Package 'gfoRmula'

March 23, 2020

Title Parametric G-Formula

Version 0.3.1

Description Implements the parametric g-formula algorithm of Robins (1986) <doi:10.1016/0270-0255(86)90088-6>. The g-formula can be used to estimate the causal effects of hypothetical time-varying treatment interventions on the mean or risk of an outcome from longitudinal data with time-varying confounding. This package allows: 1) binary or continuous/multi-level time-varying treatments; 2) different types of outcomes (survival or continuous/binary end of follow-up); 3) data with competing events or truncation by death and loss to follow-up and other types of censoring events; 4) different options for handling competing events in the case of survival outcomes; 5) a random measurement/visit process; 6) joint interventions on multiple treatments; and 7) general incorporation of a priori knowledge of the data structure.

```
Depends R (>= 3.4.0)
```

License GPL-3

Encoding UTF-8

LazyData true

RoxygenNote 6.1.1

Imports data.table, ggplot2, ggpubr, grDevices, nnet, parallel, progress, stats, stringr, survival, truncnorm, truncreg, utils

Suggests Hmisc

URL https://github.com/CausalInference/gfoRmula,
 https://arxiv.org/abs/1908.07072

BugReports https://github.com/CausalInference/gfoRmula/issues

NeedsCompilation no

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2 basicdata

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Date/Publication 2020-03-23 17:20:10 UTC

R topics documented:

static	43
print.gformula_survival	40
plot.gformula_continuous_eof	
lagged	
gformula_survival	26
gformula_binary_eof	
continuous_eofdata_pb	
coef.gformula	
binary_eofdata	4
basicdata	

basicdata

Example Dataset for a Survival Outcome with Censoring

Description

A dataset consisting of 11,332 observations on 2,500 individuals over 7 time points. Each row in the dataset corresponds to the record of one individual at one time point. Individuals who are censored at time k+1 only have a total of k+1 records, which correspond to time indices 0, ..., k.

Usage

basicdata

basicdata_nocomp 3

Format

A data table with 11,332 rows and 8 variables:

- t0 Time index.
- id Unique identifier for each individual.
- L1 Binary time-varying covariate.
- L2 Continuous time-varying covariate.
- **L3** Continuous baseline covariate. For each individual, the baseline values are repeated at each time point.
- A Binary treatment variable.
- **D** Competing event; time-varying indicator of failure.
- Y Outcome of interest; time-varying indicator of failure.

basicdata_nocomp

Example Dataset for a Survival Outcome without Censoring

Description

A dataset consisting of 13,170 observations on 2,500 individuals over 7 time points. Each row in the dataset corresponds to the record of one individual at one time point.

Usage

basicdata_nocomp

Format

A data table with 13,170 rows and 7 variables:

- t0 Time index.
- id Unique identifier for each individual.
- L1 Binary covariate.
- L2 Continuous covariate.
- **L3** Continuous baseline covariate. For each individual, the baseline values are repeated at each time point.
- A Binary treatment variable.
- Y Outcome of interest; time-varying indicator of failure.

4 carry_forward

binary_eofdata

Example Dataset for a Binary Outcome at End of Follow-Up

Description

A dataset consisting of 17,500 observations on 2,500 individuals over 7 time points. Each row in the dataset corresponds to the record of one individual at one time point.

Usage

binary_eofdata

Format

A data table with 17,500 rows and 7 variables:

time Time index.

id num Unique identifier for each individual.

cov1 Binary time-varying covariate.

cov2 Continuous time-varying covariate.

cov3 Continuous baseline covariate. For each individual, the baseline values are repeated at each time point.

treat Binary treatment variable.

outcome Binary outcome of interest. Because this outcome is only defined at the end of follow-up, values of NA are given in all other time points.

carry_forward

Carry Forward

Description

This function assists the implemention of a restriction on a covariate in the date table newdf. A particular covariate is simulated only when some condition (usually a covariate representing whether a doctor's visit occurred or not) is TRUE. If the condition is FALSE, the covariate value is not simulated for that time point and the value is instead carried over from the previous time point.

Usage

```
carry_forward(newdf, pool, restriction, time_name, t)
```

carry_forward 5

Arguments

newdf Data table containing the simulated data at time t.

Data table containing the simulated data at times before t.

restriction List of vectors. Each vector contains as its first entry the covariate affected by

the restriction; its second entry the condition that must be TRUE for the covariate to be modeled; its third entry a function that executes other specific actions based on the condition (in this case, this function); and its fourth entry some value used

by the function (in this case, this entry is not used).

time_name Character string specifying the name of the time variable in pool and newdf.

t Integer specifying the current time index.

Value

No value is returned. The data table newdf is modified in place.

```
## Estimating the effect of static treatment strategies on risk of a
## failure event
id <- 'id'
time_points <- 7
time_name <- 't0'
covnames <- c('L1', 'L2', 'A')
outcome_name <- 'Y'
covtypes <- c('binary', 'bounded normal', 'binary')</pre>
histories <- c(lagged, lagavg)
histvars <- list(c('A', 'L1', 'L2'), c('L1', 'L2'))
covparams <- list(covmodels = c(L1 ~ lag_LA + lag_cumavg1_L1 + lag_cumavg1_L2 +</pre>
                                    L3 + t0,
                                  L2 \sim lag1_A + L1 + lag\_cumavg1_L1 +
                                    lag_cumavg1_L2 + L3 + t0,
                                  A \sim lag1_A + L1 + L2 + lag_cumavg1_L1 +
                                    lag_cumavg1_L2 + L3 + t0))
ymodel \leftarrow Y \sim A + L1 + L2 + L3 + lag1_A + lag1_L1 + lag1_L2 + t0
intvars <- list('A', 'A')</pre>
interventions <- list(list(c(static, rep(0, time_points))),</pre>
                       list(c(static, rep(1, time_points))))
int_descript <- c('Never treat', 'Always treat')</pre>
nsimul <- 10000
# At t0 == 5, assign L1 its value at the previous time point
restrictions <- list(c('L2', 't0 != 5', carry_forward))
gform_basic <- gformula_survival(obs_data = basicdata_nocomp, id = id,</pre>
                                   time_points = time_points,
                                   time_name = time_name, covnames = covnames,
                                   outcome_name = outcome_name,
                                   covtypes = covtypes,
                                   covparams = covparams, ymodel = ymodel,
```

6 coef.gformula

```
intvars = intvars,
interventions = interventions,
int_descript = int_descript,
restrictions = restrictions,
histories = histories, histvars = histvars,
basecovs = c('L3'), nsimul = nsimul,
seed = 1234)
```

gform_basic

coef.gformula

Coefficient method for objects of class "gformula"

Description

This function extracts the coefficients of the fitted models for the time-varying covariates, outcome, and compevent event (if applicable).

Usage

```
## S3 method for class 'gformula'
coef(object, ...)
```

Arguments

object Object of class "gformula". . . . Other arguments.

Value

If bootdiag was set to FALSE in gformula, this function returns a list of the coefficients of the fitted models to the observed data set. If bootstrapping was used and bootdiag was set to TRUE in gformula, this function returns a list described as follows. The first element (named 'Original sample') is a list of the coefficients of the fitted models to the observed data set. The kth element (named 'Bootstrap sample k-1') is a list of the coefficients of the fitted models corresponding to the k-1th bootstrap sample.

See Also

```
gformula
```

```
## Estimating the effect of static treatment strategies on risk of a
## failure event
id <- 'id'
time_points <- 7</pre>
```

continuous_eofdata 7

```
time_name <- 't0'</pre>
covnames <- c('L1', 'L2', 'A')
outcome_name <- 'Y'
outcome_type <- 'survival'</pre>
covtypes <- c('binary', 'bounded normal', 'binary')</pre>
histories <- c(lagged, lagavg)</pre>
histvars <- list(c('A', 'L1', 'L2'), c('L1', 'L2'))
covparams <- list(covmodels = c(L1 \sim lag_1_A + lag_cumavg_1_L1 + lag_cumavg_1_L2 + lag_cumavg_1_L2 + lag_cumavg_1_L3 +
                                                                                               L3 + t0,
                                                                                          L2 \sim lag1_A + L1 + lag\_cumavg1_L1 +
                                                                                                lag_cumavg1_L2 + L3 + t0,
                                                                                          A \sim lag1_A + L1 + L2 + lag_cumavg1_L1 +
                                                                                                lag_cumavg1_L2 + L3 + t0))
ymodel \leftarrow Y \sim A + L1 + L2 + L3 + lag1_A + lag1_L1 + lag1_L2 + t0
intvars <- list('A', 'A')</pre>
interventions <- list(list(c(static, rep(0, time_points))),</pre>
                                                              list(c(static, rep(1, time_points))))
int_descript <- c('Never treat', 'Always treat')</pre>
nsimul <- 10000
gform_basic <- gformula(obs_data = basicdata_nocomp, id = id,</pre>
                                                                   time_points = time_points,
                                                                   time_name = time_name, covnames = covnames,
                                                                   outcome_name = outcome_name,
                                                                   outcome_type = outcome_type, covtypes = covtypes,
                                                                   covparams = covparams, ymodel = ymodel,
                                                                    intvars = intvars,
                                                                    interventions = interventions,
                                                                   int_descript = int_descript,
                                                                   histories = histories, histvars = histvars,
                                                                   basecovs = c('L3'), nsimul = nsimul,
                                                                   seed = 1234)
coef(gform_basic)
```

continuous_eofdata

Example Dataset for a Continuous Outcome at End of Follow-Up

Description

A dataset consisting of 17,500 observations on 2,500 individuals over 7 time points. Each row in the dataset corresponds to the record of one individual at one time point.

Usage

continuous_eofdata

Format

A data table with 17,500 rows and 7 variables:

- t0 Time index.
- id Unique identifier for each individual.
- L1 Categorical time-varying covariate.
- L2 Continuous time-varying covariate.
- **L3** Continuous baseline covariate. For each individual, the baseline values are repeated at each time point.
- A Binary treatment variable.
- Y Continuous outcome of interest. Because this outcome is only defined at the end of follow-up, values of NA are given in all other time points.

continuous_eofdata_pb Example Dataset for a Continuous Outcome at End of Follow-Up with Pre-Baseline Times

Description

A dataset consisting of 22,500 observations on 2,500 individuals over 2 pre-baseline time points and follow-up 7 time points. Each row in the dataset corresponds to the record of one individual at one time point.

Usage

continuous_eofdata_pb

Format

A data table with 22,500 rows and 7 variables:

- to Time index.
- id Unique identifier for each individual.
- L1 Categorical time-varying covariate.
- **L2** Continuous time-varying covariate.
- **L3** Continuous baseline covariate. For each individual, the baseline values are repeated at each time point.
- A Binary treatment variable.
- Y Continuous outcome of interest. Because this outcome is only defined at the end of follow-up, values of NA are given in all other time points.

gformula	Estimation of Survival Outcome, Continuous End-of-Follow-Up Outcome, or Binary End-of-Follow-Up Outcome Under the Parametric
	G-Formula

Description

Based on an observed data set, this function estimates the risk over time (for survival outcomes), outcome mean at end-of-follow-up (for continuous end-of-follow-up outcomes), or outcome probability at end-of-follow-up (for binary end-of-follow-up outcomes) under multiple user-specified interventions using the parametric g-formula. See Lin et al. (2019) for further details concerning the application and implementation of the parametric g-formula.

