create more
ans <- gammaImpute(formula=Surv(edrel,rel)~histol + instit,
                   data = nwtco, m=2, gamma.factor=1, DCO.time=6209)

#subject specific gamma (multiplied by gamma.factor to give the jump)
#NA for subjects that are not to be imputed
jumps <- c(rep(NA,10),rep(1,490))
DCO.values <- rep(6209,500)

ans.2 <- gammaImpute(formula=Surv(edrel,rel)~histol + instit + strata(stage),
                   data = nwtco, m=2, bootstrap.strata=strata(nwtco$stage),
                   gamma=jumps, gamma.factor=1, DCO.time=DCO.values)

#can also use column names
nwtco$gamma <- jumps
nwtco$DCO.time <- DCO.values
ans.3 <- gammaImpute(formula=Surv(edrel,rel)~histol + instit + strata(stage),
                   data = nwtco, m=2, bootstrap.strata=strata(nwtco$stage),
                   gamma="gamma", DCO.time="DCO.time")

## End(Not run)
```

`GammaImputedData.object`
`GammaImputedData` *object*

Description

An object which contains

Slots

`data` A data frame containing the time to event data with 3 new columns impute.time and impute.event, the imputed event/censoring times and event indicators (for subjects whose data is not imputed these columns contain the unchanged event/censoring time and event indicator) and internal_gamma_val which is the value of gamma used for each subject in this data set

`default.formula` The default model formula which will be used when fitting the imputed data

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`GammaImputedSet.object`
`GammaImputedSet` *object*

Description

An object which contains the set of gamma imputed data frames. Use the `ExtractSingle` function to extract a single `GammaImputedData` objects. Use the ImputeStat function to fit models to the entire set of imputed data frames

Details

It contains the following:

Slots

`data` A data frame containing the unimputed time to event data (along with a column internal_gamma_val which is the value of gamma used for each subject in this data set)

`m` The number of imputed data sets

`gamma.factor` The value of gamma.factor used with the imputation

`impute.time` A matrix (1 column per imputed data set) containing the imputed times

`impute.event` A matrix (1 column per imputed data set) containing the imputed event indicators

`default.formula` The default model formula which will be used when fitting the imputed data

See Also

`GammaImputedData.object`

GammaStat.object GammaStat *object*

Description

An S3 object which contains the point estimate and test statistic after fitting a model to a GammaImputedData object.

Details

The function print.GammaStat has been implemented

The object contains the following:

Slots

model The model used to create the fit

method The model used for the fit

estimate A point estimate of the test statistic

var The estimate for the variance of the test statistic

GammaStatList.object GammaStatList *object*

Description

The object containing the results of fitting models to a GammaImputedSet object.

Details

A summary.GammaStatList has been implemented which performs Rubin's multiple imputation rules.

The object contains the following

Slots

fits A list of GammaStat objects containing the model fits for the imputed data sets

statistics A list with two elements: estimates and vars which contain the coefficient estimates and their variances one column per covariate one row per imputed data set

m The number of model fits

ImputeStat *S3 generic to fit model(s) to risk score/gamma Imputed objects*

Description

S3 generic to fit model(s) to risk score/gamma Imputed objects

Usage

```
## S3 method for class 'GammaImputedData'
ImputeStat(object, method = c("Cox", "weibull",
  "exponential")[1], formula = NULL, ...)

## S3 method for class 'GammaImputedSet'
ImputeStat(object, method = c("Cox", "weibull",
  "exponential")[1], formula = NULL, ..., parallel = c("no", "multicore",
  "snow")[1], ncpus = 1L, cl = NULL)

ImputeStat(object, method = c("logrank", "Wilcoxon", "Cox", "weibull",
  "exponential")[1], formula, ...)

## S3 method for class 'ScoreImputedSet'
ImputeStat(object, method = c("logrank", "Wilcoxon",
  "Cox")[1], formula = NULL, ..., parallel = c("no", "multicore",
  "snow")[1], ncpus = 1L, cl = NULL)
```

Arguments

object	A ScoreImputedData, ScoreImputedSet, GammaImputedData or GammaImputedSet object to fit the model to
method	The type of statistical model to fit. There are three methods which can be performed when using Risk Score imputation "logrank": a logrank test using survival::survdiff "Wilcoxon": Peto & Peto modification of the Gehan-Wilcoxon test using survival::survdiff with rho=1 "Cox": Fit a cox model using survival::coxph For gamma imputation the model can be "Cox" (using survival::coxph), "weibull" or "exponential" both using survival::coxph
formula	The model formula to fit. If no formula argument is used, then object$default.formula will be used. For risk score imputation this is ~ treatment.group and for gamma imputation this is the formula used when fitting the Cox model For method="Cox", additional covariates can be included by explictily giving a formula argument. For logrank/Wilcoxon only additional strata terms can be included.

	In all cases only the right hand side of the formula is required The survival object on the left hand side is created automatically E.g. for a Cox model could use formula=~arm + covar1. The cluster and tt options cannot be used See the vignettes for further details
...	Additional arguments which are passed into the model fit function
parallel	The type of parallel operation to be used (if any), can be used for GammaImputedSet and ScoreImputedSet
ncpus	integer: number of processes to be used in parallel operation: typically one would chose this to be the number of available CPUs, can be used for GammaImputedSet and ScoreImputedSet.
cl	An optional parallel or snow cluster for use if parallel="snow". If not supplied, a cluster on the local machine is created for the duration of the call, can be used for GammaImputedSet and ScoreImputedSet.

See Also

ScoreStat.object ScoreImputedData.object

MakeTimeDepScore *Create a valid* ScoreTD *object*

Description

Create a valid ScoreTD object

Usage

