# Package 'gfoRmula'

October 1, 2024

<a href="https://doi:10.1016/0270-0255(86)90088-6">doi:10.1016/0270-0255(86)90088-6</a>, Hernán and Robins (2024, ISBN:9781420076165)).

**Description** Implements the non-iterative conditional expectation (NICE)

The g-formula can estimate an outcome's counterfactual mean or risk under hypothetical treatment strategies (interventions) when there is sufficient

algorithm of the g-formula algorithm (Robins (1986)

Title Parametric G-Formula

NeedsCompilation no

Version 1.1.0

information on time-varying treatments and confounders. This package can be used for discrete or continuous time-varying treatments and for failure time outcomes or continuous/binary end of follow-up outcomes. The package can handle a random measurement/visit process and a priori knowledge of the data structure, as well as censoring (e.g., by loss to follow-up) and two options for handling competing events for failure time outcomes. Interventions can be flexibly specified, both as interventions on a single treatment or as joint interventions on multiple treatments. See McGrath et al. (2020) <doi:10.1016/j.patter.2020.100008> for a guide on how to use the package. **Depends** R (>= 3.5.0) License GPL-3 **Encoding** UTF-8 LazyData true RoxygenNote 7.3.2 Imports data.table, ggplot2, ggpubr, grDevices, nnet, parallel, progress, stats, stringr, survival, truncnorm, truncreg, utils **Suggests** Hmisc, knitr, randomForest, rmarkdown, testthat (>= 3.0.0) VignetteBuilder knitr URL https://github.com/CausalInference/gfoRmula, https://doi.org/10.1016/j.patter.2020.100008 BugReports https://github.com/CausalInference/gfoRmula/issues Config/testthat/edition 3

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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

#### **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

4 binary\_eofdata

## **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.

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 5

## **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, int_visit_type, intvar)
```

## **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, 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.
int_visit_type	Logical scalar specifying whether to carry forward the intervened value (rather than the natural value) of the treatment variables(s) when performing a carry forward restriction type
intvar	A vector specifying the name(s) of the variable(s) to be intervened on.

#### Value

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

# **Examples**

```
## 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'
covtypes <- c('binary', 'bounded normal', 'binary')</pre>
```

6 censor\_data

```
histories <- c(lagged, lagavg)</pre>
histvars <- list(c('A', 'L1', 'L2'), c('L1', 'L2'))
covparams <- list(covmodels = c(L1 \sim lag_LA + lag_cumavg1_L1 + lag_cumavg1_L2 + lag_cumavg1_L2 + lag_cumavg1_L3 + lag_cumav
                                                                                              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
intervention1.A <- list(static, rep(0, time_points))</pre>
intervention2.A <- list(static, rep(1, time_points))</pre>
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))</pre>
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,
                                                                   intervention1.A = intervention1.A,
                                                                    intervention2.A = intervention2.A,
                                                                   int_descript = int_descript,
                                                                   restrictions = restrictions,
                                                                   histories = histories, histvars = histvars,
                                                                   basecovs = c('L3'), nsimul = nsimul,
                                                                   seed = 1234)
gform_basic
```

censor\_data

Example Dataset for a Survival Outcome with an Indicator of Censoring Variable

# Description

A dataset consisting of 118,725 observations on 20,000 individuals over 10 time points. Each row in the dataset corresponds to the record of one individual at one time point.

#### **Usage**

censor\_data

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## **Format**

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

- t0 Time index.
- id Unique identifier for each individual.
- L Binary time-varying covariate.
- A Continuous treatment variable.
- C Censoring indicator.
- Y Outcome of interest; time-varying indicator of failure.

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 <code>gformula</code>, 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 <code>gformula</code>, 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
```

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## **Examples**

```
## 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
intervention1.A <- list(static, rep(0, time_points))</pre>
intervention2.A <- list(static, rep(1, time_points))</pre>
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,
                         intervention1.A = intervention1.A,
                         intervention2.A = intervention2.A,
                         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.

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## 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.

## 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:

- 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.

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 McGrath et al. (2020) 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,
  ymodel_fit_custom = NULL,
  ymodel_predict_custom = NULL,
  compevent_name = NULL,
  compevent_model = NA,
  compevent_cens = FALSE,
  censor_name = NULL,
  censor\_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,
  ipw_cutoff_quantile = NULL,
  ipw_cutoff_value = NULL,
  int_visit_type = NULL,
  sim_trunc = TRUE,
)
```

#### **Arguments**

obs\_data Data table containing the observed data.

id Character string specifying the name of the ID variable in obs\_data.

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 plus 1.

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 accurage. The default is NA.

not be included in covnames. The default is NA.

outcome\_name Character string specifying the name of the outcome variable in obs\_data.

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

"survival", "continuous\_eof", and "binary\_eof".

ymodel Model statement for the outcome variable.

ymodel\_fit\_custom

Function specifying a custom outcome model. See the vignette "Using Custom Outcome Models in gfoRmula" for details. The default is NULL.

ymodel\_predict\_custom

Function obtaining predictions from the custom outcome model specified in ymodel\_fit\_custom. See the vignette "Using Custom Outcome Models in gfoRmula" for details. The default is NULL.

compevent\_name Character string specifying the name of the competing event variable in obs\_data.

