# Package 'postcard'

April 8, 2025

Type Package

Title Estimating Marginal Effects with Prognostic Covariate Adjustment

Version 1.0.0

**Description** Conduct power analyses and inference of marginal effects. Uses plug-in estimation and influence functions to perform robust inference, optionally leveraging historical data to increase precision with prognostic covariate adjustment. The methods are described in Højbjerre-Frandsen et al. (2025) <doi:10.48550/arXiv.2503.22284>.

License MIT + file LICENSE

URL https://novonordisk-opensource.github.io/postcard/,

https://github.com/NovoNordisk-OpenSource/postcard

BugReports https://github.com/NovoNordisk-OpenSource/postcard/issues

**Imports** cli, Deriv, dplyr, earth, generics, magrittr, options, parsnip, rlang, rsample, stats, stringr, tidyselect, tune, utils, workflowsets, xgboost, yardstick

**Suggests** gggrid, ggplot2, knitr, LiblineaR, MASS, ranger, rmarkdown, testthat (>= 3.0.0), withr

Config/testthat/edition 3

**Encoding** UTF-8

RoxygenNote 7.3.2

VignetteBuilder knitr

NeedsCompilation no

Author Mathias Lerbech Jeppesen [aut, cre], Emilie Hojbjerre-Frandsen [aut], Novo Nordisk A/S [cph]

Maintainer Mathias Lerbech Jeppesen <mathiasljeppesen@outlook.com>

**Repository** CRAN

Date/Publication 2025-04-08 15:40:02 UTC

# Contents

2	25
rctglm_with_prognosticscore	20
rctglm_methods	18
rctglm	15
prog	14
power_marginaleffect	10
power_linear	6
options	5
glm_data	4
fit_best_learner	3
default_learners	2

default\_learners Creates a list of learners

#### Description

Index

This function creates a list of learners compatible with the learners argument of fit\_best\_learner, which is used as the default argument.

#### Usage

default\_learners()

### Value

a named list of learners, where each element consists of a

- model: A parsnip model specification
- grid: A data.frame with columns corresponding to tuning parameters

### Examples

default\_learners()

fit\_best\_learner

#### Description

Find the best learner in terms of RMSE among specified learners using cross validation

#### Usage

```
fit_best_learner(
    preproc,
    data,
    cv_folds = 5,
    learners = default_learners(),
    verbose = options::opt("verbose")
)
```

#### Arguments

preproc	A list (preferably named) with preprocessing objects: formulas, recipes, or workflows::workflow_variables(). Passed to workflowsets::workflow_set().
data	A data frame.
cv_folds	a numeric with the number of cross-validation folds used when fitting and eval- uating models
learners	a list (preferably named) containing named lists of elements model and option- ally grid. The model element should be a parsnip model specification, which is passed to workflowsets::workflow_set as the model argument, while the grid element is passed as the grid argument of workflowsets::option_add
verbose	numeric verbosity level. Higher values means more information is printed in console. A value of 0 means nothing is printed to console during execution (Defaults to 2, overwritable using option 'postcard.verbose' or environment variable 'R_POSTCARD_VERBOSE')

#### Details

Ensure data compatibility with the learners.

#### Value

a trained workflow

#### See Also

See rctglm\_with\_prognosticscore() for a function that utilises this function to perform prognostic covariate adjustment.

#### Examples

```
# Generate some synthetic 2-armed RCT data along with historical controls
n <- 100
dat_rct <- glm_data(</pre>
  Y \sim 1 + 2 \times x + 3 \times a,
  x1 = rnorm(n, 2),
  a = rbinom (n, 1, .5),
  family = gaussian()
)
dat_hist <- glm_data(</pre>
  Y \sim 1+2*x1,
  x1 = rnorm(n, 2),
  family = gaussian()
)
# Fit a learner to the historical control data
learners <- list(</pre>
  mars = list(
    model = parsnip::set_engine(
      parsnip::mars(
        mode = "regression", prod_degree = 3
      ),
       "earth"
    )
  )
)
fit <- fit_best_learner(</pre>
  preproc = list(mod = Y ~ .),
  data = dat_hist,
  learners = learners
)
# Use it fx. to predict the "control outcome" in the 2-armed RCT
predict(fit, new_data = dat_rct)
```

glm\_data

Generate data simulated from a GLM

#### Description

Provide a formula, variables and a family to generate a linear predictor using the formula and provided variables before using the inverse link of the family to generate the GLM modelled mean, mu, which is then used to simulate the response with this mean from the generating function according to the chosen family.