Usage

```
gformula(obs_data, id, time_points = NULL, time_name, covnames, covtypes,
  covparams, covfits_custom = NA, covpredict_custom = NA,
  histvars = NULL, histories = NA, basecovs = NA, outcome_name,
  outcome_type, ymodel, compevent_name = NULL, compevent_model = NA,
  intvars = NULL, interventions = NULL, int_times = NULL,
  int_descript = NULL, ref_int = 0, intcomp = NA,
  visitprocess = NA, restrictions = NA, yrestrictions = NA,
  compevent_restrictions = NA, baselags = FALSE, nsimul = NA,
  sim_data_b = FALSE, seed, nsamples = 0, parallel = FALSE,
  ncores = NA, ci_method = "percentile", threads, model_fits = FALSE,
  boot_diag = FALSE, show_progress = TRUE, ...)
```

Arguments

obs_data	Data table containing the observed data.
id	Character string specifying the name of the ID variable in obs_data.
time_points	Number of time points to simulate. By default, this argument is set equal to the maximum number of records that obs_data contains for any individual.
time_name	Character string specifying the name of the time variable in obs_data.
covnames	Vector of character strings specifying the names of the time-varying covariates in obs_data.
covtypes	Vector of character strings specifying the "type" of each time-varying covariate included in covnames. The possible "types" are: "binary", "normal", "categorical", "bounded normal", "zero-inflated normal", "truncated normal", "absorbing", "categorical time", and "custom".
covparams	List of vectors, where each vector contains information for one parameter used in the modeling of the time-varying covariates (e.g., model statement, family, link function, etc.). Each vector must be the same length as covnames and in the same order. If a parameter is not required for a certain covariate, it should be set to NA at that index.

covfits_custom Vector containing custom fit functions for time-varying covariates that do not fall within the pre-defined covariate types. It should be in the same order covnames. If a custom fit function is not required for a particular covariate (e.g., if the first covariate is of type "binary" but the second is of type "custom"), then that index should be set to NA. The default is NA.

covpredict_custom

Vector containing custom prediction functions for time-varying covariates that do not fall within the pre-defined covariate types. It should be in the same order as covnames. If a custom prediction function is not required for a particular covariate, then that index should be set to NA. The default is NA.

histvars List of vectors. The kth vector specifies the names of the variables for which the

kth history function in histories is to be applied.

histories Vector of history functions to apply to the variables specified in histvars. The

default is NA.

basecovs Vector of character strings specifying the names of baseline covariates in obs_data.

> These covariates are not simulated using a model but rather carry their value over all time points from the first time point of obs_data. These covariates should

not be included in covnames. The default is NA.

Character string specifying the name of the outcome variable in obs_data. outcome_name

Character string specifying the "type" of outcome. The possible "types" are: outcome_type

"survival", "continuous_eof", and "binary_eof".

ymodel Model statement for the outcome variable.

Character string specifying the name of the competing event variable in obs_data. compevent_name

Only applicable for survival outcomes.

compevent_model

Model statement for the competing event variable. The default is NA. Only ap-

plicable for survival outcomes.

intvars List, whose elements are vectors of character strings. The kth vector in intvars

specifies the name(s) of the variable(s) to be intervened on in each round of the

simulation under the kth intervention in interventions.

List, whose elements are lists of vectors. Each list in interventions specifies a interventions

> unique intervention on the relevant variable(s) in intvars. Each vector contains a function implementing a particular intervention on a single variable, optionally followed by one or more "intervention values" (i.e., integers used to specify the

treatment regime).

int_times List, whose elements are lists of vectors. The kth list in int_times corresponds

to the kth intervention in interventions. Each vector specifies the time points in which the relevant intervention is applied on the corresponding variable in intvars. When an intervention is not applied, the simulated natural course value is used. By default, this argument is set so that all interventions are applied

in all time points.

int_descript Vector of character strings, each describing an intervention. It must be in same

order as the entries in interventions.

ref_int Integer denoting the intervention to be used as the reference for calculating the

risk ratio and risk difference. 0 denotes the natural course, while subsequent

integers denote user-specified interventions in the order that they are named in interventions. The default is 0.

intcomp List of two numbers indicating a pair of interventions to be compared by a haz-

ard ratio. The default is NA, resulting in no hazard ratio calculation.

visitprocess List of vectors. Each vector contains as its first entry the covariate name of a

visit process; its second entry the name of a covariate whose modeling depends on the visit process; and its third entry the maximum number of consecutive visits that can be missed before an individual is censored. The default is NA.

restrictions List of vectors. Each vector contains as its first entry a covariate for which a pri-

ori knowledge of its distribution is available; its second entry a condition under which no knowledge of its distribution is available and that must be TRUE for the distribution of that covariate given that condition to be estimated via a parametric model or other fitting procedure; its third entry a function for estimating the distribution of that covariate given the condition in the second entry is false such that *a priori* knowledge of the covariate distribution is available; and its fourth entry a value used by the function in the third entry. The default is NA.

yrestrictions List of vectors. Each vector containins as its first entry a condition and its second

entry an integer. When the condition is TRUE, the outcome variable is simulated according to the fitted model; when the condition is FALSE, the outcome variable

takes on the value in the second entry. The default is NA.

compevent_restrictions

List of vectors. Each vector containins as its first entry a condition and its second entry an integer. When the condition is TRUE, the competing event variable is simulated according to the fitted model; when the condition is FALSE, the competing event variable takes on the value in the second entry. The default is NA.

Only applicable for survival outcomes.

baselags Logical scalar for specifying the convention used for lagi and lag_cumavgi terms

in the model statements when pre-baseline times are not included in obs_data and when the current time index, t, is such that t < i. If this argument is set to FALSE, the value of all lagi and lag_cumavgi terms in this context are set to 0 (for non-categorical covariates) or the reference level (for categorical covariates). If this argument is set to TRUE, the value of lagi and lag_cumavgi terms are set to

their values at time 0. The default is FALSE.

nsimul Number of subjects for whom to simulate data. By default, this argument is set

equal to the number of subjects in obs_data.

sim_data_b Logical scalar indicating whether to return the simulated data set. If bootstrap

samples are used (i.e., nsamples is set to a value greater than 0), this argument

must be set to FALSE. The default is FALSE.

seed Starting seed for simulations and bootstrapping.

nsamples Integer specifying the number of bootstrap samples to generate. The default is

0.

parallel Logical scalar indicating whether to parallelize simulations of different inter-

ventions to multiple cores.

ncores Integer specifying the number of CPU cores to use in parallel simulation. This

argument is required when parallel is set to TRUE. In many applications, users

may wish to set this argument equal to parallel::detectCores() -1.

ci_method Character string specifying the method for calculating the bootstrap 95% confi-

dence intervals, if applicable. The options are "percentile" and "normal".

threads Integer specifying the number of threads to be used in data.table. See setDTthreads

for further details.

model_fits Logical scalar indicating whether to return the fitted models. Note that if this

argument is set to TRUE, the output of this function may use a lot of memory.

The default is FALSE.

boot_diag Logical scalar indicating whether to return the coefficients, standard errors, and

variance-covariance matrices of the parameters of the fitted models in the boot-

strap samples. The default is FALSE.

show_progress Logical scalar indicating whether to print a progress bar for the number of boot-

strap samples completed in the R console. This argument is only applicable when parallel is set to FALSE and bootstrap samples are used (i.e., nsamples

is set to a value greater than 0). The default is TRUE.

.. Other arguments, which are passed to the functions in covpredict_custom.

Value

An object of class gformula_survival. The object is a list with the following components:

result Results table. For survival outcomes, this contains the estimated risk, risk dif-

ference, and risk ratio for all interventions (inculding the natural course) at each time point. For continuous end-of-follow-up outcomes, this contains estimated mean outcome, mean difference, and mean ratio for all interventions (inculding natural course) at the last time point. For binary end-of-follow-up outcomes, this contains the estimated outcome probability, probability difference, and probability ratio for all interventions (inculding natural course) at the last time point. If bootstrapping was used, the results table includes the bootstrap risk / mean /

probability difference, ratio, standard error, and 95% confidence interval.

coeffs A list of the coefficients of the fitted models.

stderrs A list of the standard errors of the coefficients of the fitted models.

vcovs A list of the variance-covariance matrices of the parameters of the fitted models.

rmses A list of root mean square error (RMSE) values of the fitted models.

hazardratio_val

Hazard ratio between two interventions (if applicable).

fits A list of the fitted models for the time-varying covariates, outcome, and com-

peting event (if applicable). If model_fits is set to FALSE, a value of NULL is

given.

sim_data A list of data tables of the simulated data. Each element in the list corresponds

to one of the interventions. If the argument sim_data_b is set to FALSE, a value

of NA is given.

bootcoeefs A list, where the kth element is a list containing the coefficients of the fitted

models corresponding to the kth bootstrap sample. If boot_diag is set to FALSE,

a value of NULL is given.

bootstderrs A list, where the kth element is a list containing the standard errors of the co-

efficients of the fitted models corresponding to the kth bootstrap sample. If

boot_diag is set to FALSE, a value of NULL is given.

bootvcovs A list, where the kth element is a list containing the variance-covariance matrices

of the parameters of the fitted models corresponding to the kth bootstrap sample.

If boot_diag is set to FALSE, a value of NULL is given.

. . . Some additional elements.

The results for the g-formula simulation are printed with the print.gformula_survival, print.gformula_continuous_ec and print.gformula_binary_eof functions. To generate graphs comparing the mean estimated covariate values and risks over time and mean observed covariate values and risks over time, use the plot.gformula_survival, plot.gformula_continuous_eof, and plot.gformula_binary_eof functions.

References

Lin V, McGrath S, Zhang Z, Petito LC, Logan RW, Hernán MA, and JG Young. gfoRmula: An R package for estimating effects of general time-varying treatment interventions via the parametric g-formula. arXiv e-prints. 2019. https://arxiv.org/abs/1908.07072.