Only applicable for survival outcomes.

compevent\_model

Model statement for the competing event variable. The default is NA. Only applicable for survival outcomes.

compevent\_cens Logical scalar indicating whether to treat competing events as censoring events.

This argument is only applicable for survival outcomes and when a competing even model is supplied (i.e., compevent\_name and compevent\_model are specified). If this argument is set to TRUE, the competing event model will only be used to construct inverse probability weights to estimate the natural course means / risk from the observed data. If this argument is set to FALSE, the competing event model will be used in the parametric g-formula estimates of the risk and will not be used to construct inverse probability weights. See "Details". The

default is FALSE.

censor\_name Character string specifying the name of the censoring variable in obs\_data.

Only applicable when using inverse probability weights to estimate the natural

course means / risk from the observed data. See "Details".

censor\_model Model statement for the censoring variable. Only applicable when using inverse

probability weights to estimate the natural course means  $\slash$  risk from the observed

data. See "Details".

intvars (Deprecated. See the ... argument) List, whose elements are vectors of char-

acter 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

(Deprecated. See the ... argument) 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

(Deprecated. See the ... argument) 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 specified interventions (see the . . . argument).

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 (see the . . . argument). The default is 0.

intcomp

List of two numbers indicating a pair of interventions to be compared by a hazard 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 contains 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 contains 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. Number of subjects for whom to simulate data. By default, this argument is set nsimul 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. Integer specifying the number of bootstrap samples to generate. The default is nsamples parallel Logical scalar indicating whether to parallelize simulations of different interventions to multiple cores. Integer specifying the number of CPU cores to use in parallel simulation. This ncores 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". Integer specifying the number of threads to be used in data.table. See setDTthreads threads 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 parametric g-formula estimates as well as 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. ipw\_cutoff\_quantile Percentile by which to truncate inverse probability weights. The default is NULL (i.e., no truncation). See "Details". ipw\_cutoff\_value Cutoff value by which to truncate inverse probability weights. The default is NULL (i.e., no truncation). See "Details". int\_visit\_type Vector of logicals. The kth element is a logical specifying whether to carry forward the intervened value (rather than the natural value) of the treatment variables(s) when performing a carry forward restriction type for the kth intervention in interventions. When the kth element is set to FALSE, the natural value of the treatment variable(s) in the kth intervention in interventions will be carried forward. By default, this argument is set so that the intervened value of the treatment variable(s) is carried forward for all interventions. sim\_trunc Logical scalar indicating whether to truncate simulated covariates to their range in the observed data set. This argument is only applicable for covariates of type "normal", "bounded normal", "truncated normal", and "zero-inflated normal".

The default is TRUE.

Other arguments, including (a) those that specify the interventions and (b) those that are passed to the functions in covpredict\_custom. To specify interventions, users can supply arguments with the following naming requirements

- Each intervention argument begins with a prefix of intervention.
- After the prefix, the intervention number is specified and followed by a period.
- After the period, the treatment variable name is specified.

Each intervention argument takes as input a list with the following elements:

- The first element specifies the intervention function.
- The subsequent elements specify any intervention values.
- (Optional) The named element int\_times specifies the time points to apply the intervention. By default, all interventions are applied at all time points.

For example, an "always treat" intervention on A is given by intervention1.A = list(static, rep(1, time\_points))
See the vignette "A Simplified Approach for Specifying Interventions in gfoR-mula" and "Examples" section for more examples.

#### **Details**

. . .

To assess model misspecification in the parametric g-formula, users can obtain inverse probability (IP) weighted estimates of the natural course risk and/or means of the time-varying covariates from the observed data. See Chiu et al. (2023) for details. In addition to the general requirements described in McGrath et al. (2020), the requirements for the input data set and the call to the gformula function for such analyses are described below.

Users need to include a column in obs\_data with a time-varying censoring variable. Users need to indicate the name of the censoring variable and a model statement for the censoring variable with parameters censor\_name and censor\_model, respectively. When competing events are present, users need to include a column in obs\_data with a time-varying indicator of the competing event variable and need to indicate the name of the competing event variable and the corresponding model statement with parameters compevent\_name and compevent\_model, respectively. Users need to indicate whether to treat competing events as censoring events with the compevent\_cens parameter. Finally, users can specify how to truncate IP weights with the ipw\_cutoff\_quantile or ipw\_cutoff\_value parameters.

In addition to the package output described in McGrath et al. (2020), the output will display estimates of the "cumulative percent intervened on" and the "average percent intervened on". When using a custom intervention function, users need to specify whether each individual at that time point is eligible to contribute person-time to the percent intervened on calculations. Specifically, this must be specified in the eligible\_pt column of newdf. By default, eligible\_pt is set to TRUE for each individual at each time point in custom interventions.

## Value

An object of class "gformula\_survival" (for survival outcomes), "gformula\_continuous\_eof" (for continuous end-of-follow-up outcomes), or "gformula\_binary\_eof" (for binary end-of-follow-up outcomes). 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. For all outcome types, this also contains the "cumulative percent intervened on" and the "average percent intervened on". 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.

