# **Package: medoutcon (via r-universe)**

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Title Efficient Natural and Interventional Causal Mediation Analysis

Version 0.2.2

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**Description** Efficient estimators of interventional (in)direct effects in the presence of mediator-outcome confounding affected by exposure. The effects estimated allow for the impact of the exposure on the outcome through a direct path to be disentangled from that through mediators, even in the presence of intermediate confounders that complicate such a relationship. Currently supported are non-parametric efficient one-step and targeted minimum loss estimators based on the formulation of Díaz, Hejazi, Rudolph, and van der Laan (2020) <doi:10.1093/biomet/asaa085>. Support for efficient estimation of the natural (in)direct effects is also provided, appropriate for settings in which intermediate confounders are absent. The package also supports estimation of these effects when the mediators are measured using outcome-dependent two-phase sampling designs (e.g., case-cohort).

**Depends** R (>= 3.2.0)

- **Imports** stats, data.table, assertthat, tibble, dplyr, zeallot, scales, stringr, origami (>= 1.0.3), glm2, sl3 (>= 1.4.3)
- **Suggests** testthat, knitr, rmarkdown, covr, Rsolnp, nnls, SuperLearner, glmnet, hal9001 (>= 0.4.1), speedglm, xgboost, ranger, arm
- Remotes github::tlverse/hal9001, github::tlverse/sl3@devel

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URL https://github.com/nhejazi/medoutcon

BugReports https://github.com/nhejazi/medoutcon/issues

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confint.medoutcon	Confidence intervals for natural/interventional (in)direct effect esti-
	mates

# Description

Compute confidence intervals for objects of class medoutcon, which contain estimates produced by medoutcon.

# Usage

```
## S3 method for class 'medoutcon'
confint(object, parm = seq_len(object$theta), level = 0.95, ...)
```

object	An object of class medoutcon, as produced by invoking medoutcon, for which a confidence interval is to be computed.
parm	A numeric vector indicating indices of <code>object</code> for which to return confidence intervals.
level	A numeric indicating the level of the confidence interval to be computed.
	Other arguments. Not currently used.

 $\texttt{fit\_moc\_mech}$ 

# Description

Fit intermediate confounding mechanism with(out) conditioning on mediators

# Usage

```
fit_moc_mech(
   train_data,
   valid_data = NULL,
   contrast,
   learners,
   m_names,
   w_names,
   type = c("q", "r")
)
```

train_data	A data.table containing observed data, with columns in the order specified by the NPSEM (Y, M, R, Z, A, W), with column names set appropriately based on the input data. Such a structure is a convenience utility to passing data around to the various core estimation routines and is automatically generated by medoutcon.
valid_data	A holdout data set, with columns exactly matching those appearing in the pre- ceding argument data, to be used for estimation via cross-fitting. Optional, defaulting to NULL.
contrast	A numeric double indicating the two values of the intervention A to be com- pared. The default value of $c(0, 1)$ assumes a binary intervention node A.
learners	Stack, or other learner class (inheriting from Lrnr_base), containing a set of learners from sl3, to be used in fitting a model for the intermediate confounding mechanism, i.e., $q = E[zla',W]$ and $r = E[zla',m,w]$ ).
m_names	A character vector of the names of the columns that correspond to mediators (M). The input for this argument is automatically generated by a call to the wrapper function medoutcon.
w_names	A character vector of the names of the columns that correspond to base- line covariates (W). The input for this argument is automatically generated by medoutcon.
type	A character vector indicating whether to condition on the mediators (M) or not. Specifically, this is an option for specifying one of two types of nuisance regressions: "r" is defined as the component that conditions on the mediators (i.e., $r = E[z a',m,w]$ ) while "q" is defined as the component that does not (i.e., q = E[z a',w]).