```
MakeTimeDepScore(data, Id, time.start, time.end)
```

Arguments

data	A data frame of time dependent covariates
Id	The column name of the subject Id
time.start	The covariates are valid for the time [time.start,time.end] where time.start is the column name of time.start
time.end	The covariates are valid for the time [time.start,time.end] where time.end is the column name of time.end

Value

A ScoreTD object

NN.options — *Create a list of options which control the nearest neighbour algorithm for risk score imputation*

Description

Create a list of options which control the nearest neighbour algorithm for risk score imputation

Usage

```
NN.options(NN = 5, w.censoring = 0.2, min.subjects = 20)
```

Arguments

NN	The (maximum) number of subjects to be included in the risk set
w.censoring	The weighting on the censoring risk score when calculating distances for the nearest neighbour calculation A weighting of (1-w.censoring) is used for the event risk score
min.subjects	If using time dependent score imputation include at least this number of subjects when fitting the Cox model (i.e. include some subjects who were censored/had event earlier than the cenosred observation if neccessary)

Value

A list of options used within the ScoreImputedData function

ScoreImpute — *Perform risk score multiple imputation method*

Description

Perform risk score multiple imputation method

Usage

```
ScoreImpute(data, event.model, censor.model = event.model, col.control,
  NN.control = NN.options(), time.dep = NULL, m, bootstrap.strata = rep(1,
  nrow(data)), ..., parallel = c("no", "multicore", "snow")[1], ncpus = 1L,
  cl = NULL)
```

Arguments

`data`	The data set for which imputation is required
`event.model`	The right hand side of the formula to be used for fitting the Cox model for calculating the time to event score e.g. ~Z1+Z2+Z3.
`censor.model`	The right hand side of the formula to be used for fitting the Cox model for calculating the time to censoring score if not included then `event.model` will be used
`col.control`	A list of the columns names of `data` which are used by the imputation algorithm See example below and for further details of these columns and their purpose see `col.headings`
`NN.control`	Parameters which control the nearest neighbour algorithm. See `NN.options`
`time.dep`	A ScoreTD object, to be included if the time dependent score imputation method is to be used, otherwise it should be NULL
`m`	The number of data sets to impute
`bootstrap.strata`	When performing the bootstrap procedure for fitting the models, how should the data be stratified (see strata argument to `boot::boot`). if argument is not used then standard sampling with replacement is used to generate the bootstrap data
`...`	Additional arguments passed into the Cox model Note the subset and na.action arguments should not be used (na.fail will be used when fitting the Cox model)
`parallel`	The type of parallel operation to be used (if any).
`ncpus`	integer: number of processes to be used in parallel operation: typically one would chose this to be the number of available CPUs
`cl`	An optional parallel or snow cluster for use if `parallel="snow"`. If not supplied, a cluster on the local machine is created for the duration of the call.

Details

Note that coxph may fail to converge and the following output Warning in fitter(X, Y, strats, offset, init, control, weights = weights, : Ran out of iterations and did not converge

It is possible to use ridge regression by including a ridge term in the model formula (e.g. `~Z1+ridge(Z2,theta=1)`). See `ridge` for further details

Value

A `ScoreImputedSet` object

See Also

`ScoreImputedSet.object`

Examples

```
data(ScoreInd)

col.control <- col.headings(has.event="event", time="time",
                            Id="Id",arm="arm",
                            DCO.time="DCO.time",
                            to.impute="to.impute")

## Not run:
ans <- ScoreImpute(data=ScoreInd,event.model=~Z1+Z2+Z3+Z4+Z5,
                   col.control=col.control, m=5,
                   bootstrap.strata=ScoreInd$arm,
                   NN.control=NN.options(NN=5,w.censoring = 0.2))