IP\_weights A numeric vector specifying the inverse probability weights. See "Details".

bootests A data table containing the bootstrap replicates of the parametric g-formula es-

timates. If boot\_diag is set to FALSE, a value of NULL is given.

bootcoeffs 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.

bootvoovs 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

Chiu YH, Wen L, McGrath S, Logan R, Dahabreh IJ, Hernán MA. Evaluating model specification when using the parametric g-formula in the presence of censoring. American Journal of Epidemiology. 2023;192:1887–1895.

McGrath S, Lin V, Zhang Z, Petito LC, Logan RW, Hernán MA, and JG Young. gfoRmula: An R package for estimating the effects of sustained treatment strategies via the parametric g-formula. Patterns. 2020;1:100008.

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.].

# **Examples**

```
## 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 <- Y ~ A + L1 + L2 + L3 + lag1_A + lag1_L1 + lag1_L2 + t0</pre>
intervention1.A <- list(static, rep(0, time_points))</pre>
intervention2.A <- list(static, rep(1, time_points))</pre>
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,
                         intervention1.A = intervention1.A,
                         intervention2.A = intervention2.A,
                         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) 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)))  $ymodel \leftarrow Y \sim A + L1 + L2 + lag1_A + lag1_L1 + lag1_L2 + L3 + as.factor(t0)$  $compevent\_model <- D ~A + L1 + L2 + lag1\_A + lag1\_L1 + lag1\_L2 + L3 + as.factor(t0)$ intervention1.A <- list(static, rep(0, time\_points))</pre> intervention2.A <- list(static, rep(1, time\_points))</pre> 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, intervention1.A = intervention1.A, intervention2.A = intervention2.A, 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)</pre>
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
intervention1.A <- list(static, rep(0, 7))</pre>
intervention2.A <- list(static, rep(1, 7))</pre>
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,
                             intervention1.A = intervention1.A,
                             intervention2.A = intervention2.A,
                             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')</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 +</pre>
                                    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>
intervention1.treat <- list(static, rep(0, 7))</pre>
intervention2.treat <- list(threshold, 1, Inf)</pre>
```

```
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,
                           intervention1.treat = intervention1.treat,
                           intervention2.treat = intervention2.treat,
                           int_descript = int_descript, histories = histories,
                           histvars = histvars, basecovs = c("cov3"),
                           seed = 1234, parallel = TRUE, nsamples = 5,
                           nsimul = nsimul, ncores = ncores)
gform_bin_eof
## Using IP weighting to estimate natural course risk
## Only the natural course intervention is included for simplicity
covnames <- c('L', 'A')
histories <- c(lagged)
histvars <- list(c('A', 'L'))
ymodel <- Y \sim L + A
covtypes <- c('binary', 'normal')</pre>
covparams <- list(covmodels = c(L \sim lag1_L + lag1_A),
                                 A \sim lag1_L + L + lag1_A))
censor_name <- 'C'</pre>
censor_model <- C ~ L
res_censor <- gformula(obs_data = censor_data, id = 'id',
                        time_name = 't0', covnames = covnames,
                        outcome_name = 'Y', outcome_type = 'survival',
                        censor_name = censor_name, censor_model = censor_model,
                        covtypes = covtypes,
                        covparams = covparams, ymodel = ymodel,
                        histories = histories, histvars = histvars,
                        seed = 1234)
plot(res_censor)
```

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-offollow-up under multiple user-specified interventions using the parametric g-formula. See McGrath et al. (2020) for further details concerning the application and implementation of the parametric g-formula.

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# Usage

```
gformula_binary_eof(
 obs_data,
  id,
  time_name,
  covnames,
  covtypes,
  covparams,
  covfits_custom = NA,
  covpredict_custom = NA,
 histvars = NULL,
 histories = NA,
 basecovs = NA,
  censor_name = NULL,
  censor_model = NA,
 outcome_name,
  ymodel,
 ymodel_fit_custom = NULL,
 ymodel_predict_custom = NULL,
  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,
  ipw_cutoff_quantile = NULL,
  ipw_cutoff_value = NULL,
  int_visit_type = NULL,
  sim_trunc = TRUE,
)
```

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#### **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.

censor\_name Character string specifying the name of the censoring variable in obs\_data.

Only applicable when using inverse probability weights to estimate the natural

course means / risk from the observed data. See "Details".

censor\_model Model statement for the censoring variable. Only applicable when using inverse

probability weights to estimate the natural course means / risk from the observed  $\,$ 

data. See "Details".

outcome\_name Character string specifying the name of the outcome variable in obs\_data.

ymodel Model statement for the outcome variable.

ymodel\_fit\_custom

Function specifying a custom outcome model. See the vignette "Using Custom Outcome Models in gfoRmula" for details. The default is NULL.

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ymodel\_predict\_custom

Function obtaining predictions from the custom outcome model specified in ymodel\_fit\_custom. See the vignette "Using Custom Outcome Models in gfoRmula" for details. The default is NULL.