Robins JM. A new approach to causal inference in mortality studies with a sustained exposure period: application to the healthy worker survivor effect. Mathematical Modelling. 1986;7:1393–1512. [Errata (1987) in Computers and Mathematics with Applications 14, 917.-921. Addendum (1987) in Computers and Mathematics with Applications 14, 923-.945. Errata (1987) to addendum in Computers and Mathematics with Applications 18, 477.].

```
## Estimating the effect of static treatment strategies on risk of a
## failure event
id <- 'id'
time_points <- 7
time_name <- 't0'
covnames <- c('L1', 'L2', 'A')
outcome_name <- 'Y'
outcome_type <- 'survival'</pre>
covtypes <- c('binary', 'bounded normal', 'binary')</pre>
histories <- c(lagged, lagavg)
histvars <- list(c('A', 'L1', 'L2'), c('L1', 'L2'))
covparams <- list(covmodels = c(L1 ~ lag1_A + lag_cumavg1_L1 + lag_cumavg1_L2 +
                                    L3 + t0,
                                  L2 \sim lag1_A + L1 + lag\_cumavg1_L1 +
                                    lag_cumavg1_L2 + L3 + t0,
                                  A \sim lag1_A + L1 + L2 + lag_cumavg1_L1 +
                                    lag_cumavg1_L2 + L3 + t0))
ymodel <- Y ~ A + L1 + L2 + L3 + lag1_A + lag1_L1 + lag1_L2 + t0</pre>
intvars <- list('A', 'A')</pre>
interventions <- list(list(c(static, rep(0, time_points))),</pre>
                       list(c(static, rep(1, time_points))))
int_descript <- c('Never treat', 'Always treat')</pre>
```

```
nsimul <- 10000
gform_basic <- gformula(obs_data = basicdata_nocomp, id = id,</pre>
                         time_points = time_points,
                         time_name = time_name, covnames = covnames,
                         outcome_name = outcome_name,
                         outcome_type = outcome_type, covtypes = covtypes,
                         covparams = covparams, ymodel = ymodel,
                         intvars = intvars,
                         interventions = interventions,
                         int_descript = int_descript,
                         histories = histories, histvars = histvars,
                         basecovs = c('L3'), nsimul = nsimul,
                         seed = 1234)
gform_basic
## Estimating the effect of treatment strategies on risk of a failure event
## when competing events exist
id <- 'id'
time_points <- 7</pre>
time_name <- 't0'</pre>
covnames <- c('L1', 'L2', 'A')
outcome_name <- 'Y'
compevent_name <- 'D'</pre>
outcome_type <- 'survival'</pre>
covtypes <- c('binary', 'bounded normal', 'binary')</pre>
histories <- c(lagged, lagavg)</pre>
histvars <- list(c('A', 'L1', 'L2'), c('L1', 'L2'))
covparams <- list(covlink = c('logit', 'identity', 'logit'),</pre>
                   covmodels = c(L1 ~ lag1_A + lag_cumavg1_L1 + lag_cumavg1_L2 +
                                    L3 + as.factor(t0),
                                  L2 \sim lag1_A + L1 + lag\_cumavg1_L1 +
                                    lag_cumavg1_L2 + L3 + as.factor(t0),
                                  A \sim lag1_A + L1 + L2 + lag_cumavg1_L1 +
                                    lag_cumavg1_L2 + L3 + as.factor(t0)))
ymodel \leftarrow Y \sim A + L1 + L2 + lag1_A + lag1_L1 + lag1_L2 + L3 + as.factor(t0)
compevent_model <- D \sim A + L1 + L2 + lag1_A + lag1_L1 + lag1_L2 + L3 + as.factor(t0)
intvars <- list('A', 'A')</pre>
interventions <- list(list(c(static, rep(0, time_points))),</pre>
                       list(c(static, rep(1, time_points))))
int_descript <- c('Never treat', 'Always treat')</pre>
nsimul <- 10000
gform_basic <- gformula(obs_data = basicdata, id = id,</pre>
                         time_points = time_points,
                         time_name = time_name, covnames = covnames,
                         outcome_name = outcome_name,
                         outcome_type = outcome_type,
                         compevent_name = compevent_name,
                         covtypes = covtypes,
```

```
covparams = covparams, ymodel = ymodel,
                         compevent_model = compevent_model,
                         intvars = intvars, interventions = interventions,
                         int_descript = int_descript,
                         histories = histories, histvars = histvars,
                         basecovs = c('L3'), nsimul = nsimul,
                         seed = 1234)
gform_basic
## Estimating the effect of treatment strategies on the mean of a continuous
## end of follow-up outcome
library('Hmisc')
id <- 'id'
time_name <- 't0'</pre>
covnames <- c('L1', 'L2', 'A')
outcome_name <- 'Y'
outcome_type <- 'continuous_eof'</pre>
covtypes <- c('categorical', 'normal', 'binary')</pre>
histories <- c(lagged)
histvars <- list(c('A', 'L1', 'L2'))
covparams <- list(covmodels = c(L1 \sim lag1_A + lag1_L1 + L3 + t0 +
                                   rcspline.eval(lag1_L2, knots = c(-1, 0, 1)),
                                 L2 \sim lag1_A + L1 + lag1_L1 + lag1_L2 + L3 + t0,
                                 A \sim lag1_A + L1 + L2 + lag1_L1 + lag1_L2 + L3 + t0))
ymodel <- Y \sim A + L1 + L2 + lag1_A + lag1_L1 + lag1_L2 + L3
intvars <- list('A', 'A')</pre>
interventions <- list(list(c(static, rep(0, 7))),</pre>
                       list(c(static, rep(1, 7))))
int_descript <- c('Never treat', 'Always treat')</pre>
nsimul <- 10000
gform_cont_eof <- gformula(obs_data = continuous_eofdata,</pre>
                            id = id, time_name = time_name,
                            covnames = covnames, outcome_name = outcome_name,
                            outcome_type = outcome_type, covtypes = covtypes,
                            covparams = covparams, ymodel = ymodel,
                            intvars = intvars, interventions = interventions,
                            int_descript = int_descript,
                            histories = histories, histvars = histvars,
                            basecovs = c("L3"), nsimul = nsimul, seed = 1234)
gform_cont_eof
## Estimating the effect of threshold interventions on the mean of a binary
## end of follow-up outcome
outcome_type <- 'binary_eof'</pre>
id <- 'id_num'</pre>
time_name <- 'time'</pre>
```

```
covnames <- c('cov1', 'cov2', 'treat')
outcome_name <- 'outcome'
histories <- c(lagged, cumavg)</pre>
histvars <- list(c('treat', 'cov1', 'cov2'), c('cov1', 'cov2'))</pre>
covtypes <- c('binary', 'zero-inflated normal', 'normal')</pre>
covparams <- list(covmodels = c(cov1 ~ lag1_treat + lag1_cov1 + lag1_cov2 +</pre>
                                    cov3 + time,
                                  cov2 ~ lag1_treat + cov1 + lag1_cov1 +
                                    lag1_cov2 + cov3 + time,
                                  treat \sim lag1\_treat + cumavg\_cov1 +
                                    cumavg_cov2 + cov3 + time))
ymodel <- outcome ~ treat + cov1 + cov2 + lag1_cov1 + lag1_cov2 + cov3</pre>
intvars <- list('treat', 'treat')</pre>
interventions <- list(list(c(static, rep(0, 7))),</pre>
                       list(c(threshold, 1, Inf)))
int_descript <- c('Never treat', 'Threshold - lower bound 1')</pre>
nsimul <- 10000
ncores <- 2
gform_bin_eof <- gformula(obs_data = binary_eofdata,</pre>
                           outcome_type = outcome_type, id = id,
                            time_name = time_name, covnames = covnames,
                            outcome_name = outcome_name, covtypes = covtypes,
                            covparams = covparams, ymodel = ymodel,
                            intvars = intvars, interventions = interventions,
                            int_descript = int_descript, histories = histories,
                            histvars = histvars, basecovs = c("cov3"),
                            seed = 1234, parallel = TRUE, nsamples = 5,
                            nsimul = nsimul, ncores = ncores)
gform_bin_eof
```

gformula_binary_eof Estimation of Binary End-of-Follow-Up Outcome Under the Parametric G-Formula

Description

Based on an observed data set, this internal function estimates the outcome probability at end-of-follow-up under multiple user-specified interventions using the parametric g-formula. See Lin et al. (2019) for further details concerning the application and implementation of the parametric g-formula.

Usage

```
gformula_binary_eof(obs_data, id, time_name, covnames, covtypes, covparams,
   covfits_custom = NA, covpredict_custom = NA, histvars = NULL,
   histories = NA, basecovs = NA, outcome_name, ymodel,
   intvars = NULL, interventions = NULL, int_times = NULL,
```

gformula_binary_eof 17

```
int_descript = NULL, ref_int = 0, visitprocess = NA,
restrictions = NA, yrestrictions = NA, baselags = FALSE,
nsimul = NA, sim_data_b = FALSE, seed, nsamples = 0,
parallel = FALSE, ncores = NA, ci_method = "percentile", threads,
model_fits = FALSE, boot_diag = FALSE, show_progress = TRUE, ...)
```

Arguments

obs_data Data table containing the observed data.

id Character string specifying the name of the ID variable in obs_data.

time_name Character string specifying the name of the time variable in obs_data.

covnames Vector of character strings specifying the names of the time-varying covariates

in obs_data.

covtypes Vector of character strings specifying the "type" of each time-varying covari-

ate included in covnames. The possible "types" are: "binary", "normal", "categorical", "bounded normal", "zero-inflated normal", "truncated

normal", "absorbing", "categorical time", and "custom".

covparams List of vectors, where each vector contains information for one parameter used

in the modeling of the time-varying covariates (e.g., model statement, family, link function, etc.). Each vector must be the same length as covnames and in the same order. If a parameter is not required for a certain covariate, it should be set

to NA at that index.

 ${\tt covfits_custom} \ \ Vector\ containing\ custom\ fit\ functions\ for\ time-varying\ covariates\ that\ do\ not\ fall$

within the pre-defined covariate types. It should be in the same order covnames. If a custom fit function is not required for a particular covariate (e.g., if the first covariate is of type "binary" but the second is of type "custom"), then that

index should be set to NA. The default is NA.

covpredict_custom

Vector containing custom prediction functions for time-varying covariates that do not fall within the pre-defined covariate types. It should be in the same order as covnames. If a custom prediction function is not required for a particular

covariate, then that index should be set to NA. The default is NA.

histvars List of vectors. The kth vector specifies the names of the variables for which the

kth history function in histories is to be applied.

histories Vector of history functions to apply to the variables specified in histvars. The

default is NA.

basecovs Vector of character strings specifying the names of baseline covariates in obs_data.

These covariates are not simulated using a model but rather carry their value over all time points from the first time point of obs_data. These covariates should

not be included in covnames. The default is NA.

outcome_name Character string specifying the name of the outcome variable in obs_data.

ymodel Model statement for the outcome variable.

intvars List, whose elements are vectors of character strings. The kth vector in intvars

specifies the name(s) of the variable(s) to be intervened on in each round of the

simulation under the kth intervention in interventions.

interventions

List, whose elements are lists of vectors. Each list in interventions specifies a unique intervention on the relevant variable(s) in intvars. Each vector contains a function implementing a particular intervention on a single variable, optionally followed by one or more "intervention values" (i.e., integers used to specify the treatment regime).

int_times

List, whose elements are lists of vectors. The kth list in int_times corresponds to the kth intervention in interventions. Each vector specifies the time points in which the relevant intervention is applied on the corresponding variable in intvars. When an intervention is not applied, the simulated natural course value is used. By default, this argument is set so that all interventions are applied in all time points.

int_descript

Vector of character strings, each describing an intervention. It must be in same order as the entries in interventions.

ref_int

Integer denoting the intervention to be used as the reference for calculating the end-of-follow-up mean ratio and mean difference. 0 denotes the natural course, while subsequent integers denote user-specified interventions in the order that they are named in interventions. The default is 0.

visitprocess

List of vectors. Each vector contains as its first entry the covariate name of a visit process; its second entry the name of a covariate whose modeling depends on the visit process; and its third entry the maximum number of consecutive visits that can be missed before an individual is censored. The default is NA.

restrictions

List of vectors. Each vector contains as its first entry a covariate for which *a priori* knowledge of its distribution is available; its second entry a condition under which no knowledge of its distribution is available and that must be TRUE for the distribution of that covariate given that condition to be estimated via a parametric model or other fitting procedure; its third entry a function for estimating the distribution of that covariate given the condition in the second entry is false such that *a priori* knowledge of the covariate distribution is available; and its fourth entry a value used by the function in the third entry. The default is NA.

yrestrictions

List of vectors. Each vector containins as its first entry a condition and its second entry an integer. When the condition is TRUE, the outcome variable is simulated according to the fitted model; when the condition is FALSE, the outcome variable takes on the value in the second entry. The default is NA.

baselags

Logical scalar for specifying the convention used for lagi and lag_cumavgi terms in the model statements when pre-baseline times are not included in obs_data and when the current time index, t, is such that t < i. If this argument is set to FALSE, the value of all lagi and lag_cumavgi terms in this context are set to 0 (for non-categorical covariates) or the reference level (for categorical covariates). If this argument is set to TRUE, the value of lagi and lag_cumavgi terms are set to their values at time 0. The default is FALSE.

nsimul

Number of subjects for whom to simulate data. By default, this argument is set equal to the number of subjects in obs_data.

sim_data_b

Logical scalar indicating whether to return the simulated data set. If bootstrap samples are used (i.e., nsamples is set to a value greater than 0), this argument must be set to FALSE. The default is FALSE.

seed

Starting seed for simulations and bootstrapping.

nsamples	Integer specifying the number of bootstrap samples to generate. The default is 0.
parallel	Logical scalar indicating whether to parallelize simulations of different interventions to multiple cores.
ncores	Integer specifying the number of CPU cores to use in parallel simulation. This argument is required when parallel is set to TRUE. In many applications, users may wish to set this argument equal to parallel::detectCores() -1.
ci_method	Character string specifying the method for calculating the bootstrap 95% confidence intervals, if applicable. The options are "percentile" and "normal".
threads	Integer specifying the number of threads to be used in data.table. See setDTthreads for further details.
model_fits	Logical scalar indicating whether to return the fitted models. Note that if this argument is set to TRUE, the output of this function may use a lot of memory. The default is FALSE.
boot_diag	Logical scalar indicating whether to return the coefficients, standard errors, and variance-covariance matrices of the parameters of the fitted models in the bootstrap samples. The default is FALSE.
show_progress	Logical scalar indicating whether to print a progress bar for the number of bootstrap samples completed in the R console. This argument is only applicable when parallel is set to FALSE and bootstrap samples are used (i.e., nsamples is set to a value greater than 0). The default is TRUE.
	Other arguments, which are passed to the functions in covpredict_custom.