#### Usage

```
glm_data(formula, ..., family = gaussian(), family_args = list(sd = 1))
```

#### options

#### Arguments

formula	an object of class "formula" (or one that can be coerced to that class): a symbolic description of the model to be fitted. The details of model specification are given under 'Details' in the glm documentation.
	a data.frame with columns corresponding to variables used in formula, a named list of those variables, or individually provided named arguments of variables from
family	the family of the response. this can be a character string naming a family function, a family function or the result of a call to a family function
family_args	a named list with values of arguments passed to family relevant r <family_name> function for simulating the data</family_name>

#### Value

a data.frame

#### Examples

```
# Generate a gaussian response from a single covariate
glm_data(Y ~ 1+2*x1,
                x1 = rnorm(10))
# Generate a gaussian response from a single covariate with non-linear
# effects. Specify that the response should have standard deviation sqrt(3)
glm_data(Y ~ 1+2*abs(sin(x1)),
                x1 = runif(10, min = -2, max = 2),
                family_args = list(sd = sqrt(3)))
# Generate a negative binomial response
glm_data(Y \sim 1+2*x1-x2)
                x1 = rnorm(10),
                x2 = rgamma(10, shape = 2),
                family = MASS::negative.binomial(2))
# Provide variables as a list/data.frame
glm_data(resp ~ 1+2*x1-x2,
                data.frame(
                  x1 = rnorm(10),
                  x^2 = rgamma(10, shape = 2)
                ),
                family = MASS::negative.binomial(2))
```

options

#### Description

Internally used, package-specific options. All options will prioritize R options() values, and fall back to environment variables if undefined. If neither the option nor the environment variable is set, a default value is used.

#### Arguments

verbose

numeric verbosity level. Higher values means more information is printed in console. A value of 0 means nothing is printed to console during execution (Defaults to 2, overwritable using option 'postcard.verbose' or environment variable 'R\_POSTCARD\_VERBOSE')

#### **Checking Option Values**

Option values specific to postcard can be accessed by passing the package name to env.

```
options::opts(env = "postcard")
options::opt(x, default, env = "postcard")
```

#### Options

**verbose** numeric verbosity level. Higher values means more information is printed in console. A value of 0 means nothing is printed to console during execution

default: 2option: postcard.verboseenvvar: R\_POSTCARD\_VERBOSE (evaluated if possible, raw string otherwise)

#### See Also

options getOption Sys.setenv Sys.getenv

power\_linear Power and sample size estimation for linear models

#### Description

variance\_ancova provides a convenient function for estimating a variance to use for power and sample size approximation.

The power\_gs and samplesize\_gs functions calculate the Guenther-Schouten power approximation for ANOVA or ANCOVA. The approximation is based in (Guenther WC. Sample Size Formulas for Normal Theory T Tests. The American Statistician. 1981;35(4):243–244) and (Schouten HJA. Sample size formula with a continuous outcome for unequal group sizes and unequal variances. Statistics in Medicine. 1999;18(1):87–91).

The function power\_nc calculates the power for ANOVA or ANCOVA based on the non-centrality parameter and the exact t-distributions.

See more details about each function in Details and in sections after Value.

#### Usage

```
variance_ancova(formula, data, inflation = 1, deflation = 1)
power_gs(variance, ate, n, r = 1, margin = 0, alpha = 0.025)
samplesize_gs(variance, ate, r = 1, margin = 0, power = 0.9, alpha = 0.025)
power_nc(variance, df, ate, n, r = 1, margin = 0, alpha = 0.025)
```

#### Arguments

formula	an object of class "formula" (or one that can be coerced to that class): a symbolic description used in stats::model.frame() to create a data.frame with response and covariates. This data.frame is used to estimate the $R^2$ , which is then used to find the variance. See more in details.
data	a data frame, list or environment (or object coercible by as.data.frame to a data frame), containing the variables in formula. Neither a matrix nor an array will be accepted.
inflation	a numeric to multiply the marginal variance of the response by. Default is 1 which estimates the variance directly from data. Use values above 1 to obtain a more conservative estimate of the marginal response variance.
deflation	a numeric to multiply the $R^2$ by. Default is 1 which means the estimate of $R^2$ is unchanged. Use values below 1 to obtain a more conservative estimate of the coefficient of determination. See details about how $R^2$ related to the estimation.
variance	a numeric variance to use for the approximation. See more details in documen- tation sections of each power approximating function.
ate	a numeric minimum effect size that we should be able to detect.
n	a numeric with number of participants in total. From this number of participants in the treatment group is $n1 = (r/(1+r))n$ and the control group is $n1 = (1/(1+r))n$ .
r	a numeric allocation ratio $r = n1/n0$ . For one-to-one randomisation r=1.
margin	a numeric superiority margin (for non-inferiority margin, a negative value can be provided).
alpha	a numeric significance level. Due to regulatory guidelines when using a one-sided test, half the specified significance level is used. Thus, for standard significance level of 5%, the default is $alpha = 0.025$ .
power	a numeric giving the desired power when calculating the sample size
df	a numeric degrees of freedom to use in the t-distribution.

#### Details

This details section provides information about relation between arguments to functions and the formulas described in sections below for each power approximation formula.

