# Package 'RCTrep'

# December 16, 2021

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DR\_base

DR

R6 class: Doubly robust estimator class

# **Description**

A R6 class for doubly robust estimator that implements its own fit method.

# Super classes

```
RCTrep::Estimator -> RCTrep::DR_base -> DR
```

#### Methods

#### **Public methods:**

```
• DR$new()
```

```
• DR$clone()
```

#### Method new():

```
Usage:
DR$new(
    df,
    vars_name,
    outcome_method,
    outcome_formula,
    treatment_method,
    treatment_formula,
    two_models,
    ...
)
```

**Method** clone(): The objects of this class are cloneable with this method.

```
Usage:
DR$clone(deep = FALSE)
Arguments:
deep Whether to make a deep clone.
```

DR\_base

R6 class: Doubly robust estimator base class

# Description

A base R6 class for doubly robust estimator of average treatment effect that implements comment methods.

# **Super class**

```
RCTrep::Estimator -> DR_base
```

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#### Methods

#### **Public methods:**

```
    DR_base$new()
    DR_base$clone()
    Method new():
        Usage:
        DR_base$new(df, vars_name)
    Method clone(): The objects of this class are cloneable with this method.
        Usage:
        DR_base$clone(deep = FALSE)
        Arguments:
```

Estimate

Estimate average treatment effect

# **Description**

The function Estimate is used to estimate the average treatment effect obtained from data.

#### Usage

```
Estimate(
   Estimator,
   data,
   vars_name,
   outcome_method = "glm",
   treatment_method = "glm",
   two_models = NULL,
   outcome_formula,
   treatment_formula,
   stratification,
   stratification_joint,
   strata_cut,
   ...
)
```

deep Whether to make a deep clone.

#### **Arguments**

Estimator

A character specifying an estimator for average treatment effect. The allowed estimators for Estimator are: "G\_computation", "IPW", and "DR". The corresponding object will be created by the wrapper function Estimate(). The default is "G\_computation", which, along with outcome\_method="glm" model the potential outcomes.

data

A data frame containing variables in vars\_name.

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vars\_name

A list containing four vectors confounders\_internal, confounders\_external, treatment\_name, and outcome\_name. confounders\_internal is a character vector containing the adjustment variables, which, along with Estimator and the corresponding outcome\_method or treatment\_method to correct for confounding; confounders\_external is a character vector containing variables for weighting as to generalize estimates from source.data to target.data; outcome\_name is a character vector of length one containing the variable name of outcome; treatment\_name is a character vector of length one containing the variable name of treatment.

outcome\_method

A string specifying which model for outcome, treatment, and selection to use. Possible values are found using names(getModelInfo()). See http://topepo. github.io/caret/train-models-by-tag.html. A list of functions can also be passed for a custom model function. See http://topepo.github.io/caret/ using-your-own-model-in-train.html for details.

treatment\_method

A string specifying which model for outcome, treatment, and selection to use. Possible values are found using names (getModelInfo()). See http://topepo. github.io/caret/train-models-by-tag.html. A list of functions can also be passed for a custom model function. See http://topepo.github.io/caret/ using-your-own-model-in-train.html for details.

two\_models

An optional logical indicating whether potential outcomes should be modeled separately when Estimator="DR". Default is FALSE.

outcome\_formula

An optional object of class formula describing the outcome model, treatment model, and selection model.

treatment\_formula

An optional object of class formula describing the outcome model, treatment model, and selection model.

stratification An optional string vector containing variables to define subgroups. source.obj will compute both weighted and unweighted conditional average treatment effect, targe.obj will calculate the conditional average treatment effect based on these variables.

stratification\_joint

An optional logical defining the subgroup based on joint distribution of variables or univariate distribution in stratification when stratification is specified.

strata\_cut

An optional list containing lists. Each component is a list with tag named by a variable to discretize, containing break which is a vector specifying the interval of range of the variable to divide, lable which is a string vector specifying how to code value in the variable according to which interval they fall. The leftmost interval corresponds to level one, the next leftmost to level two and so on. This parameter is useful in the case we concern the integrated treatment effect conditioning on variables with multiple levels (for instance, continuous variable or ordinal variable with multiple levels). Note that we first model based on these continuous variables, then we discretize these variables according to strata\_cut by modifying the public variable data of Estimator object in wrap function Estimate, and calculate the weight for generalization based on the discretized variables.