Value

An object of class gformula_binary_eof. The object is a list with the following components:

result	Results table containing the estimated outcome probability for all interventions (inculding natural course) at the last time point. If bootstrapping was used, the results table includes the bootstrap end-of-follow-up mean ratio, standard error, and 95% confidence interval.
coeffs	A list of the coefficients of the fitted models.
stderrs	A list of the standard errors of the coefficients of the fitted models.
vcovs	A list of the variance-covariance matrices of the parameters of the fitted models.
rmses	A list of root mean square error (RMSE) values of the fitted models.
fits	A list of the fitted models for the time-varying covariates and outcome. If model_fits is set to FALSE, a value of NULL is given.
sim_data	A list of data tables of the simulated data. Each element in the list corresponds to one of the interventions. If the argument sim_data_b is set to FALSE, a value of NA is given.
bootcoeefs	A list, where the kth element is a list containing the coefficients of the fitted models corresponding to the kth bootstrap sample. If boot_diag is set to FALSE, a value of NULL is given.

bootstderrs A list, where the kth element is a list containing the standard errors of the co-

efficients of the fitted models corresponding to the kth bootstrap sample. If

boot_diag is set to FALSE, a value of NULL is given.

bootvcovs A list, where the kth element is a list containing the variance-covariance matrices

of the parameters of the fitted models corresponding to the kth bootstrap sample.

If boot_diag is set to FALSE, a value of NULL is given.

... Some additional elements.

The results for the g-formula simulation under various interventions for the last time point are printed with the print.gformula_binary_eof function. To generate graphs comparing the mean estimated and observed covariate values over time, use the plot.gformula_binary_eof function.

References

Lin V, McGrath S, Zhang Z, Petito LC, Logan RW, Hernán MA, and JG Young. gfoRmula: An R package for estimating effects of general time-varying treatment interventions via the parametric g-formula. arXiv e-prints. 2019. https://arxiv.org/abs/1908.07072.

Robins JM. A new approach to causal inference in mortality studies with a sustained exposure period: application to the healthy worker survivor effect. Mathematical Modelling. 1986;7:1393–1512. [Errata (1987) in Computers and Mathematics with Applications 14, 917.-921. Addendum (1987) in Computers and Mathematics with Applications 14, 923-.945. Errata (1987) to addendum in Computers and Mathematics with Applications 18, 477.].

See Also

gformula

```
## Estimating the effect of threshold interventions on the mean of a binary
## end of follow-up outcome
id <- 'id_num'</pre>
time_name <- 'time'</pre>
covnames <- c('cov1', 'cov2', 'treat')</pre>
outcome_name <- 'outcome'
histories <- c(lagged, cumavg)</pre>
histvars <- list(c('treat', 'cov1', 'cov2'), c('cov1', 'cov2'))</pre>
covtypes <- c('binary', 'zero-inflated normal', 'normal')</pre>
covparams <- list(covmodels = c(cov1 ~ lag1_treat + lag1_cov1 + lag1_cov2 + cov3 +</pre>
                                     time.
                                   cov2 ~ lag1_treat + cov1 + lag1_cov1 + lag1_cov2 +
                                     cov3 + time,
                                   treat ~ lag1_treat + cumavg_cov1 +
                                     cumavg_cov2 + cov3 + time))
ymodel <- outcome ~ treat + cov1 + cov2 + lag1_cov1 + lag1_cov2 + cov3</pre>
intvars <- list('treat', 'treat')</pre>
interventions <- list(list(c(static, rep(0, 7))),</pre>
                        list(c(threshold, 1, Inf)))
```

```
int_descript <- c('Never treat', 'Threshold - lower bound 1')</pre>
nsimul <- 10000
ncores <- 2
gform_bin_eof <- gformula_binary_eof(obs_data = binary_eofdata, id = id,</pre>
                                      time_name = time_name,
                                      covnames = covnames,
                                      outcome_name = outcome_name,
                                      covtypes = covtypes,
                                      covparams = covparams,
                                      ymodel = ymodel,
                                      intvars = intvars,
                                      interventions = interventions,
                                      int_descript = int_descript,
                                      histories = histories, histvars = histvars,
                                      basecovs = c("cov3"), seed = 1234,
                                      parallel = TRUE, nsamples = 5,
                                      nsimul = nsimul, ncores = ncores)
gform_bin_eof
```

gformula_continuous_eof

Estimation of Continuous End-of-Follow-Up Outcome Under the Parametric G-Formula

Description

Based on an observed data set, this internal function estimates the outcome mean at end-of-follow-up under multiple user-specified interventions using the parametric g-formula. See Lin et al. (2019) for further details concerning the application and implementation of the parametric g-formula.

Usage

```
gformula_continuous_eof(obs_data, id, time_name, covnames, covtypes,
  covparams, covfits_custom = NA, covpredict_custom = NA,
  histvars = NULL, histories = NA, basecovs = NA, outcome_name,
  ymodel, intvars = NULL, interventions = NULL, int_times = NULL,
  int_descript = NULL, ref_int = 0, visitprocess = NA,
  restrictions = NA, yrestrictions = NA, baselags = FALSE,
  nsimul = NA, sim_data_b = FALSE, seed, nsamples = 0,
  parallel = FALSE, ncores = NA, ci_method = "percentile", threads,
  model_fits = FALSE, boot_diag = FALSE, show_progress = TRUE, ...)
```

Arguments

obs_data Data table containing the observed data.

id Character string specifying the name of the ID variable in obs_data.

time_name Character string specifying the name of the time variable in obs_data.

covnames Vector of character strings specifying the names of the time-varying covariates

in obs_data.

covtypes Vector of character strings specifying the "type" of each time-varying covari-

ate included in covnames. The possible "types" are: "binary", "normal", "categorical", "bounded normal", "zero-inflated normal", "truncated

normal", "absorbing", "categorical time", and "custom".

covparams List of vectors, where each vector contains information for one parameter used

in the modeling of the time-varying covariates (e.g., model statement, family, link function, etc.). Each vector must be the same length as covnames and in the same order. If a parameter is not required for a certain covariate, it should be set

to NA at that index.

covfits_custom Vector containing custom fit functions for time-varying covariates that do not fall

within the pre-defined covariate types. It should be in the same order covnames. If a custom fit function is not required for a particular covariate (e.g., if the first covariate is of type "binary" but the second is of type "custom"), then that

index should be set to NA. The default is NA.

covpredict_custom

Vector containing custom prediction functions for time-varying covariates that do not fall within the pre-defined covariate types. It should be in the same order as covnames. If a custom prediction function is not required for a particular

covariate, then that index should be set to NA. The default is NA.

histvars List of vectors. The kth vector specifies the names of the variables for which the

kth history function in histories is to be applied.

histories Vector of history functions to apply to the variables specified in histvars. The

default is NA.

basecovs Vector of character strings specifying the names of baseline covariates in obs_data.

These covariates are not simulated using a model but rather carry their value over all time points from the first time point of obs_data. These covariates should

not be included in covnames. The default is NA.

outcome_name Character string specifying the name of the outcome variable in obs_data.

ymodel Model statement for the outcome variable.

intvars List, whose elements are vectors of character strings. The kth vector in intvars

specifies the name(s) of the variable(s) to be intervened on in each round of the

simulation under the kth intervention in interventions.

interventions List, whose elements are lists of vectors. Each list in interventions specifies a

unique intervention on the relevant variable(s) in intvars. Each vector contains a function implementing a particular intervention on a single variable, optionally followed by one or more "intervention values" (i.e., integers used to specify the

treatment regime).

int_times List, whose elements are lists of vectors. The kth list in int_times corresponds

to the kth intervention in interventions. Each vector specifies the time points in which the relevant intervention is applied on the corresponding variable in intvars. When an intervention is not applied, the simulated natural course value is used. By default, this argument is set so that all interventions are applied

in all time points.

int_descript Vector of character strings, each describing an intervention. It must be in same

order as the entries in interventions.

ref_int Integer denoting the intervention to be used as the reference for calculating the

end-of-follow-up mean ratio and mean difference. 0 denotes the natural course, while subsequent integers denote user-specified interventions in the order that

they are named in interventions. The default is 0.

visitprocess List of vectors. Each vector contains as its first entry the covariate name of a

visit process; its second entry the name of a covariate whose modeling depends on the visit process; and its third entry the maximum number of consecutive visits that can be missed before an individual is censored. The default is NA.

restrictions List of vectors. Each vector contains as its first entry a covariate for which a pri-

ori knowledge of its distribution is available; its second entry a condition under which no knowledge of its distribution is available and that must be TRUE for the distribution of that covariate given that condition to be estimated via a parametric model or other fitting procedure; its third entry a function for estimating the distribution of that covariate given the condition in the second entry is false such that *a priori* knowledge of the covariate distribution is available; and its fourth

entry a value used by the function in the third entry. The default is NA.

yrestrictions List of vectors. Each vector containing as its first entry a condition and its second

entry an integer. When the condition is TRUE, the outcome variable is simulated according to the fitted model; when the condition is FALSE, the outcome variable

takes on the value in the second entry. The default is NA.

baselags Logical scalar for specifying the convention used for lagi and lag_cumavgi terms

in the model statements when pre-baseline times are not included in obs_data and when the current time index, t, is such that t < i. If this argument is set to FALSE, the value of all lagi and lag_cumavgi terms in this context are set to 0 (for non-categorical covariates) or the reference level (for categorical covariates). If this argument is set to TRUE, the value of lagi and lag_cumavgi terms are set to

their values at time 0. The default is FALSE.

nsimul Number of subjects for whom to simulate data. By default, this argument is set

equal to the number of subjects in obs_data.

sim_data_b Logical scalar indicating whether to return the simulated data set. If bootstrap

samples are used (i.e., nsamples is set to a value greater than 0), this argument

must be set to FALSE. The default is FALSE.

seed Starting seed for simulations and bootstrapping.

nsamples Integer specifying the number of bootstrap samples to generate. The default is

0.

parallel Logical scalar indicating whether to parallelize simulations of different inter-

ventions to multiple cores.

ncores Integer specifying the number of CPU cores to use in parallel simulation. This

argument is required when parallel is set to TRUE. In many applications, users

may wish to set this argument equal to parallel::detectCores() -1.

ci_method Character string specifying the method for calculating the bootstrap 95% confi-

dence intervals, if applicable. The options are "percentile" and "normal".

threads Integer specifying the number of threads to be used in data. table. See setDTthreads

for further details.

model_fits Logical scalar indicating whether to return the fitted models. Note that if this

argument is set to TRUE, the output of this function may use a lot of memory.

The default is FALSE.

boot_diag Logical scalar indicating whether to return the coefficients, standard errors, and

variance-covariance matrices of the parameters of the fitted models in the boot-

strap samples. The default is FALSE.

show_progress Logical scalar indicating whether to print a progress bar for the number of boot-

strap samples completed in the R console. This argument is only applicable when parallel is set to FALSE and bootstrap samples are used (i.e., nsamples

is set to a value greater than 0). The default is TRUE.

... Other arguments, which are passed to the functions in covpredict_custom.