Note that all entities that carry the same name as an argument and in the formula will not be mentioned below, as they are obviously linked (n, r, alpha)

- ate:  $\beta_1 \beta_0$
- margin:  $\Delta_s$
- variance:  $\hat{\sigma}^2(1-\hat{R}^2)$

#### Finding the variance to use for approximation:

The variance\_ancova function estimates  $\sigma^2(1-R^2)$  in data and returns it as a numeric that can be passed directly as the variance in power\_gs. Corresponds to estimating the power from using an 1m with the same formula as specified in variance\_ancova.

The user can estimate the variance any way they see fit.

#### Value

All functions return a numeric. variance\_ancova returns a numeric with a variance estimated from data to used for power estimation and sample size estimation. power\_xx and samplesize\_xx functions return a numeric with the power or sample size approximation.

#### **Guenther-Schouten power approximation**

The estimation formula in the case of an ANCOVA model with multiple covariate adjustment is (see description for reference):

$$n = \frac{(1+r)^2}{r} \frac{(z_{1-\alpha} + z_{1-\beta})^2 \widehat{\sigma}^2 (1-\widehat{R}^2)}{(\beta_1 - \beta_0 - \Delta_s)^2} + \frac{(z_{1-\alpha})^2}{2}$$

where  $\widehat{R}^2 = \frac{\widehat{\sigma}_{XY}^\top \widehat{\Sigma}_X^{-1} \widehat{\sigma}_{XY}}{\widehat{\sigma}^2}$ , we denote by  $\widehat{\sigma^2}$  an estimate of the variance of the outcome,  $\widehat{\Sigma}_X$  and estimate of the covariance matrix of the covariates, and  $\widehat{\sigma}_{XY}$  a *p*-dimensional column vector consisting of an estimate of the covariance between the outcome variable and each covariate. In the univariate case  $R^2$  is replaced by  $\rho^2$ 

#### Power approximation using non-centrality parameter

The prospective power estimations are based on (Kieser M. Methods and Applications of Sample Size Calculation and Recalculation in Clinical Trials. Springer; 2020). The ANOVA power is calculated based on the non-centrality parameter given as

$$nc = \sqrt{\frac{r}{(1+r)^2} \cdot n} \cdot \frac{\beta_1 - \beta_0 - \Delta_s}{\sigma},$$

where we denote by  $\sigma^2$  the variance of the outcome, such that the power can be estimated as

$$1 - \beta = 1 - F_{t,n-2,nc} \left( F_{t,n-2,0}^{-1} (1 - \alpha) \right).$$

The power of ANCOVA with univariate covariate adjustment and no interaction is calculated based on the non-centrality parameter given as

$$nc = \sqrt{\frac{rn}{(1+r)^2}} \frac{\beta_1 - \beta_0 - \Delta_s}{\sigma \sqrt{1-\rho^2}},$$

such that the power can be estimated as

$$1 - \beta = 1 - F_{t,n-3,nc} \left( F_{t,n-3,0}^{-1} (1 - \alpha) \right).$$

The power of ANCOVA with either univariate covariate adjustment and interaction or multiple covariate adjustement with or without interaction is calculated based on the non-centrality parameter given as

$$nc = \frac{\beta_1 - \beta_0 - \Delta_s}{\sqrt{\left(\frac{1}{n_1} + \frac{1}{n_0} + X_d^\top \left((n-2)\Sigma_X\right)^{-1} X_d\right) \sigma^2 \left(1 - \hat{R}^2\right)}}.$$

where  $X_d = \left(\overline{X}_1^1 - \overline{X}_0^1, \dots, \overline{X}_1^p - \overline{X}_0^p\right)^\top$ ,  $\widehat{R}^2 = \frac{\widehat{\sigma}_{XY}^\top \widehat{\Sigma}_X^{-1} \widehat{\sigma}_{XY}}{\widehat{\sigma}^2}$ , we denote by  $\widehat{\sigma^2}$  an estimate of

the variance of the outcome,  $\widehat{\Sigma}_X$  and estimate of the covariance matrix of the covariates, and  $\widehat{\sigma}_{XY}$  a *p*-dimensional column vector consisting of an estimate of the covariance between the outcome variable and each covariate. Since we are in the case of randomized trials the expected difference between the covariate values between the to groups is 0. Furthermore, the elements of  $\Sigma_X^{-1}$  will be small, unless the variances are close to 0, or the covariates exhibit strong linear dependencies, so that the correlations are close to 1. These scenarios are excluded since they could lead to potentially serious problems regarding inference either way. These arguments are used by Zimmermann et. al (Zimmermann G, Kieser M, Bathke AC. Sample Size Calculation and Blinded Recalculation for Analysis of Covariance Models with Multiple Random Covariates. Journal of Biopharmaceutical Statistics. 2020;30(1):143–159.) to approximate the non-centrality parameter as in the univariate case where  $\rho^2$  is replaced by  $R^2$ .