fit\_nuisance\_u

# Description

Fit pseudo-outcome regression conditioning on mediator-outcome confounder

# Usage

```
fit_nuisance_u(
    train_data,
    valid_data,
    learners,
    b_out,
    q_out,
    r_out,
    g_out,
    h_out,
    w_names
)
```

train_data	A data.table containing observed data, with columns in the order specified by the NPSEM (Y, M, R, Z, A, W), with column names set appropriately based on the input data. Such a structure is a convenience utility to passing data around to the various core estimation routines and is automatically generated by medoutcon.	
valid_data	A holdout data set, with columns exactly matching those appearing in the pre- ceding argument data, to be used for estimation via cross-fitting. NOT optional for this nuisance parameter.	
learners	Stack, or other learner class (inheriting from Lrnr_base), containing a set of learners from <b>sl3</b> , to be used in fitting a model for this nuisance parameter.	
b_out	Output from the internal function for fitting the outcome regression fit_out_mech.	
q_out	Output from the internal function for fitting the mechanism of the intermediate confounder while conditioning on mediators, i.e., fit_moc_mech, setting type = "q".	
r_out	Output from the internal function for fitting the mechanism of the intermedi- ate confounder without conditioning on mediators, i.e., fit_moc_mech, setting type = "r".	
g_out	Output from the internal function for fitting the treatment mechanism without conditioning on mediators fit_treat_mech.	
h_out	Output from the internal function for fitting the treatment mechanism condition- ing on the mediators fit_treat_mech.	

# fit\_nuisance\_v

w\_names A character vector of the names of the columns that correspond to baseline covariates (W). The input for this argument is automatically generated by medoutcon.

fit\_nuisance\_v Fit pseudo-outcome regression conditioning on treatment and baseline

# Description

Fit pseudo-outcome regression conditioning on treatment and baseline

# Usage

```
fit_nuisance_v(
   train_data,
   valid_data,
   contrast,
   learners,
   b_out,
   q_out,
   m_names,
   w_names
)
```

train_data	A data.table containing observed data, with columns in the order specified by the NPSEM (Y, M, R, Z, A, W), with column names set appropriately based on the input data. Such a structure is a convenience utility to passing data around to the various core estimation routines and is automatically generated by medoutcon.
valid_data	A holdout data set, with columns exactly matching those appearing in the pre- ceding argument data, to be used for estimation via cross-fitting. Not optional for this nuisance parameter.
contrast	A numeric double indicating the two values of the intervention A to be com- pared. The default value of c(0, 1) assumes a binary intervention node A.
learners	Stack, or other learner class (inheriting from Lrnr_base), containing a set of learners from <b>sl3</b> , to be used in fitting a model for this nuisance parameter.
b_out	Output from the internal function for fitting the outcome regression fit_out_mech.
q_out	Output from the internal function for fitting the mechanism of the intermediate confounder while conditioning on the mediators, i.e., fit_moc_mech, setting type = "q".
m_names	A character vector of the names of the columns that correspond to mediators $(M)$ . The input for this argument is automatically generated by a call to the wrapper function medoutcon.

w\_names A character vector of the names of the columns that correspond to baseline covariates (W). The input for this argument is automatically generated by medoutcon.

fit\_out\_mech Fit outcome regression

# Description

Fit outcome regression

# Usage

```
fit_out_mech(
   train_data,
   valid_data = NULL,
   contrast,
   learners,
   m_names,
   w_names
)
```

train_data	A data.table containing the observed data, with columns in the order specified by the NPSEM (Y, M, R, Z, A, W), with column names set based on the input data. Such a structure is a convenience utility to passing data around to the various core estimation routines and is automatically generated medoutcon.
valid_data	A holdout data set, with columns exactly matching those appearing in the pre- ceding argument data, to be used for estimation via cross-fitting. Optional, defaulting to NULL.
contrast	A numeric double indicating the two values of the intervention A to be compared. The default of $c(0, 1)$ assumes a binary intervention node A.
learners	Stack, or other learner class (inheriting from Lrnr_base), containing a set of learners from <b>sl3</b> , to be used in fitting the outcome regression, i.e., $b(A,Z,M,W)$ .
m_names	A character vector of the names of the columns that correspond to mediators $(M)$ . The input for this argument is automatically generated by medoutcon.
w_names	A character vector of the names of the columns that correspond to base- line covariates (W). The input for this argument is automatically generated by medoutcon.