Value

An object of class gformula_continuous_eof. The object is a list with the following components:

result Results table containing the estimated mean outcome for all interventions (in-

culding natural course) at the last time point. If bootstrapping was used, the results table includes the bootstrap end-of-follow-up mean ratio, standard error,

and 95% confidence interval.

coeffs A list of the coefficients of the fitted models.

stderrs A list of the standard errors of the coefficients of the fitted models.

vcovs A list of the variance-covariance matrices of the parameters of the fitted models.

rmses A list of root mean square error (RMSE) values of the fitted models.

fits A list of the fitted models for the time-varying covariates and outcome. If

model_fits is set to FALSE, a value of NULL is given.

sim_data A list of data tables of the simulated data. Each element in the list corresponds

to one of the interventions. If the argument sim_data_b is set to FALSE, a value

of NA is given.

bootcoeefs A list, where the kth element is a list containing the coefficients of the fitted

models corresponding to the kth bootstrap sample. If boot_diag is set to FALSE,

a value of NULL is given.

bootstderrs A list, where the kth element is a list containing the standard errors of the co-

efficients of the fitted models corresponding to the kth bootstrap sample. If

boot_diag is set to FALSE, a value of NULL is given.

bootvcovs A list, where the kth element is a list containing the variance-covariance matrices

of the parameters of the fitted models corresponding to the kth bootstrap sample.

If boot_diag is set to FALSE, a value of NULL is given.

... Some additional elements.

The results for the g-formula simulation under various interventions for the last time point are printed with the print.gformula_continuous_eof function. To generate graphs comparing the mean estimated and observed covariate values over time, use the print.gformula_continuous_eof function.

References

Lin V, McGrath S, Zhang Z, Petito LC, Logan RW, Hernán MA, and JG Young. gfoRmula: An R package for estimating effects of general time-varying treatment interventions via the parametric g-formula. arXiv e-prints. 2019. https://arxiv.org/abs/1908.07072.

Robins JM. A new approach to causal inference in mortality studies with a sustained exposure period: application to the healthy worker survivor effect. Mathematical Modelling. 1986;7:1393–1512. [Errata (1987) in Computers and Mathematics with Applications 14, 917.-921. Addendum (1987) in Computers and Mathematics with Applications 14, 923-.945. Errata (1987) to addendum in Computers and Mathematics with Applications 18, 477.].

See Also

gformula

```
## Estimating the effect of treatment strategies on the mean of a continuous
## end of follow-up outcome
library('Hmisc')
id <- 'id'
time_name <- 't0'
covnames <- c('L1', 'L2', 'A')
outcome_name <- 'Y'</pre>
covtypes <- c('categorical', 'normal', 'binary')</pre>
histories <- c(lagged)
histvars <- list(c('A', 'L1', 'L2'))
covparams <- list(covmodels = c(L1 ~ lag1_A + lag1_L1 + L3 + t0 +
                                    rcspline.eval(lag1_L2, knots = c(-1, 0, 1)),
                                  L2 \sim lag1_A + L1 + lag1_L1 + lag1_L2 + L3 + t0,
                                  A \sim lag1_A + L1 + L2 + lag1_L1 + lag1_L2 + L3 + t0))
ymodel <- Y ~ A + L1 + L2 + lag1_A + lag1_L1 + lag1_L2 + L3</pre>
intvars <- list('A', 'A')</pre>
interventions <- list(list(c(static, rep(0, 7))),</pre>
                       list(c(static, rep(1, 7))))
int_descript <- c('Never treat', 'Always treat')</pre>
nsimul <- 10000
gform_cont_eof <- gformula_continuous_eof(obs_data = continuous_eofdata,</pre>
                                            id = id,
                                            time_name = time_name,
                                            covnames = covnames,
                                            outcome_name = outcome_name,
                                            covtypes = covtypes,
                                            covparams = covparams, ymodel = ymodel,
                                            intvars = intvars,
                                            interventions = interventions,
                                            int_descript = int_descript,
                                            histories = histories, histvars = histvars,
                                            basecovs = c("L3"),
```

```
nsimul = nsimul, seed = 1234)
```

gform_cont_eof

gformula_survival

Estimation of Survival Outcome Under the Parametric G-Formula

Description

Based on an observed data set, this internal function estimates the risk over time under multiple user-specified interventions using the parametric g-formula. See Lin et al. (2019) for further details concerning the application and implementation of the parametric g-formula.

Usage

```
gformula_survival(obs_data, id, time_points = NULL, time_name, covnames,
  covtypes, covparams, covfits_custom = NA, covpredict_custom = NA,
  histvars = NULL, histories = NA, basecovs = NA, outcome_name,
  ymodel, compevent_name = NULL, compevent_model = NA,
  intvars = NULL, interventions = NULL, int_times = NULL,
  int_descript = NULL, ref_int = 0, intcomp = NA,
  visitprocess = NA, restrictions = NA, yrestrictions = NA,
  compevent_restrictions = NA, baselags = FALSE, nsimul = NA,
  sim_data_b = FALSE, seed, nsamples = 0, parallel = FALSE,
  ncores = NA, ci_method = "percentile", threads, model_fits = FALSE,
  boot_diag = FALSE, show_progress = TRUE, ...)
```

Arguments

obs_data	Data table containing the observed data.
id	Character string specifying the name of the ID variable in obs_data.
time_points	Number of time points to simulate. By default, this argument is set equal to the maximum number of records that obs_data contains for any individual.
time_name	Character string specifying the name of the time variable in obs_data.
covnames	Vector of character strings specifying the names of the time-varying covariates in obs_data.
covtypes	Vector of character strings specifying the "type" of each time-varying covariate included in covnames. The possible "types" are: "binary", "normal", "categorical", "bounded normal", "zero-inflated normal", "truncated normal", "absorbing", "categorical time", and "custom".
covparams	List of vectors, where each vector contains information for one parameter used in the modeling of the time-varying covariates (e.g., model statement, family, link function, etc.). Each vector must be the same length as covnames and in the same order. If a parameter is not required for a certain covariate, it should be set to NA at that index.

covfits_custom Vector containing custom fit functions for time-varying covariates that do not fall within the pre-defined covariate types. It should be in the same order covnames. If a custom fit function is not required for a particular covariate (e.g., if the first covariate is of type "binary" but the second is of type "custom"), then that index should be set to NA. The default is NA.

covpredict_custom

Vector containing custom prediction functions for time-varying covariates that do not fall within the pre-defined covariate types. It should be in the same order as covnames. If a custom prediction function is not required for a particular covariate, then that index should be set to NA. The default is NA.

histvars List of vectors. The kth vector specifies the names of the variables for which the

kth history function in histories is to be applied.

histories Vector of history functions to apply to the variables specified in histvars. The

default is NA.

basecovs Vector of character strings specifying the names of baseline covariates in obs_data.

These covariates are not simulated using a model but rather carry their value over all time points from the first time point of obs_data. These covariates should

not be included in covnames. The default is NA.

Character string specifying the name of the outcome variable in obs_data. outcome_name

ymodel Model statement for the outcome variable.

compevent_name Character string specifying the name of the competing event variable in obs_data.

compevent_model

Model statement for the competing event variable. The default is NA.

List, whose elements are vectors of character strings. The kth vector in intvars intvars

specifies the name(s) of the variable(s) to be intervened on in each round of the

simulation under the kth intervention in interventions.

interventions List, whose elements are lists of vectors. Each list in interventions specifies a

> unique intervention on the relevant variable(s) in intvars. Each vector contains a function implementing a particular intervention on a single variable, optionally followed by one or more "intervention values" (i.e., integers used to specify the

treatment regime).

int_times List, whose elements are lists of vectors. The kth list in int_times corresponds

to the kth intervention in interventions. Each vector specifies the time points in which the relevant intervention is applied on the corresponding variable in intvars. When an intervention is not applied, the simulated natural course value is used. By default, this argument is set so that all interventions are applied

in all time points.

int_descript Vector of character strings, each describing an intervention. It must be in same

order as the entries in interventions.

ref_int Integer denoting the intervention to be used as the reference for calculating the

> risk ratio and risk difference. 0 denotes the natural course, while subsequent integers denote user-specified interventions in the order that they are named in

interventions. The default is 0.

intcomp List of two numbers indicating a pair of interventions to be compared by a haz-

ard ratio. The default is NA, resulting in no hazard ratio calculation.

visitprocess

List of vectors. Each vector contains as its first entry the covariate name of a visit process; its second entry the name of a covariate whose modeling depends on the visit process; and its third entry the maximum number of consecutive visits that can be missed before an individual is censored. The default is NA.

restrictions

List of vectors. Each vector contains as its first entry a covariate for which *a priori* knowledge of its distribution is available; its second entry a condition under which no knowledge of its distribution is available and that must be TRUE for the distribution of that covariate given that condition to be estimated via a parametric model or other fitting procedure; its third entry a function for estimating the distribution of that covariate given the condition in the second entry is false such that *a priori* knowledge of the covariate distribution is available; and its fourth entry a value used by the function in the third entry. The default is NA.

yrestrictions

List of vectors. Each vector containins as its first entry a condition and its second entry an integer. When the condition is TRUE, the outcome variable is simulated according to the fitted model; when the condition is FALSE, the outcome variable takes on the value in the second entry. The default is NA.

compevent_restrictions

List of vectors. Each vector containins as its first entry a condition and its second entry an integer. When the condition is TRUE, the competing event variable is simulated according to the fitted model; when the condition is FALSE, the competing event variable takes on the value in the second entry. The default is NA.

baselags

Logical scalar for specifying the convention used for lagi and lag_cumavgi terms in the model statements when pre-baseline times are not included in obs_data and when the current time index, t, is such that t < i. If this argument is set to FALSE, the value of all lagi and lag_cumavgi terms in this context are set to 0 (for non-categorical covariates) or the reference level (for categorical covariates). If this argument is set to TRUE, the value of lagi and lag_cumavgi terms are set to their values at time 0. The default is FALSE.

nsimul

Number of subjects for whom to simulate data. By default, this argument is set equal to the number of subjects in obs_data.

sim_data_b

Logical scalar indicating whether to return the simulated data set. If bootstrap samples are used (i.e., nsamples is set to a value greater than 0), this argument must be set to FALSE. The default is FALSE.

seed

Starting seed for simulations and bootstrapping.

nsamples

Integer specifying the number of bootstrap samples to generate. The default is 0

parallel

Logical scalar indicating whether to parallelize simulations of different interventions to multiple cores.

ncores

Integer specifying the number of CPU cores to use in parallel simulation. This argument is required when parallel is set to TRUE. In many applications, users may wish to set this argument equal to parallel::detectCores() -1.

ci_method

Character string specifying the method for calculating the bootstrap 95% confidence intervals, if applicable. The options are "percentile" and "normal".

threads

Integer specifying the number of threads to be used in data. table. See setDTthreads for further details.

. . .

argument is set to TRUE, the output of this function may use a lot of memory.

The default is FALSE.

boot_diag Logical scalar indicating whether to return the coefficients, standard errors, and

variance-covariance matrices of the parameters of the fitted models in the boot-

strap samples. The default is FALSE.

show_progress Logical scalar indicating whether to print a progress bar for the number of boot-

strap samples completed in the R console. This argument is only applicable when parallel is set to FALSE and bootstrap samples are used (i.e., nsamples

is set to a value greater than 0). The default is TRUE.

... Other arguments, which are passed to the functions in covpredict_custom.

Value

An object of class gformula_survival. The object is a list with the following components:

result Results table containing the estimated risk and risk ratio for all interventions

(inculding the natural course) at each time point. If bootstrapping was used, the results table includes the bootstrap mean risk ratio, standard error, and 95%

confidence interval.

coeffs A list of the coefficients of the fitted models.

stderrs A list of the standard errors of the coefficients of the fitted models.

vcovs A list of the variance-covariance matrices of the parameters of the fitted models.

rmses A list of root mean square error (RMSE) values of the fitted models.

hazardratio_val

Hazard ratio between two interventions (if applicable).

fits A list of the fitted models for the time-varying covariates, outcome, and com-

peting event (if applicable). If model_fits is set to FALSE, a value of NULL is

given.

sim_data A list of data tables of the simulated data. Each element in the list corresponds

to one of the interventions. If the argument sim_data_b is set to FALSE, a value

of NA is given.

bootcoeefs A list, where the kth element is a list containing the coefficients of the fitted

models corresponding to the kth bootstrap sample. If boot_diag is set to FALSE,

a value of NULL is given.

bootstderrs A list, where the kth element is a list containing the standard errors of the co-

efficients of the fitted models corresponding to the kth bootstrap sample. If

boot_diag is set to FALSE, a value of NULL is given.

bootvcovs A list, where the kth element is a list containing the variance-covariance matrices

of the parameters of the fitted models corresponding to the kth bootstrap sample.