An optional arguments passed to fit() of each estimator object for model training and tuning. See https://topepo.github.io/caret/model-training-and-tuning. html for details.

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#### Value

An object of class Estimator.

Estimator

R6 class: Estimator base class

#### **Description**

A base R6 class for estimator of average treatment effect that implements the common methods, such as RCTrep, get\_CATE, plot\_CATE, inheritted by G\_computation\_base, IPW\_base, and DR\_base class.

#### Methods

#### **Public methods:**

```
• Estimator$new()
```

- Estimator\$RCTrep()
- Estimator\$get\_CATE()
- Estimator\$plot\_CATE()
- Estimator\$clone()

Method new(): Create a new Estimator object

Usage:

Estimator\$new(df, vars\_name)

Arguments:

df A data frame containing variables in vars\_name

vars\_name vars\_name A list containing four vectors confounders\_internal, confounders\_external, treatment\_name, and outcome\_name. confounders\_internal is a character vector containing the adjustment variables, which, along with Estimator and the corresponding outcome\_method or treatment\_method to correct for confounding; confounders\_external is a character vector containing variables for weighting as to generalize estimates from source.data to target.data; outcome\_name is a character vector of length one containing the variable name of outcome; treatment\_name is a character vector of length one containing the variable name of treatment.

**Method** RCTrep(): Replicating the average treatment effect of target.obj. If stratification is specified, then replicating the conditional average treatment effect stratified by stratification and stratification\_joint by weighting based on the residual variables, namely, variables that are specified in confounders\_external\_name while not in stratification.

```
Usage:
Estimator$RCTrep(
   target.obj,
   weighting_estimator,
   weighting_method,
   stratification,
   stratification_joint
)
Arguments:
```

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target.obj An object of class Estimator or list.

weighting\_estimator A string specifying a weighting estimator for generalizing/transporting the estimates to target.obj. The allowed estimators are: "balancing", and "modeling".

weighting\_method A string specifying which model for selection to use. Possible values are found using names(getModelInfo()). See http://topepo.github.io/caret/train-models-by-tag. html

stratification An optional string vector containing variables to define subgroup. If !is.NULL(stratification) source.obj will compute both weighted and unweighted conditional average treatment effect based on these variables, target.obj will calculate the conditional average treatment effect based on these variables.

stratification\_joint An optional logical defining the subgroup based on joint distribution of variables or univariate distribution in stratification when stratification is specified.

**Method** get\_CATE(): Get conditional average treatment effect of subgroups defined by stratification and stratification\_joint. If stratification\_joint=FALSE, then the method return conditional average treatment effect of subgroups stratified by each of variables in stratification.

Usage:

Estimator\$get\_CATE(stratification, stratification\_joint)

Arguments:

stratification An string vector containing variables to define subgroup.

stratification\_joint An logical defining the subgroup based on joint distribution of variables or univariate distribution in stratification.

Returns: A data frame. If stratification\_joint=TRUE, then the method returns a data frame with N rows and J columns, where N represents the number of subgroups, and J is equal to the sum of number of variables in stratification and 3 (three additional columns with name cate, se, and size, representing the estimated conditional average treatment effect of this subgroup, standard error of the estimate, and the sample size of the subgroup). If stratification\_joint=FALSE, then the method returns a data frame with N rows and 5 columns, where N represents the number of subgroups stratified by each variable in stratification and 5 columns with name name, value, cate, se, and size, representing the name of a variable used to stratify the population, a level of the variable, the estimated conditional average treatment effect of this subgroup, standard error of the estimate, and the sample size of the subgroup).