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intvars

(Deprecated. See the ... argument) 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

(Deprecated. See the ... argument) 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

(Deprecated. See the ... argument) 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 specified interventions (see the . . . argument).

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 contains 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

nsimul

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.

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.

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 parametric g-formula estimates as

well as 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 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.

ipw\_cutoff\_quantile

Percentile by which to truncate inverse probability weights. The default is NULL

(i.e., no truncation). See "Details".

ipw\_cutoff\_value

Cutoff value by which to truncate inverse probability weights. The default is

NULL (i.e., no truncation). See "Details".

int\_visit\_type Vector of logicals. The kth element is a logical specifying whether to carry

forward the intervened value (rather than the natural value) of the treatment variables(s) when performing a carry forward restriction type for the kth intervention in interventions. When the kth element is set to FALSE, the natural value of the treatment variable(s) in the kth intervention in interventions will be carried forward. By default, this argument is set so that the intervened value

of the treatment variable(s) is carried forward for all interventions.

sim\_trunc Logical scalar indicating whether to truncate simulated covariates to their range

in the observed data set. This argument is only applicable for covariates of type "normal", "bounded normal", "truncated normal", and "zero-inflated normal".

The default is TRUE.

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• • •

Other arguments, including (a) those that specify the interventions and (b) those that are passed to the functions in covpredict\_custom. To specify interventions, users can supply arguments with the following naming requirements

- Each intervention argument begins with a prefix of intervention.
- After the prefix, the intervention number is specified and followed by a period.
- After the period, the treatment variable name is specified.

Each intervention argument takes as input a list with the following elements:

- The first element specifies the intervention function.
- The subsequent elements specify any intervention values.
- (Optional) The named element int\_times specifies the time points to apply the intervention. By default, all interventions are applied at all time points.

For example, an "always treat" intervention on A is given by intervention1.A = list(static, rep(1, time\_points))

See the vignette "A Simplified Approach for Specifying Interventions in gfoR-mula" and "Examples" section for more examples.

#### **Details**

To assess model misspecification in the parametric g-formula, users can obtain inverse probability (IP) weighted estimates of the natural course means of the time-varying covariates from the observed data. See Chiu et al. (2023) for details. In addition to the general requirements described in McGrath et al. (2020), the requirements for the input data set and the call to the gformula function for such analyses are described below.

Users need to include a column in obs\_data with a time-varying censoring variable. Users need to indicate the name of the censoring variable and a model statement for the censoring variable with parameters censor\_name and censor\_model, respectively. Finally, users can specify how to truncate IP weights with the ipw\_cutoff\_quantile or ipw\_cutoff\_value parameters.

In addition to the package output described in McGrath et al. (2020), the output will display estimates of the "cumulative percent intervened on" and the "average percent intervened on". When using a custom intervention function, users need to specify whether each individual at that time point is eligible to contribute person-time to the percent intervened on calculations. Specifically, this must be specified in the eligible\_pt column of newdf. By default, eligible\_pt is set to TRUE for each individual at each time point in custom interventions.

# Value

An object of class "gformula\_binary\_eof". The object is a list with the following components:

Results table containing the estimated outcome probability for all interventions (inculding natural course) at the last time point as well as the "cumulative percent intervened on" and the "average percent intervened on". 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.
IP_weights	A numeric vector specifying the inverse probability weights. See "Details".
bootests	A data.table containing the bootstrap replicates of the parametric g-formula estimates. If boot_diag is set to FALSE, a value of NULL is given.
bootcoeffs	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 coefficients 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

Chiu YH, Wen L, McGrath S, Logan R, Dahabreh IJ, Hernán MA. Evaluating model specification when using the parametric g-formula in the presence of censoring. American Journal of Epidemiology. 2023;192:1887–1895.

McGrath S, Lin V, Zhang Z, Petito LC, Logan RW, Hernán MA, and JG Young. gfoRmula: An R package for estimating the effects of sustained treatment strategies via the parametric g-formula. Patterns. 2020;1:100008.