Then the power for ANCOVA with d degrees of freedom can be estimated as

$$1 - \beta = 1 - F_{t,d,nc} \left( F_{t,d,0),0}^{-1} (1 - \alpha) \right).$$

#### Examples

```
# Approximate the sample size needed to obtain 90% power with same model as
# above
samplesize_gs(
  variance = va_cov, ate = 1.8, power = 0.9, margin = 1, r = 2
)
# No adjustment covariates
power_nc(n = 200, variance = va_nocov, df = 199, ate = 1)
# Adjusting for all covariates in data generating process
power_nc(n = 200, variance = va_cov, df = 196, ate = 1.8, margin = 1, r = 2)
```

power\_marginaleffect Power approximation for estimating marginal effects in GLMs

#### Description

The functions implements the algorithm for power estimation described in Powering RCTs for marginal effects with GLMs using prognostic score adjustment by Højbjerre-Frandsen et. al (2025). See a bit more context in details and all details in reference.

#### Usage

```
power_marginaleffect(
  response,
  predictions,
  target_effect,
  exposure_prob,
  var1 = NULL,
  kappa1_squared = NULL,
  estimand_fun = "ate",
  estimand_fun_deriv0 = NULL,
  estimand_fun_deriv1 = NULL,
  inv_estimand_fun = NULL,
  margin = estimand_fun(1, 1),
  alpha = 0.025,
  tolerance = 0.001,
  verbose = options::opt("verbose"),
)
```

## Arguments

response	the response variable from comparator participants
predictions	predictions of the response
target_effect	a numeric minimum effect size that we should be able to detect. See more in details.

exposure_prob	a numeric with the probability of being in "group 1" (rather than group 0). See more in details.
var1	a numeric variance of the potential outcome corresponding to group 1, or a function with a single argument meant to obtain var1 as a tranformation of the variance of the potential outcome corresponding to group 0. See more in details.
kappa1_squared	a numeric mean-squared error from predicting potential outcome corresponding to group 1, or a function with a single arguments meant to obtain kappa1_squared as a transformation of the MSE in group 0. See more in details.
estimand_fun	a function with arguments psi1 and psi0 specifying the estimand. Alternative, specify "ate" or "rate_ratio" as a character to use one of the default estimand functions. See more details in the "Estimand" section of rctglm.
estimand_fun_de	riv0
	a function specifying the derivative of estimand_fun wrt. psi0. As a default the algorithm will use symbolic differentiation to automatically find the derivative from estimand_fun
estimand_fun_de	riv1
	a function specifying the derivative of estimand_fun wrt. psi1. As a default the algorithm will use symbolic differentiation to automatically find the derivative from estimand_fun
inv_estimand_fu	n
	<pre>(optional) a function with arguments psi0 and target_effect, so estimand_fun(psi1 = y, psi0 = x) = z and inv_estimand_fun(psi0 = x, target_effect = z) = y for all x, y, z. If left as NULL, the inverse will be found automatically</pre>
margin	a numeric superiority margin. As a default, the estimand_fun is evaluated with the same counterfactual means psi1 and psi0, corresponding to a superiority margin assuming no difference (fx. 0 for ATE and 1 for rate ratio).
alpha	a numeric significance level. Due to regulatory guidelines when using a one- sided test, half the specified significance level is used. Thus, for standard signif- icance level of 5%, the default is $alpha = 0.025$ .
tolerance	passed to all.equal when comparing calculated target_effect from derivations and given target_effect.
verbose	numeric verbosity level. Higher values means more information is printed in console. A value of 0 means nothing is printed to console during execution (Defaults to 2, overwritable using option 'postcard.verbose' or environment variable 'R_POSTCARD_VERBOSE')

... arguments passed to [stats::uniroot], which is used to find the inverse of estimand\_fun, when inv\_estimand\_fun is NULL.

#### Details

$$v_{\infty}^{\uparrow 2} = r_0^{\prime 2} \sigma_0^2 + r_1^{\prime 2} \sigma_1^2 + \pi_0 \pi_1 \left( \frac{|r_0^{\prime}|\kappa_0}{\pi_0} + \frac{|r_1^{\prime}|\kappa_1}{\pi_1} \right)^2$$

where  $r'_a$  is the derivative of the estimand\_fun with respect to  $\Psi_a$ ,  $\sigma_a^2$  is the variance of the potential outcome corresponding to group a,  $\pi_a$  is the probability of being assigned to group a, and  $\kappa_a$  is the expected mean-squared error when predicting the potential outcome corresponding to group a.

The variance bound is then used for calculating a lower bound of the power using the distributions corresponding to the null and alternative hypotheses  $\mathcal{H}_0: \hat{\Psi} \sim F_0 = \mathcal{N}(\Delta, v_{\infty}^{\uparrow 2}/n)$  and  $\mathcal{H}_1: \hat{\Psi} \sim F_1 = \mathcal{N}(\Psi, v_{\infty}^{\uparrow 2}/n)$ . See more details in the reference.