## End(Not run)
```

ScoreImputedData.object

ScoreImputedData *object*

Description

An object which contains

Slots

`data` A data frame containing the time to event data with 2 new columns impute.time and impute.event, the imputed event/censoring times and event indicators (for subjects whose data is not imputed these columns contain the unchanged event/censoring time and event indicator)

`col.control` The list of column names the risk score imputation method requires see `col.headings` for further details. If censor.type was not used then `col.control$censor.type="using_has.event_col"`

`default.formula` The default model formula which will be used when fitting the imputed data using a Cox model

---

ScoreImputedSet.object

ScoreImputedSet *object*

Description

An object which contains the set of score imputed data frames. Use the `ExtractSingle` function to extract a single `ScoreImputedData` object. Use the `ScoreStat` function to fit models to the entire set of imputed data frames

Details

It contains the following:

Slots

`data` A data frame containing the unimputed time to event data

`col.control` The list of column names the score imputation method requires see `col.headings` for further details

`m` The number of imputed data sets

`impute.time` A matrix (1 column per imputed data set) containing the imputed times

`impute.event` A matrix (1 column per imputed data set) containing the imputed event indicators

`default.formula` The default model formula which will be used when fitting the imputed data using a Cox model

See Also

`ScoreImputedData.object`

`ScoreInd` *Simulated time to event data with 5 time independent covariates*

Description

This dataset is inspired by the simulation described in Hsu and Taylor, Statistics in Medicine (2009) 28:462-475 with an additional DCO.time column

Format

A data.frame containing a row per subject with eleven columns:

Fields

`Id` subject identifier

`arm` factor for treatment group control=0, active=1

`Z1` binary time independent covariate

`Z2` continuous time independent covariate

`Z3` binary time independent covariate

`Z4` continuous time independent covariate

`Z5` binary time independent covariate

`event` event indicator (1 yes, 0 no)

`time` subject censoring/event time (in years)

`to.impute` logical, should an event time be imputed for this subject? (this is ignored if subject has event time)

`DCO.time` The time the subject would have been censored if they had not had an event or been censored before the data cut off date

ScoreStat.object *ScoreStat object*

Description

An S3 object which contains the point estimate and test statistic after fitting a model to a `ScoreImputedData` object.

Details

The functions `print.ScoreStat` and `as.vector.ScoreStat` have been included

The object contains the following:

The test statistic should be normally distributed and hence for the logrank test Z = (O_2 - E_2)/sqrt(V_2), i.e. the square root of the standard Chi squared statistic (with the appropriate sign)

Slots

`model` The model used to create the fit

`method` The method used for the fit

`estimate` A point estimate of the test statistic

`var` The estimate for the variance of the test statistic

`statistic` The test statistic given by `estimate/sqrt(var)`

ScoreStatList.object *ScoreStatList*

Description

The object containing the results of fitting models to a `ScoreImputedSet` object.

Details

A `summary.ScoreStatList` has been implemented.

The object contains the following

Slots

`fits` A list of `ScoreStat` objects containing the model fits for the imputed data sets

`statistics` A `ScoreStatSet` object containing the statistics

`m` The number of model fits

See Also

`ScoreStatSet.object` `ScoreStat.object`

ScoreStatSet *S3 generic to create a* ScoreStatSet *object*

Description

S3 generic to create a ScoreStatSet object

Usage

```
ScoreStatSet(x)
```

Arguments

x	The object to convert into a ScoreStatSet object

Value

A ScoreStatSet object

See Also

ScoreStatSet.object

ScoreStatSet.object *An object which contains the test statistic and estimators for a set of model fits to imputed data using risk score imputation*

Description

The object is a Mx3 matrix, one row per imputed data set and columns: estimate (the point estimates), var (their variances) and Z (the test statistic). M must be > 4

Details

Note the Z should be ~ standard normal (so we do not use the chi_squared test statistic see ScoreStat.object for further details)

The summary.ScoreStatSet function will apply the MI averaging procedures and estimates of the test statistic and p-value

See Also

summary.ScoreStatSet

ScoreTD.object *A* ScoreTD *object*

Description

This data frame holds time dependent covariates for use with risk score imputation

Details

The data frame contains the following columns: 'Id' for subject ID
'time.start' and 'time.end' the range of time for which the covariate values are valid - i.e. [time.start,time.end]
Additional columns are the time dependent covariates

All data for a single subject should be stored in consecutive rows, sorted by time and the starting time of a row should match the ending time of the previous row

See Also

MakeTimeDepScore

ScoreTimeDep *Simulated time dependent variables for time to event data*

Description

This data set contains time dependent covariates for the ScoreInd time to event data.

Format

A data.frame containing 1 row per subject-visit

Fields

Id The Subject Id

start The covariate given in each row are for a given subject from time 'start'...

end ... until time end

W1 The value of a (binary) time dependent variable for the subject with the given 'Id' between times 'start' and 'end'

W2 The value of a (continuous) time dependent variable for the subject with the given 'Id' between times 'start' and 'end'

`summary.ScoreStatSet` *Summary object of* `ScoreStatSet` *object*

Description

This object contains the multiple imputed averages/p-values of a set of estimates from risk score imputed data sets.

Details

A `print.summary.ScoreStatSet` function has been implemented

This object contains three lists meth1 and meth2 and methRubin meth1 averages the point estimates to produce an F test statistic, meth2 averages the test statistics and prodcues a t test statistic and methRubin follows Rubin's standard rules and is used for calculating confidence intervals

See the vignette for further details.

meth1, meth2 and methRubin are lists with the following elements: estimate: average estimator for meth1, NOTE: for meth2 this is the average test statistic,
var: estimate of variance of "estimate" field
test.stat: test statistic
distribution: distribution of statistical test (i.e. F or t)
p.value: p-value of test

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