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

## **Examples**

```
## Estimating the effect of threshold interventions on the mean of a binary
## end of follow-up outcome
id <- 'id num'
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 +</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>
intervention1.treat <- list(static, rep(0, 7))</pre>
intervention2.treat <- list(threshold, 1, Inf)</pre>
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,
                                       intervention1.treat = intervention1.treat,
                                       intervention2.treat = intervention2.treat,
                                       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-followup under multiple user-specified interventions using the parametric g-formula. See McGrath et al. (2020) 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,
 ymodel_fit_custom = NULL,
  ymodel_predict_custom = NULL,
  censor_name = NULL,
  censor_model = NA,
  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,
  ipw_cutoff_quantile = NULL,
  ipw_cutoff_value = NULL,
  int_visit_type = NULL,
  sim_trunc = 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.

ymodel\_fit\_custom

Function specifying a custom outcome model. See the vignette "Using Custom

Outcome Models in gfoRmula" for details. The default is NULL.

ymodel\_predict\_custom

Function obtaining predictions from the custom outcome model specified in ymodel\_fit\_custom. See the vignette "Using Custom Outcome Models in

gfoRmula" for details. The default is NULL.

censor\_name Character string specifying the name of the censoring variable in obs\_data.

Only applicable when using inverse probability weights to estimate the natural

course means / risk from the observed data. See "Details".

censor\_model Model statement for the censoring variable. Only applicable when using inverse

probability weights to estimate the natural course means / risk from the observed  $\,$ 

data. See "Details".

intvars (Deprecated. See the ... argument) List, whose elements are vectors of char-

acter 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 (Deprecated. See the ... argument) 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 on a single variable, optionally followed by one or more "intervention on a single variable, optionally followed by one or more "intervention on the relevant variables in intervention on the relevant variables in intervention on the relevant variables."

tion values" (i.e., integers used to specify the treatment regime).

int\_times (Deprecated. See the ... argument) 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 specified interventions (see the . . . argument).

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,

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.

while subsequent integers denote user-specified interventions in the order that

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 contains 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. Logical scalar indicating whether to return the simulated data set. If bootstrap sim\_data\_b 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. Starting seed for simulations and bootstrapping. seed nsamples Integer specifying the number of bootstrap samples to generate. The default is Logical scalar indicating whether to parallelize simulations of different interparallel 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% 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. Logical scalar indicating whether to return the parametric g-formula estimates as boot\_diag well as 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 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.

ipw\_cutoff\_quantile

Percentile by which to truncate inverse probability weights. The default is NULL (i.e., no truncation). See "Details".

ipw\_cutoff\_value

Cutoff value by which to truncate inverse probability weights. The default is NULL (i.e., no truncation). See "Details".

int\_visit\_type Vector of logicals. The kth element is a logical specifying whether to carry forward the intervened value (rather than the natural value) of the treatment variables(s) when performing a carry forward restriction type for the kth intervention in interventions. When the kth element is set to FALSE, the natural value of the treatment variable(s) in the kth intervention in interventions will be carried forward. By default, this argument is set so that the intervened value of the treatment variable(s) is carried forward for all interventions.

sim\_trunc

Logical scalar indicating whether to truncate simulated covariates to their range in the observed data set. This argument is only applicable for covariates of type "normal", "bounded normal", "truncated normal", and "zero-inflated normal". The default is TRUE.

... Other arguments, including (a) those that specify the interventions and (b) those that are passed to the functions in covpredict\_custom. To specify interventions, users can supply arguments with the following naming requirements

- Each intervention argument begins with a prefix of intervention.
- After the prefix, the intervention number is specified and followed by a period.
- After the period, the treatment variable name is specified.

Each intervention argument takes as input a list with the following elements:

- The first element specifies the intervention function.
- The subsequent elements specify any intervention values.
- (Optional) The named element int\_times specifies the time points to apply the intervention. By default, all interventions are applied at all time points.

For example, an "always treat" intervention on A is given by intervention1.A = list(static, rep(1, time\_points))

See the vignette "A Simplified Approach for Specifying Interventions in gfoR-mula" and "Examples" section for more examples.

#### **Details**

To assess model misspecification in the parametric g-formula, users can obtain inverse probability (IP) weighted estimates of the natural course means of the time-varying covariates from the observed data. See Chiu et al. (2023) for details. In addition to the general requirements described in McGrath et al. (2020), the requirements for the input data set and the call to the gformula function for such analyses are described below.

Users need to include a column in obs\_data with a time-varying censoring variable. Users need to indicate the name of the censoring variable and a model statement for the censoring variable with parameters censor\_name and censor\_model, respectively. Finally, users can specify how to truncate IP weights with the ipw\_cutoff\_quantile or ipw\_cutoff\_value parameters.

In addition to the package output described in McGrath et al. (2020), the output will display estimates of the "cumulative percent intervened on" and the "average percent intervened on". When using a custom intervention function, users need to specify whether each individual at that time point is eligible to contribute person-time to the percent intervened on calculations. Specifically, this must be specified in the eligible\_pt column of newdf. By default, eligible\_pt is set to TRUE for each individual at each time point in custom interventions.

#### Value

An object of class "gformula\_continuous\_eof". The object is a list with the following components:

Results table containing the estimated mean outcome for all interventions (inculding natural course) at the last time point as well as the "cumulative percent intervened on" and the "average percent intervened on". 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.
IP_weights	A numeric vector specifying the inverse probability weights. See "Details".
bootests	A data.table containing the bootstrap replicates of the parametric g-formula estimates. If boot_diag is set to FALSE, a value of NULL is given.
bootcoeffs	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 coefficients 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

Chiu YH, Wen L, McGrath S, Logan R, Dahabreh IJ, Hernán MA. Evaluating model specification when using the parametric g-formula in the presence of censoring. American Journal of Epidemiology. 2023;192:1887–1895.

McGrath S, Lin V, Zhang Z, Petito LC, Logan RW, Hernán MA, and JG Young. gfoRmula: An R package for estimating the effects of sustained treatment strategies via the parametric g-formula. Patterns. 2020;1:100008.

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

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## **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'
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 ~ 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 \leftarrow Y \sim A + L1 + L2 + lag1_A + lag1_L1 + lag1_L2 + L3
intervention1.A <- list(static, rep(0, 7))</pre>
intervention2.A <- list(static, rep(1, 7))</pre>
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,
                                            intervention1.A = intervention1.A,
                                            intervention2.A = intervention2.A,
                                            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 McGrath et al. (2020) for further details concerning the application and implementation of the parametric g-formula.

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# 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,
  ymodel_fit_custom = NULL,
  ymodel_predict_custom = NULL,
  compevent_name = NULL,
  compevent_model = NA,
  compevent_cens = FALSE,
  censor_name = NULL,
  censor_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,
  ipw_cutoff_quantile = NULL,
  ipw_cutoff_value = NULL,
  int_visit_type = NULL,
```