#### **Relating arguments to formulas:**

- response: Used to obtain both  $\sigma_0^2$  (by taking the sample variance of the response) and  $\kappa_0$ .
- predictions: Used when calculating the MSE  $\kappa_0$ .
- var1:  $\sigma_1^2$ . As a default, chosen to be the same as  $\sigma_0^2$ . Can specify differently through this argument fx. by
  - Inflating or deflating the value of  $\sigma_0^2$  by a scalar according to prior beliefs. Fx. specify var1 = function(x) 1.2 \* x to inflate  $\sigma_0^2$  by 1.2.
  - If historical data is available for group 1, an estimate of the variance from that data can be provided here.
- kappa1\_squared: κ<sub>1</sub>. Same as for var1, default is to assume the same value as kappa0\_squared, which is found by using the response and predictions vectors. Adjust the value according to prior beliefs if relevant.
- target\_effect:  $\Psi$ .
- exposure\_prob:  $\pi_1$

#### Value

a numeric with the estimated power.

#### See Also

See power\_linear for power approximation functionalities for linear models.

#### Examples

```
glm2 \leftarrow glm(Y \sim X1 + X2 + A, data = gaus2)
preds_glm1 <- predict(glm2, newdata = gaus1, type = "response")</pre>
preds_glm2 <- predict(glm1, newdata = gaus2, type = "response")</pre>
preds_glm <- c(preds_glm1, preds_glm2)</pre>
# Obtain power
power_marginaleffect(
 response = dat_gaus$Y,
 predictions = preds_glm,
 target_effect = 2,
 exposure_prob = exposure_prob
)
#
                                _____
# Get OOS predictions using discrete super learner and adjust variance
# -----
learners <- list(</pre>
 mars = list(
   model = parsnip::set_engine(
     parsnip::mars(
       mode = "regression", prod_degree = 3
     ),
      "earth"
   )
),
   lm = list(
     model = parsnip::set_engine(
       parsnip::linear_reg(),
        "lm"
     )
   )
)
lrnr1 <- fit_best_learner(preproc = list(mod = Y ~ X1 + X2 + A),</pre>
                         data = gaus1,
                         learners = learners)
lrnr2 <- fit_best_learner(preproc = list(mod = Y ~ X1 + X2 + A),</pre>
                         data = gaus2,
                         learners = learners)
preds_lrnr1 <- dplyr::pull(predict(lrnr2, new_data = gaus1))</pre>
preds_lrnr2 <- dplyr::pull(predict(lrnr1, new_data = gaus2))</pre>
preds_lrnr <- c(preds_lrnr1, preds_lrnr2)</pre>
# Estimate the power AND adjust the assumed variance in the "unknown"
# group 1 to be 20% larger than in group 0
power_marginaleffect(
 response = dat_gaus$Y,
 predictions = preds_lrnr,
 target_effect = 2,
 exposure_prob = exposure_prob,
 var1 = function(var0) 1.2 * var0
)
```

#### prog

#### Description

Extracts the prognostic\_info list element from an rctglm\_prog object. See 'Value' at rctglm\_with\_prognosticscore for more details.

#### Usage

prog(x)

## S3 method for class 'rctglm\_prog'
prog(x)

#### Arguments

х

an object of class rctglm\_prog (returned by rctglm\_with\_prognosticscore)

#### Value

a list with the structure described of prognostic\_info in the Value section of rctglm\_with\_prognosticscore.

#### See Also

The generic rctglm\_with\_prognosticscore() for which this method works.

#### Examples

```
# Generate some data
n <- 100
b0 <- 1
b1 <- 1.5
b2 <- 2
W1 <- runif(n, min = -2, max = 2)
exposure_prob <- .5</pre>
dat_treat <- glm_data(</pre>
  Y ~ b0+b1*abs(sin(W1))+b2*A,
  W1 = W1,
  A = rbinom(n, 1, exposure_prob)
)
dat_notreat <- glm_data(</pre>
  Y \sim b0+b1*abs(sin(W1)),
  W1 = W1
)
learners <- list(</pre>
```

#### rctglm

```
mars = list(
   model = parsnip::set_engine(
      parsnip::mars(
        mode = "regression", prod_degree = 3
      ),
      "earth"
   )
 )
)
ate <- rctglm_with_prognosticscore(</pre>
 formula = Y \sim .,
 exposure_indicator = A,
 exposure_prob = exposure_prob,
 data = dat_treat,
 family = gaussian(),
 estimand_fun = "ate",
 data_hist = dat_notreat,
 learners = learners)
prog(ate)
```

rctglm

Fit GLM and find any estimand (marginal effect) using plug-in estimation with variance estimation using influence functions

#### Description

The procedure uses plug-in-estimation and influence functions to perform robust inference of any specified estimand in the setting of a randomised clinical trial, even in the case of heterogeneous effect of covariates in randomisation groups. See Powering RCTs for marginal effects with GLMs using prognostic score adjustment by Højbjerre-Frandsen et. al (2025) for more details on methodology.