If boot_diag is set to FALSE, a value of NULL is given.

... Some additional elements.

The results for the g-formula simulation under various interventions only for the first and last time points are printed with the print.gformula_survival function. To generate graphs comparing the mean estimated covariate values and risks over time and mean observed covariate values and risks over time, use the plot.gformula_survival function.

References

Lin V, McGrath S, Zhang Z, Petito LC, Logan RW, Hernán MA, and JG Young. gfoRmula: An R package for estimating effects of general time-varying treatment interventions via the parametric g-formula. arXiv e-prints. 2019. https://arxiv.org/abs/1908.07072.

Robins JM. A new approach to causal inference in mortality studies with a sustained exposure period: application to the healthy worker survivor effect. Mathematical Modelling. 1986;7:1393–1512. [Errata (1987) in Computers and Mathematics with Applications 14, 917.-921. Addendum (1987) in Computers and Mathematics with Applications 14, 923-.945. Errata (1987) to addendum in Computers and Mathematics with Applications 18, 477.].

See Also

gformula

```
## Estimating the effect of static treatment strategies on risk of a
## failure event
id <- 'id'
time_points <- 7
time_name <- 't0'
covnames <- c('L1', 'L2', 'A')
outcome_name <- 'Y'
covtypes <- c('binary', 'bounded normal', 'binary')</pre>
histories <- c(lagged, lagavg)
histvars <- list(c('A', 'L1', 'L2'), c('L1', 'L2'))
covparams <- list(covmodels = c(L1 ~ lag1_A + lag_cumavg1_L1 + lag_cumavg1_L2 +</pre>
                                   L3 + t0.
                                  L2 \sim lag1_A + L1 + lag\_cumavg1_L1 +
                                    lag_cumavg1_L2 + L3 + t0,
                                  A \sim lag1_A + L1 + L2 + lag_cumavg1_L1 +
                                    lag_cumavg1_L2 + L3 + t0))
ymodel <- Y ~ A + L1 + L2 + L3 + lag1_A + lag1_L1 + lag1_L2 + t0</pre>
intvars <- list('A', 'A')</pre>
interventions <- list(list(c(static, rep(0, time_points))),</pre>
                       list(c(static, rep(1, time_points))))
int_descript <- c('Never treat', 'Always treat')</pre>
nsimul <- 10000
gform_basic <- gformula_survival(obs_data = basicdata_nocomp, id = id,</pre>
                                  time_points = time_points,
                                  time_name = time_name, covnames = covnames,
                                  outcome_name = outcome_name,
                                  covtypes = covtypes,
                                   covparams = covparams, ymodel = ymodel,
                                   intvars = intvars,
                                   interventions = interventions,
                                  int_descript = int_descript,
                                  histories = histories, histvars = histvars,
                                  basecovs = c('L3'), nsimul = nsimul,
```

lagged 31

```
seed = 1234)
gform_basic
## Estimating the effect of treatment strategies on risk of a failure event
## when competing events exist
id <- 'id'
time_points <- 7</pre>
time_name <- 't0'
covnames <- c('L1', 'L2', 'A')
outcome_name <- 'Y'
compevent_name <- 'D'</pre>
covtypes <- c('binary', 'bounded normal', 'binary')</pre>
histories <- c(lagged, lagavg)
histvars <- list(c('A', 'L1', 'L2'), c('L1', 'L2'))
covparams <- list(covlink = c('logit', 'identity', 'logit'),</pre>
                   covmodels = c(L1 \sim lag1_A + lag\_cumavg1_L1 + lag\_cumavg1_L2 +
                                   L3 + as.factor(t0),
                                  L2 \sim lag1_A + L1 + lag\_cumavg1_L1 +
                                   lag_cumavg1_L2 + L3 + as.factor(t0),
                                 A \sim lag1_A + L1 + L2 + lag_cumavg1_L1 +
                                   lag_cumavg1_L2 + L3 + as.factor(t0)))
ymodel \leftarrow Y \sim A + L1 + L2 + lag1_A + lag1_L1 + lag1_L2 + L3 + as.factor(t0)
compevent_model <- D \sim A + L1 + L2 + lag1_A + lag1_L1 + lag1_L2 + L3 + as.factor(t0)
intvars <- list('A', 'A')</pre>
interventions <- list(list(c(static, rep(0, time_points))),</pre>
                       list(c(static, rep(1, time_points))))
int_descript <- c('Never treat', 'Always treat')</pre>
nsimul <- 10000
gform_basic <- gformula_survival(obs_data = basicdata, id = id,</pre>
                                  time_points = time_points,
                                  time_name = time_name, covnames = covnames,
                                  outcome_name = outcome_name,
                                  compevent_name = compevent_name,
                                  covtypes = covtypes,
                                  covparams = covparams, ymodel = ymodel,
                                   compevent_model = compevent_model,
                                   intvars = intvars, interventions = interventions,
                                   int_descript = int_descript,
                                  histories = histories, histvars = histvars,
                                  basecovs = c('L3'), nsimul = nsimul,
                                   seed = 1234)
gform_basic
```

32 lagged

Description

These functions create new columns in an input data table for covariate histories. Users must specify which covariates are to be used in the history functions.

Usage

```
lagged(pool, histvars, histvals, time_name, t, id_name, baselags,
  below_zero_indicator)

cumavg(pool, histvars, time_name, t, id_name, below_zero_indicator)

lagavg(pool, histvars, histvals, time_name, t, id_name, baselags,
  below_zero_indicator)
```

Arguments

pool Data table containing all information prior to time t (t noninclusive).

histvars Vector of character strings specifying the names of the variables for which his-

tory functions are to be applied.

histvals For lagged, this argument is a vector specifying the lags used in the model state-

ments (e.g., if $lag1_varname$ and $lag2_varname$ were included in the model statements, this vector would be c(1,2)). For lagavg, this argument is a nu-

meric vector specifying the lag averages used in the model statements.

time_name Character string specifying the name of the time variable in pool.

t Integer specifying the current time index.

id_name Character string specifying the name of the ID variable in pool.

baselags Logical scalar for specifying the convention used for lagi and lag_cumavgi terms

in the model statements when pre-baseline times are not included in obs_data and when the current time index, t, is such that t < i. If this argument is set to FALSE, the value of all lagi and lag_cumavgi terms in this context are set to 0 (for non-categorical covariates) or the reference level (for categorical covariates). If this argument is set to TRUE, the value of lagi and lag_cumavgi terms are set to

their values at time 0. The default is FALSE.

below_zero_indicator

Logical scalar indicating whether the observed data set contains rows for time t < 0.

Details

lagged creates new columns for lagged versions of existing variables in the dataset. The user must specify which variables are to be lagged.

cumavg creates new columns for the cumulative average up until time t of existing variables in the dataset.

lagavg creates new columns for the "lagged cumulative average" (cumulative average up until time t, then lagged by one time unit) up until time t of existing variables in the dataset.

Value

No value is returned. The data table pool is modified in place.

```
## Estimating the effect of static treatment strategies on risk of a
## failure event
id <- 'id'
time_points <- 7
time_name <- 't0'
covnames <- c('L1', 'L2', 'A')
outcome_name <- 'Y'
covtypes <- c('binary', 'bounded normal', 'binary')</pre>
histories <- c(lagged, lagavg)
histvars <- list(c('A', 'L1', 'L2'), c('L1', 'L2'))
covparams <- list(covmodels = c(L1 ~ lag1_A + lag_cumavg1_L1 + lag_cumavg1_L2 +</pre>
                                   L3 + t0,
                                 L2 \sim lag1_A + L1 + lag\_cumavg1_L1 +
                                   lag_cumavg1_L2 + L3 + t0,
                                  A \sim lag1_A + L1 + L2 + lag_cumavg1_L1 +
                                    lag_cumavg1_L2 + L3 + t0))
ymodel \leftarrow Y \sim A + L1 + L2 + L3 + lag1_A + lag1_L1 + lag1_L2 + t0
intvars <- list('A', 'A')</pre>
interventions <- list(list(c(static, rep(0, time_points))),</pre>
                       list(c(static, rep(1, time_points))))
int_descript <- c('Never treat', 'Always treat')</pre>
nsimul <- 10000
gform_basic <- gformula_survival(obs_data = basicdata_nocomp, id = id,</pre>
                                  time_points = time_points,
                                  time_name = time_name, covnames = covnames,
                                  outcome_name = outcome_name,
                                  covtypes = covtypes,
                                  covparams = covparams, ymodel = ymodel,
                                   intvars = intvars,
                                   interventions = interventions,
                                   int_descript = int_descript,
                                  histories = histories, histvars = histvars,
                                  basecovs = c('L3'), nsimul = nsimul,
                                  seed = 1234)
gform_basic
```

Description

This function generates graphs of the mean simulated vs. observed values at each time point of the time-varying covariates under the natural course. For categorical covariates, the observed and simulated counts of the levels of the factors are plotted at each time point.

Usage

```
## S3 method for class 'gformula_binary_eof'
plot(x, covnames = NULL, ncol = NULL,
    nrow = NULL, common.legend = TRUE, legend = "bottom",
    xlab = NULL, ylab_cov = NULL, ...)
```

Arguments

x	Object of class "gformula_binary_eof".
covnames	Vector of character strings specifying the names of the time-varying covariates to be plotted. The ordering of covariates given here is used in the plot grid. Time-varying covariates of type "categorical time" cannot be included. By default, this argument is set equal to the covnames argument used in gformula_binary_eof, where covariates of type "categorical time" are removed.
ncol	Number of columns in the plot grid. By default, two columns are used when there is at least two plots.
nrow	Number of rows in the plot grid. By default, a maximum of six rows is used and additional plots are included in subsequent pages.
common.legend	Logical scalar indicating whether to include a legend. The default is TRUE.
legend	Character string specifying the legend position. Valid values are "top", "bottom", "left", "right", and "none". The default is "bottom".
xlab	Character string for the x axes of all plots. By default, this argument is set to the time_name argument specified in gformula_binary_eof.
ylab_cov	Vector of character strings for the y axes of the plots for the covariates. This argument must be the same length as covnames. The i-th element of this argument corresponds to the plot for the i-th element of covnames.
	Other arguments, which are passed to ggarrange.

Value

An object of class "ggarrange". See documentation of ggarrange.

See Also

```
gformula_binary_eof
```

```
## Estimating the effect of threshold interventions on the mean of a binary
## end of follow-up outcome
id <- 'id_num'</pre>
time_name <- 'time'</pre>
covnames <- c('cov1', 'cov2', 'treat')</pre>
outcome_name <- 'outcome'</pre>
histories <- c(lagged, cumavg)</pre>
histvars <- list(c('treat', 'cov1', 'cov2'), c('cov1', 'cov2'))</pre>
covtypes <- c('binary', 'zero-inflated normal', 'normal')</pre>
covparams <- list(covmodels = c(cov1 ~ lag1_treat + lag1_cov1 + lag1_cov2 + cov3 +
                                    time,
                                  cov2 ~ lag1_treat + cov1 + lag1_cov1 + lag1_cov2 +
                                    cov3 + time,
                                  treat ~ lag1_treat + cumavg_cov1 +
                                    cumavg_cov2 + cov3 + time))
ymodel <- outcome ~ treat + cov1 + cov2 + lag1_cov1 + lag1_cov2 + cov3</pre>
intvars <- list('treat', 'treat')</pre>
interventions <- list(list(c(static, rep(0, 7))),</pre>
                       list(c(threshold, 1, Inf)))
int_descript <- c('Never treat', 'Threshold - lower bound 1')</pre>
nsimul <- 10000
ncores <- 2
gform_bin_eof <- gformula_binary_eof(obs_data = binary_eofdata, id = id,</pre>
                                       time_name = time_name,
                                       covnames = covnames,
                                       outcome_name = outcome_name,
                                       covtypes = covtypes,
                                       covparams = covparams,
                                       ymodel = ymodel,
                                       intvars = intvars,
                                       interventions = interventions,
                                       int_descript = int_descript,
                                       histories = histories, histvars = histvars,
                                       basecovs = c("cov3"), seed = 1234,
                                       parallel = TRUE, nsamples = 5,
                                       nsimul = nsimul, ncores = ncores)
plot(gform_bin_eof)
```

Description

This function generates graphs of the mean simulated vs. observed values at each time point of the time-varying covariates under the natural course. For categorical covariates, the observed and simulated counts of the levels of the factors are plotted at each time point.