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```
sim_trunc = TRUE,
...
)
```

#### **Arguments**

obs\_data Data table containing the observed data.

id Character string specifying the name of the ID variable in obs\_data.

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 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.

ymodel\_fit\_custom

Function specifying a custom outcome model. See the vignette "Using Custom Outcome Models in gfoRmula" for details. The default is NULL.

ymodel\_predict\_custom

Function obtaining predictions from the custom outcome model specified in ymodel\_fit\_custom. See the vignette "Using Custom Outcome Models in gfoRmula" for details. The default is NULL.

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.

compevent\_cens Logical scalar indicating whether to treat competing events as censoring events.

This argument is only applicable for survival outcomes and when a competing even model is supplied (i.e., compevent\_name and compevent\_model are specified). If this argument is set to TRUE, the competing event model will only be used to construct inverse probability weights to estimate the natural course means / risk from the observed data. If this argument is set to FALSE, the competing event model will be used in the parametric g-formula estimates of the risk and will not be used to construct inverse probability weights. See "Details". The

default is FALSE.

censor\_name Character string specifying the name of the censoring variable in obs\_data.

Only applicable when using inverse probability weights to estimate the natural

course means / risk from the observed data. See "Details".

censor\_model Model statement for the censoring variable. Only applicable when using inverse

probability weights to estimate the natural course means / risk from the observed

data. See "Details".

intvars  $\hspace{1cm}$  (Deprecated. See the ... argument) List, whose elements are vectors of char-

acter 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 (Deprecated. See the ... argument) 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 "interven-

tion values" (i.e., integers used to specify the treatment regime).

int\_times (Deprecated. See the ... argument) 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 specified interventions (see the . . . argument).

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 contains 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 contains 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".

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

threads

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 parametric g-formula estimates as well as 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.

ipw\_cutoff\_quantile

Percentile by which to truncate inverse probability weights. The default is NULL (i.e., no truncation). See "Details".

ipw\_cutoff\_value

Cutoff value by which to truncate inverse probability weights. The default is NULL (i.e., no truncation). See "Details".

int\_visit\_type Vector of logicals. The kth element is a logical specifying whether to carry forward the intervened value (rather than the natural value) of the treatment variables(s) when performing a carry forward restriction type for the kth intervention in interventions. When the kth element is set to FALSE, the natural value of the treatment variable(s) in the kth intervention in interventions will be carried forward. By default, this argument is set so that the intervened value of the treatment variable(s) is carried forward for all interventions.

sim\_trunc

Logical scalar indicating whether to truncate simulated covariates to their range in the observed data set. This argument is only applicable for covariates of type "normal", "bounded normal", "truncated normal", and "zero-inflated normal". The default is TRUE.

Other arguments, including (a) those that specify the interventions and (b) those that are passed to the functions in covpredict\_custom. To specify interventions, users can supply arguments with the following naming requirements

- Each intervention argument begins with a prefix of intervention.
- After the prefix, the intervention number is specified and followed by a period.
- After the period, the treatment variable name is specified.

Each intervention argument takes as input a list with the following elements:

- The first element specifies the intervention function.
- The subsequent elements specify any intervention values.
- (Optional) The named element int\_times specifies the time points to apply the intervention. By default, all interventions are applied at all time points.

For example, an "always treat" intervention on A is given by intervention1.A = list(static, rep(1, time\_points)) See the vignette "A Simplified Approach for Specifying Interventions in gfoRmula" and "Examples" section for more examples.

#### **Details**

To assess model misspecification in the parametric g-formula, users can obtain inverse probability (IP) weighted estimates of the natural course risk and/or means of the time-varying covariates from the observed data. See Chiu et al. (2023) for details. In addition to the general requirements described in McGrath et al. (2020), the requirements for the input data set and the call to the gformula function for such analyses are described below.

Users need to include a column in obs\_data with a time-varying censoring variable. Users need to indicate the name of the censoring variable and a model statement for the censoring variable with parameters censor\_name and censor\_model, respectively. When competing events are present, users need to include a column in obs\_data with a time-varying indicator of the competing event variable and need to indicate the name of the competing event variable and the corresponding model statement with parameters compevent\_name and compevent\_model, respectively. Users need to indicate whether to treat competing events as censoring events with the compevent\_cens parameter. Finally, users can specify how to truncate IP weights with the ipw\_cutoff\_quantile or ipw\_cutoff\_value parameters.

In addition to the package output described in McGrath et al. (2020), the output will display estimates of the "cumulative percent intervened on" and the "average percent intervened on". When using a custom intervention function, users need to specify whether each individual at that time point is eligible to contribute person-time to the percent intervened on calculations. Specifically, this must be specified in the eligible\_pt column of newdf. By default, eligible\_pt is set to TRUE for each individual at each time point in custom interventions.

#### 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 (in-

culding the natural course) at each time point as well as the "cumulative percent intervened on" and the "average percent intervened on". 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.

IP\_weights A numeric vector specifying the inverse probability weights. See "Details".

bootests A data.table containing the bootstrap replicates of the parametric g-formula es-

timates. If boot\_diag is set to FALSE, a value of NULL is given.

bootcoeffs 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.

bootvoovs 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

Chiu YH, Wen L, McGrath S, Logan R, Dahabreh IJ, Hernán MA. Evaluating model specification when using the parametric g-formula in the presence of censoring. American Journal of Epidemiology. 2023;192:1887–1895.

McGrath S, Lin V, Zhang Z, Petito LC, Logan RW, Hernán MA, and JG Young. gfoRmula: An R package for estimating the effects of sustained treatment strategies via the parametric g-formula. Patterns. 2020;1:100008.

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