#### Usage

```
rctglm(
  formula,
  exposure_indicator,
  exposure_prob,
  data,
  family = gaussian,
  estimand_fun = "ate",
  estimand_fun_deriv0 = NULL,
  estimand_fun_deriv1 = NULL,
  cv_variance = FALSE,
  cv_variance_folds = 10,
  verbose = options::opt("verbose"),
  ...
)
```

# Arguments

formula	an object of class "formula" (or one that can be coerced to that class): a symbolic description of the model to be fitted. The details of model specification are given under 'Details' in the glm documentation.	
exposure_indica	tor	
	(name of) the <i>binary</i> variable in data that identifies randomisation groups. The variable is required to be binary to make the "orientation" of the estimand_fun clear.	
exposure_prob	a numeric with the probability of being in "group 1" (rather than group 0) in groups defined by <code>exposure_indicator</code> .	
data	an optional data frame, list or environment (or object coercible by as.data.frame to a data frame) containing the variables in the model. If not found in data, the variables are taken from environment(formula), typically the environment from which the function is called.	
family	a description of the error distribution and link function to be used in the model. For glm this can be a character string naming a family function, a family function or the result of a call to a family function. For glm.fit only the third option is supported. (See family for details of family functions.)	
estimand_fun	a function with arguments psi1 and psi0 specifying the estimand. Alternative, specify "ate" or "rate_ratio" as a character to use one of the default estimand functions. See more details in the "Estimand" section of rctglm.	
estimand_fun_de	riv0	
	a function specifying the derivative of <code>estimand_fun</code> wrt. <code>psi0</code> . As a default the algorithm will use symbolic differentiation to automatically find the derivative from <code>estimand_fun</code>	
estimand_fun_de	riv1	
	a function specifying the derivative of estimand_fun wrt. psi1. As a default the algorithm will use symbolic differentiation to automatically find the derivative from estimand_fun	
cv_variance	a logical determining whether to estimate the variance using cross-validation (see details of rctglm).	
cv_variance_folds		
	a numeric with the number of folds to use for cross validation if $\ensuremath{cv\_variance}$ is TRUE.	
verbose	numeric verbosity level. Higher values means more information is printed in console. A value of 0 means nothing is printed to console during execution (Defaults to 2, overwritable using option 'postcard.verbose' or environment variable 'R_POSTCARD_VERBOSE')	
	Additional arguments passed to stats::glm()	

#### Details

The procedure assumes the setup of a randomised clinical trial with observations grouped by a binary exposure\_indicator variable, allocated randomly with probability exposure\_prob. A GLM is fit and then used to predict the response of all observations in the event that the exposure\_indicator

#### rctglm

is 0 and 1, respectively. Taking means of these predictions produce the *counterfactual means* psi0 and psi1, and an estimand r(psi0, psi1) is calculated using any specified estimand\_fun.

The variance of the estimand is found by taking the variance of the influence function of the estimand. If  $cv\_variance$  is TRUE, then the counterfactual predictions for each observation (which are used to calculate the value of the influence function) is obtained as out-of-sample (OOS) predictions using cross validation with number of folds specified by  $cv\_variance\_folds$ . The cross validation splits are performed using stratified sampling with exposure\\_indicator as the strata argument in rsample::vfold\_cv.

Read more in vignette("model-fit").

#### Value

rctglm returns an object of class inheriting from "rctglm".

An object of class rctglm is a list containing the following components:

- estimand: A data.frame with plug-in estimate of estimand, standard error (SE) estimate and variance estimate of estimand
- estimand\_funs: A list with
  - f: The estimand\_fun used to obtain an estimate of the estimand from counterfactual means
  - d0: The derivative with respect to psi0
  - d1: The derivative with respect to psi1
- means\_counterfactual: A data.frame with counterfactual means psi0 and psi1
- fitted.values\_counterfactual: A data.frame with counterfactual mean values, obtained by transforming the linear predictors for each group by the inverse of the link function.
- glm: A glm object returned from running stats::glm within the procedure
- call: The matched call

#### Estimands

As noted in the description, psi0 and psi1 are the counterfactual means found by prediction using a fitted GLM in the binary groups defined by exposure\_indicator.

Default estimand functions can be specified via "ate" (which uses the function function(psi1, psi0) psi1-psi0) and "rate\_ratio" (which uses the function function(psi1, psi0) psi1/psi0). See more information on specifying the estimand\_fun in vignette("model-fit").

As a default, the Deriv package is used to perform symbolic differentiation to find the derivatives of the estimand\_fun.

#### See Also

See how to extract information using methods in rctglm\_methods.

Use rctglm\_with\_prognosticscore() to include prognostic covariate adjustment.