**Method** plot\_CATE(): Plot the forest plot of conditional average treatment effect of subgroups defined by stratification and stratification\_joint. The method first call public method get\_CATE(stratification, stratification\_joint), then plot the results.

Usage:

Estimator\$plot\_CATE(stratification, stratification\_joint = FALSE)

Arguments:

stratification An string vector containing variables to define subgroup.

stratification\_joint An logical defining the subgroup based on joint distribution of variables or univariate distribution in stratification.

**Method** clone(): The objects of this class are cloneable with this method.

Usage:

Estimator\$clone(deep = FALSE)

Arguments:

deep Whether to make a deep clone.

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 $G\_computation$ 

R6 class: G\_computation class

# **Description**

A R6 class for G\_computation estimator for average treatment effect

#### Super classes

```
RCTrep::Estimator -> RCTrep::G_computation_base -> G_computation
```

#### Methods

#### **Public methods:**

- G\_computation\$new()
- G\_computation\$clone()

# Method new():

```
Usage:
G_computation$new(
    df,
    vars_name,
    gc.method,
    gc.formula,
    var_approach = "Bias_adjusted",
    ...
)
```

**Method** clone(): The objects of this class are cloneable with this method.

Usage:

G\_computation\$clone(deep = FALSE)

Arguments:

deep Whether to make a deep clone.

G\_computation\_base

R6 class: G\_computation base class

# Description

A base R6 class for G\_computation estimator for average treatment effect

# Super class

```
RCTrep::Estimator -> G_computation_base
```

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#### Methods

```
Public methods:
```

```
• G_computation_base$new()
```

- G\_computation\_base\$residual\_check()
- G\_computation\_base\$clone()

```
Method new():
```

```
Usage:
```

G\_computation\_base\$new(df, vars\_name)

# Method residual\_check():

Usage:

G\_computation\_base\$residual\_check(stratification)

**Method** clone(): The objects of this class are cloneable with this method.

Usage:

G\_computation\_base\$clone(deep = FALSE)

Arguments:

deep Whether to make a deep clone.

IPW

R6 class: IPW class

#### **Description**

A R6 class for IPW estimator for average treatment effect that implements its own fit method.

#### Super classes

```
RCTrep::Estimator -> RCTrep::IPW_base -> IPW
```

#### Methods

#### **Public methods:**

- IPW\$new()
- IPW\$clone()

# Method new():

Usage:

IPW\$new(df, vars\_name, treatment\_method, treatment\_formula, ...)

**Method** clone(): The objects of this class are cloneable with this method.

Usage.

IPW\$clone(deep = FALSE)

Arguments:

deep Whether to make a deep clone.

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IPW\_base

R6 class: Inverse propensity score weighting estimator base class

#### **Description**

A base R6 class for inverse propensity score weighting estimator of average treatment effect that implements comment methods.

#### Super class

```
RCTrep::Estimator -> IPW_base
```

#### **Public fields**

model: a fitted model for treatment conditioning on covariates

method: a string specifying the method for fitting the propensity score

formula: an optional formula object. The formula is specified as Z ~ X1+X2..., where Z represents treatment variable and X1 and X2 are covariates.

ps: a numeric vector of length n where n is row number of self\$data.

#### **Active bindings**

model: a fitted model for treatment conditioning on covariates

method: a string specifying the method for fitting the propensity score

formula: an optional formula object. The formula is specified as Z ~ X1+X2..., where Z represents treatment variable and X1 and X2 are covariates.

ps: a numeric vector of length n where n is row number of self\$data.

#### Methods

# **Public methods:**

- IPW\_base\$new()
- IPW\_base\$clone()

#### Method new():

```
Usage:
```

IPW\_base\$new(df, vars\_name)

Method clone(): The objects of this class are cloneable with this method.