Usage

```
## S3 method for class 'gformula_continuous_eof'
plot(x, covnames = NULL, ncol = NULL,
    nrow = NULL, common.legend = TRUE, legend = "bottom",
    xlab = NULL, ylab_cov = NULL, ...)
```

Arguments

Χ	Object of class "gformula_continuous_eof".
covnames	Vector of character strings specifying the names of the time-varying covariates to be plotted. The ordering of covariates given here is used in the plot grid. Time-varying covariates of type "categorical time" cannot be included. By default, this argument is set equal to the covnames argument used in gformula_continuous_eof, where covariates of type "categorical time" are removed.
ncol	Number of columns in the plot grid. By default, two columns are used when there is at least two plots.
nrow	Number of rows in the plot grid. By default, a maximum of six rows is used and additional plots are included in subsequent pages.
common.legend	Logical scalar indicating whether to include a legend. The default is TRUE.
legend	Character string specifying the legend position. Valid values are "top", "bottom",
	"left", "right", and "none". The default is "bottom".
xlab	
xlab ylab_cov	"left", "right", and "none". The default is "bottom". Character string for the x axes of all plots. By default, this argument is set to the

Value

An object of class "ggarrange". See documentation of ggarrange.

See Also

```
gformula_continuous_eof
```

plot.gformula_survival

Examples

```
## Estimating the effect of treatment strategies on the mean of a continuous
## end of follow-up outcome
library('Hmisc')
id <- 'id'
time_name <- 't0'</pre>
covnames <- c('L1', 'L2', 'A')
outcome_name <- 'Y'
covtypes <- c('categorical', 'normal', 'binary')</pre>
histories <- c(lagged)
histvars <- list(c('A', 'L1', 'L2'))
covparams <- list(covmodels = c(L1 \sim lag1_A + lag1_L1 + L3 + t0 +
                                    rcspline.eval(lag1_L2, knots = c(-1, 0, 1)),
                                 L2 \sim lag1_A + L1 + lag1_L1 + lag1_L2 + L3 + t0,
                                 A \sim lag1_A + L1 + L2 + lag1_L1 + lag1_L2 + L3 + t0)
ymodel <- Y ~ A + L1 + L2 + lag1_A + lag1_L1 + lag1_L2 + L3</pre>
intvars <- list('A', 'A')</pre>
interventions <- list(list(c(static, rep(0, 7))),</pre>
                       list(c(static, rep(1, 7))))
int_descript <- c('Never treat', 'Always treat')</pre>
nsimul <- 10000
gform_cont_eof <- gformula_continuous_eof(obs_data = continuous_eofdata,</pre>
                                            id = id,
                                            time_name = time_name,
                                            covnames = covnames,
                                            outcome_name = outcome_name,
                                            covtypes = covtypes,
                                            covparams = covparams, ymodel = ymodel,
                                            intvars = intvars,
                                            interventions = interventions,
                                            int_descript = int_descript,
                                            histories = histories, histvars = histvars,
                                            basecovs = c("L3"),
                                            nsimul = nsimul, seed = 1234)
plot(gform_cont_eof)
```

```
plot.gformula_survival
```

Plot method for objects of class "gformula_survival"

Description

This function generates graphs of the mean simulated vs. observed values at each time point of the time-varying covariates, risk, and survival under the natural course. For categorical covariates, the observed and simulated counts of the levels of the factors are plotted at each time point.

Usage

```
## S3 method for class 'gformula_survival'
plot(x, covnames = NULL, risk = TRUE,
    survival = FALSE, ncol = NULL, nrow = NULL, common.legend = TRUE,
    legend = "bottom", xlab = NULL, ylab_cov = NULL,
    ylab_risk = "risk", ylab_surv = "survival", pos_risk = NULL,
    pos_surv = NULL, ci_risk = FALSE, ...)
```

Arguments

Į	guments				
	х	Object of class "gformula_survival".			
	covnames	Vector of character strings specifying the names of the time-varying covariates to be plotted. The ordering of covariates given here is used in the plot grid. Time-varying covariates of type "categorical time" cannot be included. To plot none of the time-varying covariates, set this argument to NA. By default, this argument is set equal to the covnames argument used in gformula_survival, where covariates of type 'categorical time' are removed.			
	risk	Logical scalar indicating whether to include a plot for the risk. The default is TRUE.			
	survival	Logical scalar indicating whether to include a plot for the survival. The default is FALSE.			
	ncol	Number of columns in the plot grid. By default, two columns are used when there is at least two plots.			
	nrow	Number of rows in the plot grid. By default, a maximum of six rows is used and additional plots are included in subsequent pages.			
	common.legend	Logical scalar indicating whether to include a legend. The default is TRUE.			
	legend	Character string specifying the legend position. Valid values are "top", "bottom". "left", "right", and "none". The default is "bottom".			
	xlab	Character string for the x axes of all plots. By default, this argument is set to the time_name argument specified in gformula_survival.			
	ylab_cov	Vector of character strings for the y axes of the plots for the covariates. This argument must be the same length as covnames. The i-th element of this argument corresponds to the plot for the i-th element of covnames.			
	ylab_risk	Character string for the y axis of the plot for the risk (if applicable). The default is "risk".			
	ylab_surv	Character string for the y axis of the plot for the survival (if applicable). The default is "survival".			
	pos_risk	Integer specifying the position at which to order the risk plot (if applicable). By default, this argument is set to the number of plots in the grid minus one (i.e., orders the risk plot second last).			
	pos_surv	Integer specifying the position at which to order the survival plot (if applicable). By default, this argument is set to the number of plots in the grid (i.e., orders the survival plot last).			

ci_risk

Logical scalar specifying whether to include error bars for the 95% confidence intervals of the estimated risk under the natural course. This argument is only effective if the argument nsamples was set to a positive value in gformula_survival. The default is TRUE.

... Other arguments, which are passed to ggarrange.

Value

An object of class "ggarrange". See documentation of ggarrange.

See Also

```
gformula_survival
```

```
## Estimating the effect of static treatment strategies on risk of a
## failure event
id <- 'id'
time_points <- 7
time_name <- 't0'</pre>
covnames <- c('L1', 'L2', 'A')
outcome_name <- 'Y'
covtypes <- c('binary', 'bounded normal', 'binary')</pre>
histories <- c(lagged, lagavg)
histvars <- list(c('A', 'L1', 'L2'), c('L1', 'L2'))
covparams <- list(covmodels = c(L1 ~ lag1_A + lag_cumavg1_L1 + lag_cumavg1_L2 +</pre>
                                    L3 + t0,
                                  L2 \sim lag1_A + L1 + lag\_cumavg1_L1 +
                                    lag_cumavg1_L2 + L3 + t0,
                                  A \sim lag1_A + L1 + L2 + lag_cumavg1_L1 +
                                    lag_cumavg1_L2 + L3 + t0))
ymodel <- Y ~ A + L1 + L2 + L3 + lag1_A + lag1_L1 + lag1_L2 + t0</pre>
intvars <- list('A', 'A')</pre>
interventions <- list(list(c(static, rep(0, time_points))),</pre>
                       list(c(static, rep(1, time_points))))
int_descript <- c('Never treat', 'Always treat')</pre>
nsimul <- 10000
gform_basic <- gformula_survival(obs_data = basicdata_nocomp, id = id,</pre>
                                   time_points = time_points,
                                   time_name = time_name, covnames = covnames,
                                   outcome_name = outcome_name,
                                   covtypes = covtypes,
                                   covparams = covparams, ymodel = ymodel,
                                   intvars = intvars,
                                   interventions = interventions,
                                   int_descript = int_descript,
                                   histories = histories, histvars = histvars,
                                   basecovs = c('L3'), nsimul = nsimul,
                                   seed = 1234)
```

```
plot(gform_basic)
```

```
print.gformula_survival
```

Print and summary methods for "gformula" objects

Description

Print and summary method for objects of class "gformula_survival", "gformula_continuous_eof", or "gformula_binary_eof".

Usage

```
## S3 method for class 'gformula_survival'
print(x, all_times = FALSE,
  coefficients = FALSE, stderrs = FALSE, rmses = FALSE,
 hazardratio = FALSE, fits = FALSE, ...)
## S3 method for class 'gformula_continuous_eof'
print(x, coefficients = FALSE,
  stderrs = FALSE, rmses = FALSE, fits = FALSE, ...)
## S3 method for class 'gformula_binary_eof'
print(x, coefficients = FALSE,
 stderrs = FALSE, rmses = FALSE, fits = FALSE, ...)
## S3 method for class 'gformula'
summary(object, ...)
## S3 method for class 'summary.gformula'
print(x, all_times = TRUE,
 coefficients = FALSE, stderrs = FALSE, rmses = FALSE,
 hazardratio = FALSE, fits = TRUE, ...)
```

Arguments

X	Object of class "gformula_survival", "gformula_continuous_eof", "gformula_binary_eof", or "summary.gformula" (for print).
all_times	Logical scalar indicating whether to print the results for all time points. This argument is only applicable to objects of class "gformula_survival". If this argument is set to FALSE, the results are only shown for the final time point. The default is FALSE for print and TRUE for summary.
coefficients	Logical scalar indicating whether to print the model coefficients. The default is FALSE.

stderrs Logical scalar indicating whether to print the standard error of the model coefficients. The default is FALSE.

rmses Logical scalar indicating whether to print the model root mean square errors

(RMSEs). The default is FALSE.

hazardratio Logical scalar indicating whether to print the hazard ratio between two interven-

tions (if computed). If bootstrapping was used, 95% confidence intervals will be given. This argument is only applicable to objects of class "gformula_survival".

The default is FALSE.

fits Logical scalar indicating whether to print summaries of the fitted models for the

time-varying covariates, outcome, and competing event (if applicable). This argument is only effective if the argument model_fits was set to TRUE in gformula.

The default is FALSE for print and TRUE for summary.

... Other arguments.

object of class "gformula" (for summary).

Value

No value is returned for the print functions. The summary function returns the object passed to it and adds the class "summary.gformula" to it.

See Also

gformula

```
## Estimating the effect of static treatment strategies on risk of a
## failure event
id <- 'id'
time_points <- 7
time_name <- 't0'
covnames <- c('L1', 'L2', 'A')
outcome_name <- 'Y'
outcome_type <- 'survival'</pre>
covtypes <- c('binary', 'bounded normal', 'binary')</pre>
histories <- c(lagged, lagavg)
histvars <- list(c('A', 'L1', 'L2'), c('L1', 'L2'))
covparams <- list(covmodels = c(L1 ~ lag1_A + lag_cumavg1_L1 + lag_cumavg1_L2 +
                                    L3 + t0,
                                  L2 \sim lag1_A + L1 + lag\_cumavg1_L1 +
                                    lag\_cumavg1\_L2 + L3 + t0,
                                  A \sim lag1_A + L1 + L2 + lag_cumavg1_L1 +
                                    lag_cumavg1_L2 + L3 + t0))
ymodel <- Y ~ A + L1 + L2 + L3 + lag1_A + lag1_L1 + lag1_L2 + t0
intvars <- list('A', 'A')</pre>
interventions <- list(list(c(static, rep(0, time_points))),</pre>
                       list(c(static, rep(1, time_points))))
int_descript <- c('Never treat', 'Always treat')</pre>
nsimul <- 10000
```

42 simple_restriction

simple_restriction

Simple Restriction

Description

This function assists the implementation of a restriction on a covariate in the data table newdf by setting lines where the covariate is restricted to a user-specified value.