See vignettes

#### Examples

```
# Generate some data to showcase example
n <- 100
exp_prob <- .5</pre>
dat_gaus <- glm_data(</pre>
  Y \sim 1+1.5 \times X1+2 \times A,
  X1 = rnorm(n),
  A = rbinom(n, 1, exp_prob),
  family = gaussian()
)
# Fit the model
ate <- rctglm(formula = Y ~ .,</pre>
               exposure_indicator = A,
               exposure_prob = exp_prob,
               data = dat_gaus,
               family = gaussian)
# Pull information on estimand
estimand(ate)
## Another example with different family and specification of estimand_fun
dat_binom <- glm_data(</pre>
  Y \sim 1+1.5 \times X1+2 \times A,
 X1 = rnorm(n),
  A = rbinom(n, 1, exp_prob),
  family = binomial()
)
rr <- rctglm(formula = Y ~ .,</pre>
               exposure_indicator = A,
               exposure_prob = exp_prob,
               data = dat_binom,
               family = binomial(),
               estimand_fun = "rate_ratio")
odds_ratio <- function(psi1, psi0) (psi1*(1-psi0))/(psi0*(1-psi1))</pre>
or <- rctglm(formula = Y ~ .,</pre>
               exposure_indicator = A,
               exposure_prob = exp_prob,
               data = dat_binom,
               family = binomial,
               estimand_fun = odds_ratio)
```

rctglm\_methods

Methods for objects of class rctglm

#### rctglm\_methods

#### Description

Methods mostly to extract information from model fit and inference. See details for more information on each method.

#### Usage

```
estimand(object)
## S3 method for class 'rctglm'
estimand(object)
est(object)
## S3 method for class 'rctglm'
coef(object, ...)
## S3 method for class 'rctglm'
print(x, digits = max(3L, getOption("digits") - 3L), ...)
```

#### Arguments

object	an object of class rctglm
•••	additional arguments passed to methods
х	an object of class rctglm
digits	a numeric with the number of digits to display when printing

#### Details

The function estimand (or short-hand version est) can be used to extract a data.frame with an estimated value and standard error of the estimand.

A method for the generic coef has been added for rctglm (i.e., coef.rctglm), which uses the method coef.glm to extract coefficient information from the underlying glm fit in the procedure.

#### Value

estimand/est returns a data.frame with columns Estimate and Std. Error with the estimate and standard error of the estimand.

coef returns a named numeric, being the result of the glm method of coef on the glm object contained within an rctglm object.

#### See Also

The generic rctglm() which these are methods for.

#### Examples

```
# Generate some data to showcase example
n <- 100
exposure_prob <-.5
dat_binom <- glm_data(</pre>
  Y \sim 1+1.5 \times X1+2 \times A,
 X1 = rnorm(n),
  A = rbinom(n, 1, exposure_prob),
  family = binomial()
)
# Fit the model
ate <- rctglm(formula = Y ~ .,</pre>
               exposure_indicator = A,
               exposure_prob = exposure_prob,
               data = dat_binom,
               family = binomial,
               estimand_fun = "ate")
print(ate)
estimand(ate)
coef(ate)
```

rctglm\_with\_prognosticscore

Use prognostic covariate adjustment when fitting an rctglm

#### Description

The procedure uses fit\_best\_learner to fit a prognostic model to historical data and uses the model to produce counterfactual predictions as a prognostic score that is then adjusted for as a covariate in the rctglm procedure. See Powering RCTs for marginal effects with GLMs using prognostic score adjustment by Højbjerre-Frandsen et. al (2025) for more details.

#### Usage

```
rctglm_with_prognosticscore(
   formula,
   exposure_indicator,
   exposure_prob,
   data,
   family = gaussian,
   estimand_fun = "ate",
   estimand_fun_deriv0 = NULL,
   estimand_fun_deriv1 = NULL,
   cv_variance = FALSE,
   cv_variance_folds = 10,
   ...,
```

```
data_hist,
  prog_formula = NULL,
  cv_prog_folds = 5,
  learners = default_learners(),
  verbose = options::opt("verbose")
)
```

### Arguments

formula	an object of class "formula" (or one that can be coerced to that class): a symbolic description of the model to be fitted. The details of model specification are given under 'Details' in the glm documentation.	
exposure_indica	ator	
	(name of) the <i>binary</i> variable in data that identifies randomisation groups. The variable is required to be binary to make the "orientation" of the estimand_fun clear.	
exposure_prob	a numeric with the probability of being in "group 1" (rather than group 0) in groups defined by exposure_indicator.	
data	an optional data frame, list or environment (or object coercible by as.data.frame to a data frame) containing the variables in the model. If not found in data, the variables are taken from environment(formula), typically the environment from which the function is called.	
family	a description of the error distribution and link function to be used in the model. For glm this can be a character string naming a family function, a family function or the result of a call to a family function. For glm.fit only the third option is supported. (See family for details of family functions.)	
estimand_fun	a function with arguments psi1 and psi0 specifying the estimand. Alternative, specify "ate" or "rate_ratio" as a character to use one of the default estimand functions. See more details in the "Estimand" section of rctglm.	
estimand_fun_de	eriv0	
	a function specifying the derivative of estimand_fun wrt. psi0. As a default the algorithm will use symbolic differentiation to automatically find the derivative from estimand_fun	
estimand_fun_de	eriv1	
	a function specifying the derivative of estimand_fun wrt. psi1. As a default the algorithm will use symbolic differentiation to automatically find the derivative from estimand_fun	
cv_variance	a logical determining whether to estimate the variance using cross-validation (see details of rctglm).	
cv_variance_folds		
	a numeric with the number of folds to use for cross validation if cv_variance is TRUE.	
	Additional arguments passed to stats::glm()	
data_hist	a data.frame with historical data on which to fit a prognostic model	