Usage:

IPW\_base\$clone(deep = FALSE)

Arguments:

deep Whether to make a deep clone.

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**RCTREP** 

Replicate treatment effect estimates obtained from a randomized control trial using real world data

#### **Description**

The function RCTREP is used to replicate the estimate of treatment effect from a target randomized control trial based on real-world data (RWD). This function estimate the treatment effect of RWD to ensure the internal validity of the estimates within the study population (namely, the observational data) and weight the resulting estimates to the target population (namely, the RCT) to enable external validity. The function currently implement the following types of estimators of treatment effect: G\_computation, inverse propensity score weighting (IPW), and augmented propensity score weighting. The function implement the following two types of weighting estimators to generalize the resulting estimates of treatment effect from RWD to the target RCT: exact matching weights, and selection score weights. Since we regard the sample in the RCT as the target population, weights for each individual in RWD is p/(1-p) so that the weighted population of RWD is representative to the target population.

#### Usage

```
RCTREP(
 Estimator = "G_computation",
 weighting_estimator = "Balancing",
  source.data = source.data,
  target.data = target.data,
  vars_name,
  outcome_method = "glm",
  treatment_method = "glm",
 weighting_method = "glm",
  outcome_formula = NULL,
  treatment_formula = NULL,
  selection_formula = NULL,
  stratification = NULL,
  stratification_joint = FALSE,
  strata_cut_source = NULL,
  strata_cut_target = NULL,
  two_models = NULL,
)
```

#### **Arguments**

Estimator

A character specifying an estimator for average treatment effect. The allowed estimators for Estimator are: "G\_computation", "IPW", and "DR". The corresponding object will be created by the wrapper function Estimate(). The default is "G\_computation", which, along with outcome\_method="glm" model the potential outcomes.

weighting\_estimator

A character specifying a weighting estimator for generalizing/transporting the estimates of source.obj (initiated using RWD) to target.obj (initiated using RCT) as to enable replication/comparison between source study (RWD) and

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> target study(RCT). The allowed estimators are: "balancing", and "modeling". "balancing" estimator use exact matching to compute the weight; "modeling" estimator model the probability of being selected to the target RCT (assuming combing target RCT and the source RWD as a population). The default is "Balancing", which, implements the exact matching on variables in vars\_name\$external\_confour to balance the population covariates between source.data and target.data

source data

A data frame containing variables named in vars\_name and possible other variables. If not found in source.data, the function will stop and throw error; vectors of binary treatment and binary outcome should be factor.

target.data

A data frame containing variables named in vars\_name and possible other variables, or a list of four components with four tags ATE\_mean, ATE\_se, CATE\_mean\_se, and univariate\_p reference four components with data type numeric, numeric, data.frame, and list respectively. ATE\_mean is a numeric vector of length 1 containing the point estimate of the treatment effect in target.data, ATE\_se is a numeric vector of length 1 containing the standard error the treatment effect, CATE\_mean\_se is a data frame containing five vectors name, value, cate, se, and size of length N, where name is variables that divide the target population into smaller groups, value is levels of variables in name, cate is the provided conditional average treatment effect of a subgroup defined by a variable in name with the corresponding level in value, se is the standard error of the cate, size is the group size, N is the number of stratum based on variables in the vector name and levels in value. univariate\_p is a list of length equal to the number of variables to divide the population with tags equal to variable names, each component containing a vector, which, each containing the name of a variable, number of levels of the variable, levels of the variable, and the distribution of each level by order.

vars\_name

A list containing four vectors confounders\_internal, confounders\_external, treatment\_name, and outcome\_name. confounders\_internal is a character vector containing the adjustment variables, which, along with Estimator and the corresponding outcome\_method or treatment\_method to correct for confounding; confounders\_external is a character vector containing variables for weighting as to generalize estimates from source.data to target.data; outcome\_name is a character vector of length one containing the variable name of outcome; treatment\_name is a character vector of length one containing the variable name of treatment.