Usage

```
simple_restriction(newdf, pool, restriction, time_name, t)
```

Arguments

newdf Data table containing the simulated data at time t.

pool Data table containing the simulated data at times before t.

restriction List of vectors. Each vector contains as its first entry the covariate affected by

the restriction; its second entry the condition that must be TRUE for the covariate to be modeled; its third entry a function that executes other specific actions based on the condition (in this case, this function); and its fourth entry some value used by the function (in this case, the value the user desires to assign to the covariate

when it is not modeled).

time_name Character string specifying the name of the time variable in pool and newdf.

t Integer specifying the current time index.

Value

No value is returned. The data table newdf is modified in place.

static 43

```
## Estimating the effect of static treatment strategies on risk of a
## failure event with a simple restriction
id <- 'id'
time_points <- 7</pre>
time_name <- 't0'</pre>
covnames <- c('L1', 'L2', 'A')</pre>
outcome_name <- 'Y'</pre>
covtypes <- c('binary', 'bounded normal', 'binary')</pre>
histories <- c(lagged, lagavg)
histvars <- list(c('A', 'L1', 'L2'), c('L1', 'L2'))
covparams <- list(covmodels = c(L1 ~ lag1_A + lag_cumavg1_L1 + lag_cumavg1_L2 +</pre>
                                    L3 + t0,
                                  L2 \sim lag1\_A + L1 + lag\_cumavg1\_L1 +
                                    lag_cumavg1_L2 + L3 + t0,
                                  A \sim lag1_A + L1 + L2 + lag_cumavg1_L1 +
                                    lag_cumavg1_L2 + L3 + t0)
ymodel \leftarrow Y \sim A + L1 + L2 + L3 + lag1_A + lag1_L1 + lag1_L2 + t0
intvars <- list('A', 'A')</pre>
interventions <- list(list(c(static, rep(0, time_points))),</pre>
                       list(c(static, rep(1, time_points))))
int_descript <- c('Never treat', 'Always treat')</pre>
nsimul <- 10000
# At t0 == 5, assume we have deterministic knowledge that L1 equals 0
restrictions <- list(c('L1', 't0 != 5', simple_restriction, 0))</pre>
gform_basic <- gformula_survival(obs_data = basicdata_nocomp, id = id,</pre>
                                   time_points = time_points,
                                   time_name = time_name, covnames = covnames,
                                   outcome_name = outcome_name,
                                   covtypes = covtypes,
                                   covparams = covparams, ymodel = ymodel,
                                   intvars = intvars,
                                   interventions = interventions,
                                   restrictions = restrictions,
                                   int_descript = int_descript,
                                   histories = histories, histvars = histvars,
                                   basecovs = c('L3'), nsimul = nsimul,
                                   seed = 1234)
gform_basic
```

44 static

Description

This function implements a static intervention (i.e., either constant treatment or no treatment over all time points) for the specified intervention variable in the data table newdf.

Usage

```
static(newdf, pool, intvar, intvals, time_name, t)
```

Arguments

newdf	Data table containing the simulated data at time t .
pool	Data table containing the simulated data at times before t .
intvar	Character string specifying the name of the variable to be intervened on in each round of the simulation.
intvals	A list of length 1. The entry is the value of static treatment to be assigned to intvar.
time_name	Character string specifying the name of the time variable in pool and newdf.
t	Integer specifying the current time index.

Value

No value is returned. The data table newdf is modified in place.

```
## Estimating the effect of static treatment strategies on risk of a
## failure event
id <- 'id'
time_points <- 7
time_name <- 't0'
covnames <- c('L1', 'L2', 'A')
outcome_name <- 'Y'
covtypes <- c('binary', 'bounded normal', 'binary')</pre>
histories <- c(lagged, lagavg)</pre>
histvars <- list(c('A', 'L1', 'L2'), c('L1', 'L2'))
covparams <- list(covmodels = c(L1 ~ lag1_A + lag_cumavg1_L1 + lag_cumavg1_L2 +</pre>
                                    L3 + t0,
                                  L2 \sim lag1_A + L1 + lag\_cumavg1_L1 +
                                    lag_cumavg1_L2 + L3 + t0,
                                  A \sim lag1_A + L1 + L2 + lag_cumavg1_L1 +
                                    lag_cumavg1_L2 + L3 + t0))
ymodel <- Y ~ A + L1 + L2 + L3 + lag1_A + lag1_L1 + lag1_L2 + t0</pre>
intvars <- list('A', 'A')</pre>
interventions <- list(list(c(static, rep(0, time_points))),</pre>
                       list(c(static, rep(1, time_points))))
int_descript <- c('Never treat', 'Always treat')</pre>
nsimul <- 10000
```

threshold 45

threshold

Threshold Intervention

Description

This function implements a threshold intervention (i.e., once treatment bypasses a certain threshold, it remains at that threshold until end of follow-up) for the specified intervention variable in the data table newdf.

Usage

```
threshold(newdf, pool, intvar, intvals, time_name, t)
```

Arguments

newdf	Data table containing the simulated data at time t .
pool	Data table containing the simulated data at times before t .
intvar	Character string specifying the name of the variable to be intervened on in each round of the simulation.
intvals	A list of length 2. The first entry is lower bound of the threshold, and the second entry is the upper bound.
time_name	Character string specifying the name of the time variable in pool and newdf.
t	Integer specifying the current time index.

Value

No value is returned. The data table newdf is modified in place.

46 vcov.gformula

Examples

```
## Estimating the effect of threshold interventions on the mean of a binary
## end of follow-up outcome
id <- 'id_num'</pre>
time_name <- 'time'</pre>
covnames <- c('cov1', 'cov2', 'treat')</pre>
outcome_name <- 'outcome'
histories <- c(lagged, cumavg)</pre>
histvars <- list(c('treat', 'cov1', 'cov2'), c('cov1', 'cov2'))</pre>
covtypes <- c('binary', 'zero-inflated normal', 'normal')</pre>
covparams <- list(covmodels = c(cov1 ~ lag1_treat + lag1_cov1 + lag1_cov2 + cov3 +
                                    time,
                                  cov2 ~ lag1_treat + cov1 + lag1_cov1 + lag1_cov2 +
                                    cov3 + time,
                                  treat ~ lag1_treat + cumavg_cov1 +
                                    cumavg_cov2 + cov3 + time))
ymodel <- outcome ~ treat + cov1 + cov2 + lag1_cov1 + lag1_cov2 + cov3</pre>
intvars <- list('treat', 'treat')</pre>
interventions <- list(list(c(static, rep(0, 7))),</pre>
                       list(c(threshold, 1, Inf)))
int_descript <- c('Never treat', 'Threshold - lower bound 1')</pre>
nsimul <- 10000
ncores <- 2
gform_bin_eof <- gformula_binary_eof(obs_data = binary_eofdata, id = id,</pre>
                                       time_name = time_name,
                                       covnames = covnames,
                                       outcome_name = outcome_name,
                                       covtypes = covtypes,
                                       covparams = covparams,
                                       ymodel = ymodel,
                                       intvars = intvars,
                                       interventions = interventions,
                                       int_descript = int_descript,
                                       histories = histories, histvars = histvars,
                                       basecovs = c("cov3"), seed = 1234,
                                       parallel = TRUE, nsamples = 5,
                                       nsimul = nsimul, ncores = ncores)
gform_bin_eof
```

vcov.gformula

Variance-covariance method for objects of class "gformula"

Description

This function extracts the variance-covariance matrices of the parameters of the fitted models for the time-varying covariates, outcome, and competing event (if applicable).

vcov.gformula 47

Usage

```
## S3 method for class 'gformula'
vcov(object, ...)
```

Arguments

object Object of class "gformula".
... Other arguments.

Value

If bootdiag was set to FALSE in gformula, this function returns a list of the variance-covariance matrices of the parameters of the fitted models to the observed data set. If bootstrapping was used and bootdiag was set to TRUE in gformula, this function returns a list described as follows. The first element (named 'Original sample') is a list of the variance-covariance matrices of the parameters of the fitted models to the observed data set. The kth element (named 'Bootstrap sample k-1') is a list of the variance-covariance matrices of the parameters of the fitted models corresponding to the k-1th bootstrap sample.

See Also

gformula

```
## Estimating the effect of static treatment strategies on risk of a
## failure event
id <- 'id'
time_points <- 7
time_name <- 't0'
covnames <- c('L1', 'L2', 'A')
outcome_name <- 'Y'
outcome_type <- 'survival'</pre>
covtypes <- c('binary', 'bounded normal', 'binary')</pre>
histories <- c(lagged, lagavg)
histvars <- list(c('A', 'L1', 'L2'), c('L1', 'L2'))
covparams <- list(covmodels = c(L1 ~ lag1_A + lag_cumavg1_L1 + lag_cumavg1_L2 +</pre>
                                    L3 + t0,
                                  L2 \sim lag1_A + L1 + lag\_cumavg1_L1 +
                                    lag_cumavg1_L2 + L3 + t0,
                                  A \sim lag1_A + L1 + L2 + lag_cumavg1_L1 +
                                    lag_cumavg1_L2 + L3 + t0))
ymodel \leftarrow Y \sim A + L1 + L2 + L3 + lag1_A + lag1_L1 + lag1_L2 + t0
intvars <- list('A', 'A')</pre>
interventions <- list(list(c(static, rep(0, time_points))),</pre>
                       list(c(static, rep(1, time_points))))
int_descript <- c('Never treat', 'Always treat')</pre>
nsimul <- 10000
gform_basic <- gformula(obs_data = basicdata_nocomp, id = id,</pre>
```

48 vcov.gformula

```
time_points = time_points,
time_name = time_name, covnames = covnames,
outcome_name = outcome_name,
outcome_type = outcome_type, covtypes = covtypes,
covparams = covparams, ymodel = ymodel,
intvars = intvars,
interventions = interventions,
int_descript = int_descript,
histories = histories, histvars = histvars,
basecovs = c('L3'), nsimul = nsimul,
seed = 1234)
```

vcov(gform_basic)

Index

```
*Topic datasets
                                                static, 43
    basicdata, 2
                                                summary.gformula
    basicdata_nocomp, 3
                                                         (print.gformula\_survival), 40
    binary_eofdata, 4
                                                threshold, 45
    continuous_eofdata, 7
    continuous_eofdata_pb, 8
                                                vcov.gformula, 46
basicdata. 2
basicdata_nocomp, 3
binary_eofdata, 4
carry_forward, 4
coef.gformula, 6
continuous_eofdata, 7
continuous_eofdata_pb, 8
cumavg (lagged), 31
gformula, 6, 9, 20, 25, 30, 41, 47
gformula_binary_eof, 16, 34
gformula_continuous_eof, 21, 36
gformula_survival, 26, 38, 39
ggarrange, 34, 36, 39
lagavg (lagged), 31
lagged, 31
plot.gformula_binary_eof, 13, 20, 33
plot.gformula_continuous_eof, 13, 35
plot.gformula_survival, 13, 29, 37
print.gformula_binary_eof, 13, 20
print.gformula_binary_eof
        (print.gformula_survival), 40
print.gformula_continuous_eof, 13, 24
print.gformula_continuous_eof
        (print.gformula_survival), 40
print.gformula_survival, 13, 29, 40
print.summary.gformula
        (print.gformula_survival), 40
setDTthreads, 12, 19, 24, 28
simple_restriction, 42
```