prog_formula	an object of class "formula" (or one that can be coerced to that class): a symbolic description of the prognostic model to be fitted to data_hist. Passed in a list as the preproc argument in fit_best_learner(). As a default, the formula is created by modelling the response (assumed to have the same name as in formula) using all columns in data_hist.
cv_prog_folds	a numeric with the number of cross-validation folds used when fitting and evaluating models
learners	a list (preferably named) containing named lists of elements model and option- ally grid. The model element should be a parsnip model specification, which is passed to workflowsets::workflow_set as the model argument, while the grid element is passed as the grid argument of workflowsets::option_add
verbose	numeric verbosity level. Higher values means more information is printed in console. A value of 0 means nothing is printed to console during execution (Defaults to 2, overwritable using option 'postcard.verbose' or environment variable 'R_POSTCARD_VERBOSE')

#### Details

Prognostic covariate adjustment involves training a prognostic model (using fit best learner) on historical data (data\_hist) to predict the response in that data.

Assuming that the historical data is representative of the comparator group in a "new" data set (group 0 of the binary exposure\_indicator in data), we can use the prognostic model to predict the counterfactual outcome of all observations (including the ones in the comparator group for which the prediction of counterfactual outcome coincides with a prediction of actual outcome).

This prediction, which is called the prognostic score, is then used as an adjustment covariate in the GLM (the prognostic score is added to formula before calling rctglm with the modified formula).

See much more details in the reference in the description.

#### Value

rctglm\_with\_prognosticscore returns an object of class rctglm\_prog, which inherits from rctglm.

An rctglm\_prog object is a list with the same components as an rctglm object (see the Value section of rctglm for a breakdown of the structure), but with an additional list element of:

- prognostic\_info: List with information about the fitted prognostic model on historical data. It has components:
  - formula: The formula with symbolic description of how the response is modelled as function of covariates in the models
  - model\_fit: A trained workflow the result of fit\_best\_learner
  - learners: A list of learners used for the discrete super learner
  - cv\_folds: The amount of folds used for cross validation
  - data: The historical data used for cross validation when fitting and testing models

#### See Also

Method to extract information of the prognostic model in prog. Function used to fit the prognostic model is fit\_best\_learner().

See rctglm() for the function and class this inherits from.

#### Examples

```
# Generate some data
n <- 100
b0 <- 1
b1 <- 1.5
b2 <- 2
W1 <- runif(n, min = -2, max = 2)
exp_prob <-.5
dat_treat <- glm_data(</pre>
  Y ~ b0+b1*abs(sin(W1))+b2*A,
 W1 = W1,
  A = rbinom (n, 1, exp_prob)
)
dat_notreat <- glm_data(</pre>
  Y ~ b0+b1*abs(sin(W1)),
  W1 = W1
)
learners <- list(</pre>
  mars = list(
    model = parsnip::set_engine(
      parsnip::mars(
        mode = "regression", prod_degree = 3
      ),
      "earth"
    )
 ),
    lm = list(
      model = parsnip::set_engine(
        parsnip::linear_reg(),
        "lm"
      )
    )
)
ate <- rctglm_with_prognosticscore(</pre>
  formula = Y \sim ..
  exposure_indicator = A,
  exposure_prob = exp_prob,
  data = dat_treat,
  family = gaussian(),
  estimand_fun = "ate",
  data_hist = dat_notreat,
  learners = learners)
```

rctglm\_with\_prognosticscore

# Pull information on estimand estimand(ate)

# Index

all.equal, 11

as.data.frame,7 coef, 19 coef.rctglm, 19 coef.rctglm(rctglm\_methods), 18 default\_learners, 2 est, 19 est(rctglm\_methods), 18 estimand, 19 estimand (rctglm\_methods), 18 family, *16*, *21* fit\_best\_learner, 2, 3, 20, 22 fit\_best\_learner(), 22, 23 glm, 5, 16, 21 glm\_data,4 options, 5 power\_gs (power\_linear), 6 power\_linear, 6, 12 power\_marginaleffect, 10 power\_nc (power\_linear), 6 print.rctglm(rctglm\_methods), 18 prog, 14, 23 rctglm, 11, 15, 16, 19-22 rctglm(), *19*, *23* rctglm\_methods, 17, 18 rctglm\_with\_prognosticscore, 14, 20 rctglm\_with\_prognosticscore(), 3, 14, 17 rsample::vfold\_cv, 17 samplesize\_gs(power\_linear), 6 stats::glm, **17** stats::glm(), 16, 21

stats::model.frame(),7

variance\_ancova(power\_linear), 6
workflows::workflow\_variables(), 3

workflowsets::option\_add, 3, 22
workflowsets::workflow\_set, 3, 22
workflowsets::workflow\_set(), 3