outcome\_method, treatment\_method, weighting\_method

A string specifying which model for outcome, treatment, and selection to use. Possible values are found using names (getModelInfo()). See http://topepo. github.io/caret/train-models-by-tag.html. A list of functions can also be passed for a custom model function. See http://topepo.github.io/caret/ using-your-own-model-in-train.html for details.

outcome\_formula, treatment\_formula, selection\_formula

An optional object of class formula describing the outcome model, treatment model, and selection model.

stratification

An optional string vector containing variables to define subgroups, source.obj will compute both weighted and unweighted conditional average treatment effect, targe.obj will calculate the conditional average treatment effect based on these variables.

stratification\_joint

An optional logical defining the subgroup based on joint distribution of variables or univariate distribution in stratification when stratification is specified.

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two\_models An optional logical indicating whether potential outcomes should be modeled separately when Estimator="DR". Default is FALSE.

An optional arguments passed to fit() of each estimator object for model training and tuning. See https://topepo.github.io/caret/model-training-and-tuning.html for details.

strata\_cut

An optional list containing lists. Each component is a list with tag named by a variable to discretize, containing break which is a vector specifying the interval of range of the variable to divide, lable which is a string vector specifying how to code value in the variable according to which interval they fall. The leftmost interval corresponds to level one, the next leftmost to level two and so on. This parameter is useful in the case we concern the integrated treatment effect conditioning on variables with multiple levels (for instance, continuous variable or ordinal variable with multiple levels). Note that we first model based on these continuous variables, then we discretize these variables according to strata\_cut by modifying the public variable data of Estimator object in wrap function Estimate, and calculate the weight for generalization based on the discretized variables.

#### **Details**

An R6 object for both studies are constructed by a wrapper function Estimate() with user's input of data and estimator for treatment effect. Then Estimate() return initialized objects source.obj and target.obj. source.obj replicates the target RCT estimate via the class method RCTrep() with input of target object target.obj and weighting method.

#### Value

A list of length two with two R6 class objects source.obj=source.obj and target.obj=target.obj.

# **Examples**

```
library(RCTrep)
source.data <- RCTrep::source.data</pre>
target.data <- RCT::target.data</pre>
Estimator <- "IPW"
strata <- c("Stage2","pT")</pre>
strata_joint <- TRUE</pre>
vars_name <- list(confounders_internal=c("Stage2","age","pT"),</pre>
                   confounders_external=c("Stage2", "age", "pT"),
                   treatment_name=c('combined_chemo'),
                   outcome_name=c('vitstat')
                  )
outcome_form <- vitstat~Stage2+age+combined_chemo+pT+</pre>
Stage2:combined_chemo+age:combined_chemo+pT:combined_chemo + pT:Stage2:combined_chemo
strata_cut <- list(age=list(breaks=c(min(data$age),</pre>
                                        50,60,70,max(data$age)),
                              labels=c(1,2,3,4)))
## Not run: output <- RCTREP(Estimator="G_computation", two_models=FALSE,</pre>
                            source.data=source.data, target.data=target.data,
                            vars_name=vars_name,
                            outcome_formula = outcome_form,
                   stratification=strata, stratification_joint=TRUE, strata_cut=strata_cut)
         output$source.obj
         output$target.obj
## End(Not run)
```

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source.data

Dutch Colon cancer registry data

# Description

A dataset containing synthetic dutch colon cancer registry data and other biomarkers

# Usage

```
source.data
```

#### **Format**

A data frame with 2000 rows and 9 variables

vitstat 1=death, 0=survival

Stage2 pathological stage, 1=stage2, 0=stage3

summary

Summary average treatment effect and possible conditional average treatment

# Description

Summary average treatment effect and possible conditional average treatment

#### Usage

```
summary(source.obj, target.obj)
```

#### **Arguments**

source.obj An object of class Estimator resulting from source data target.obj An object of class Estimator resulting from target data

#### Value

a plot with a forest plot and a table with numeric results

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