```
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 \sim A + L1 + L2 + L3 + lag1_A + lag1_L1 + lag1_L2 + t0
intervention1.A <- list(static, rep(0, time_points))</pre>
intervention2.A <- list(static, rep(1, time_points))</pre>
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,
                                   intervention1.A = intervention1.A,
                                   intervention2.A = intervention2.A,
                                   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')</pre>
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 < - Y \sim A + L1 + L2 + lag1_A + lag1_L1 + lag1_L2 + L3 + as.factor(t0)
compevent\_model <- D ~A + L1 + L2 + lag1\_A + lag1\_L1 + lag1\_L2 + L3 + as.factor(t0)
intervention1.A <- list(static, rep(0, time_points))</pre>
intervention2.A <- list(static, rep(1, time_points))</pre>
int_descript <- c('Never treat', 'Always treat')</pre>
nsimul <- 10000
gform_basic <- gformula_survival(obs_data = basicdata, id = id,</pre>
```

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```
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,
                                  intervention1.A = intervention1.A,
                                  intervention2.A = intervention2.A,
                                  int_descript = int_descript,
                                  histories = histories, histvars = histvars,
                                  basecovs = c('L3'), nsimul = nsimul,
                                  seed = 1234)
gform_basic
## Using IP weighting to estimate natural course risk
## Only the natural course intervention is included for simplicity
covnames <- c('L', 'A')
histories <- c(lagged)</pre>
histvars <- list(c('A', 'L'))
ymodel \leftarrow Y \sim L + A
covtypes <- c('binary', 'normal')</pre>
covparams <- list(covmodels = c(L \sim lag1_L + lag1_A),
                                 A \sim lag1_L + L + lag1_A))
censor_name <- 'C'
censor_model <- C ~ L
res_censor <- gformula(obs_data = censor_data, id = 'id',
                        time_name = 't0', covnames = covnames,
                        outcome_name = 'Y', outcome_type = 'survival',
                        censor_name = censor_name, censor_model = censor_model,
                        covtypes = covtypes,
                        covparams = covparams, ymodel = ymodel,
                        intvars = NULL, interventions = NULL, int_descript = NULL,
                        histories = histories, histvars = histvars,
                        seed = 1234)
plot(res_censor)
```

lagged

History functions

#### **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.

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#### 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

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.

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#### **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'
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 <- Y ~ A + L1 + L2 + L3 + lag1_A + lag1_L1 + lag1_L2 + t0</pre>
intervention1.A <- list(static, rep(0, time_points))</pre>
intervention2.A <- list(static, rep(1, time_points))</pre>
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,
                         intervention1.A = intervention1.A,
                         intervention2.A = intervention2.A,
                         int_descript = int_descript,
                         histories = histories, histvars = histvars,
                         basecovs = c('L3'), nsimul = nsimul,
                         seed = 1234)
gform_basic
```

```
plot.gformula_binary_eof

Plot method for objects of class "gformula_binary_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 probability of each level are plotted at each time point.

## Usage

```
## $3 method for class 'gformula_binary_eof'
plot(
    x,
    covnames = NULL,
    nrow = NULL,
    rrow = NULL,
    common.legend = TRUE,
    legend = "bottom",
    xlab = NULL,
    ylab_cov = NULL,
    ...
)
```

## **Arguments**

Х	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
outcome_type <- 'binary_eof'</pre>
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 +</pre>
                                    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>
intervention1.treat <- list(static, rep(0, 7))</pre>
intervention2.treat <- list(threshold, 1, Inf)</pre>
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,
                            intervention1.treat = intervention1.treat,
                            intervention2.treat = intervention2.treat,
                            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)
```

```
plot.gformula_continuous_eof
```

Plot method for objects of class "gformula\_continuous\_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 probability of each level are plotted at each time point.

## Usage

```
## $3 method for class 'gformula_continuous_eof'
plot(
    x,
    covnames = NULL,
    nrow = NULL,
    nrow = NULL,
    common.legend = TRUE,
    legend = "bottom",
    xlab = NULL,
    ylab_cov = NULL,
    ...
)
```

# **Arguments**

Х	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	Character string for the x axes of all plots. By default, this argument is set to the time_name argument specified in gformula_continuous_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\_continuous\_eof

```
## 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 ~ A + L1 + L2 + lag1_A + lag1_L1 + lag1_L2 + L3</pre>
intervention1.A <- list(static, rep(0, 7))</pre>
intervention2.A <- list(static, rep(1, 7))</pre>
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,
                            intervention1.A = intervention1.A,
                            intervention2.A = intervention2.A,
                            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 probability of each level are plotted at each time point.

# Usage

```
## S3 method for class 'gformula_survival'
plot(
 х,
  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**

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 $\ensuremath{TRUE}$ .
survival	Logical scalar indicating whether to include a plot for the survival. The default is FALSE.

plot.gformula\_survival

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'
covnames <- c('L1', 'L2', 'A')
outcome_name <- 'Y'</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(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
intervention1.A <- list(static, rep(0, time_points))</pre>
intervention2.A <- list(static, rep(1, time_points))</pre>
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,
                         intervention1.A = intervention1.A,
                         intervention2.A = intervention2.A,
                         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

```
## $3 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(
  Х,
  coefficients = FALSE,
  stderrs = FALSE,
  rmses = FALSE,
 fits = FALSE,
)
## S3 method for class 'gformula_binary_eof'
print(
  Х,
  coefficients = FALSE,
  stderrs = FALSE,
  rmses = FALSE,
  fits = FALSE,
)
## S3 method for class 'gformula'
summary(object, ...)
## S3 method for class 'summary.gformula'
print(
  Х,
  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 ar-

gument 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 coeffi-

cients. 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))
vmodel \leftarrow Y \sim A + L1 + L2 + L3 + lag1\_A + lag1\_L1 + lag1\_L2 + t0
```

simple\_restriction 55

```
intervention1.A <- list(static, rep(0, time_points))</pre>
intervention2.A <- list(static, rep(1, time_points))</pre>
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,
                         intervention1.A = intervention1.A,
                         intervention2.A = intervention2.A,
                         int_descript = int_descript,
                         histories = histories, histvars = histvars,
                         basecovs = c('L3'), nsimul = nsimul,
                         seed = 1234)
summary(gform_basic)
```

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.

. . . This argument is not used in this function.

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#### 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 with a simple restriction
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)</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
intervention1.A <- list(static, rep(0, time_points))</pre>
intervention2.A <- list(static, rep(1, time_points))</pre>
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))
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,
                                                          intervention1.A = intervention1.A,
                                                          intervention2.A = intervention2.A,
                                                          restrictions = restrictions,
                                                          int_descript = int_descript,
                                                          histories = histories, histvars = histvars,
                                                          basecovs = c('L3'), nsimul = nsimul,
                                                          seed = 1234)
gform_basic
```

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static	Static Intervention

#### **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'
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 ~ 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))
```

58 threshold

```
ymodel \leftarrow Y \sim A + L1 + L2 + L3 + lag1_A + lag1_L1 + lag1_L2 + t0
intervention1.A <- list(static, rep(0, time_points))</pre>
intervention2.A <- list(static, rep(1, time_points))</pre>
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,
                         intervention1.A = intervention1.A,
                         intervention2.A = intervention2.A,
                         int_descript = int_descript,
                         histories = histories, histvars = histvars,
                         basecovs = c('L3'), nsimul = nsimul,
                         seed = 1234)
gform_basic
```

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.

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#### **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>
intervention1.treat <- list(static, rep(0, 7))</pre>
intervention2.treat <- list(threshold, 1, Inf)</pre>
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,
                                       intervention1.treat = intervention1.treat,
                                       intervention2.treat = intervention2.treat,
                                       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).

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## 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)</pre>
histvars <- list(c('A', 'L1', 'L2'), c('L1', 'L2'))
covparams <- list(covmodels = c(L1 \sim 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 \leftarrow Y \sim A + L1 + L2 + L3 + lag1_A + lag1_L1 + lag1_L2 + t0
intervention1.A <- list(static, rep(0, time_points))</pre>
intervention2.A <- list(static, rep(1, time_points))</pre>
int_descript <- c('Never treat', 'Always treat')</pre>
nsimul <- 10000
gform_basic <- gformula(obs_data = basicdata_nocomp, id = id,</pre>
                          time_points = time_points,
```

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```
time_name = time_name, covnames = covnames,
outcome_name = outcome_name,
outcome_type = outcome_type, covtypes = covtypes,
covparams = covparams, ymodel = ymodel,
intervention1.A = intervention1.A,
intervention2.A = intervention2.A,
int_descript = int_descript,
histories = histories, histvars = histvars,
basecovs = c('L3'), nsimul = nsimul,
seed = 1234)
```

vcov(gform\_basic)

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