fit\_treat\_mech

# Description

Fit propensity scores for treatment contrasts

# Usage

```
fit_treat_mech(
  train_data,
  valid_data = NULL,
  contrast,
  learners,
  m_names,
  w_names,
  type = c("g", "h"),
  bounds = c(0.01, 0.99)
)
```

train_data	A data.table containing the observed data; columns are in the order specified by the NPSEM (Y, M, R, Z, A, W), with column names set appropriately based on the data. Such a structure is merely a convenience utility to passing data around to the various core estimation routines and is automatically generated medoutcon.
valid_data	A holdout data set, with columns exactly matching those appearing in the pre- ceding argument train_data, to be used for estimation via cross-fitting. Op- tional, defaulting to NULL.
contrast	A numeric double indicating the two values of the intervention A to be compared. The default value of $c(0, 1)$ assumes a binary intervention node A.
learners	Stack, or other learner class (inheriting from Lrnr_base), containing a set of learners from sl3, to be used in fitting a propensity score models, i.e., $g := P(A = 1   W)$ and $h := P(A = 1   M, W)$ .
m_names	A character vector of the names of the columns that correspond to mediators $(M)$ . The input for this argument is automatically generated by medoutcon.
w_names	A character vector of the names of the columns that correspond to base-line covariates (W). The input for this argument is automatically generated by $medoutcon$ .
type	A character indicating which of the treatment mechanism variants to estimate. Option "g" is the propensity score $g(A W)$ while option "h" is a reparameterized mediator density $h(A M,W)$ .
bounds	A numeric vector containing two values, the first being the minimum allowable estimated propensity score value and the second being the maximum allowable for estimated propensity score value.

medoutcon

#### Description

Efficient estimation of natural and interventional (in)direct effects

#### Usage

```
medoutcon(
 W,
 Α,
 Ζ,
 Μ,
  Υ,
 R = rep(1, length(Y)),
 obs_weights = rep(1, length(Y)),
  svy_weights = NULL,
  two_phase_weights = rep(1, length(Y)),
 effect = c("direct", "indirect", "pm"),
  contrast = NULL,
  g_learners = sl3::Lrnr_glm_fast$new(),
 h_learners = sl3::Lrnr_glm_fast$new(),
 b_learners = sl3::Lrnr_glm_fast$new(),
  q_learners = sl3::Lrnr_glm_fast$new(),
  r_learners = sl3::Lrnr_glm_fast$new(),
  u_learners = sl3::Lrnr_hal9001$new(),
  v_learners = sl3::Lrnr_hal9001$new(),
 d_learners = sl3::Lrnr_glm_fast$new(),
  estimator = c("tmle", "onestep"),
 estimator_args = list(cv_folds = 5L, max_iter = 5L, tiltmod_tol = 5),
  g_bounds = c(0.01, 0.99)
)
```

W	A matrix, data.frame, or similar object corresponding to a set of baseline covariates.
A	A numeric vector corresponding to a treatment variable. The parameter of in- terest is defined as a location shift of this quantity.
Z	A numeric vector corresponding to an intermediate confounder affected by treatment (on the causal pathway between the intervention A, mediators M, and outcome Y, but unaffected itself by the mediators). When set to NULL, the natural (in)direct effects are estimated.
М	A numeric vector, matrix, data.frame, or similar corresponding to a set of mediators (on the causal pathway between the intervention A and the outcome Y).

Y	A numeric vector corresponding to an outcome variable.
R	A logical vector indicating whether a sampled observation's mediator was measured via a two-phase sampling design. Defaults to a vector of ones, in- dicating that two-phase sampling was not performed.
obs_weights	A numeric vector of observation-level weights. The default is to give all observations equal weighting.
svy_weights	A numeric vector of observation-level weights that have been computed exter- nally, such as survey sampling weights. Such weights are used in the construc- tion of re-weighted efficient estimators.
<pre>two_phase_weigh</pre>	ts
	A numeric vector of known observation-level weights corresponding to the inverse probability of the mediator being measured. Defaults to a vector of ones.
effect	A character indicating whether to compute the direct or the indirect effect as discussed in <a href="https://arxiv.org/abs/1912.09936">https://arxiv.org/abs/1912.09936</a> >. This is ignored when the argument contrast is provided. By default, the direct effect is estimated.
contrast	A numeric double indicating the two values of the intervention A to be com- pared. The default value of NULL has no effect, as the value of the argument effect is instead used to define the contrasts. To override effect, provide a numeric double vector, giving the values of a' and a*, e.g., $c(0, 1)$ .
g_learners	A Stack object, or other learner class (inheriting from Lrnr_base), containing instantiated learners from <b>sl3</b> ; used to fit a model for the propensity score.
h_learners	A Stack object, or other learner class (inheriting from Lrnr_base), containing instantiated learners from <b>sl3</b> ; used to fit a model for a parameterization of the propensity score that conditions on the mediators.
b_learners	A Stack object, or other learner class (inheriting from Lrnr_base), containing instantiated learners from <b>sl3</b> ; used to fit a model for the outcome regression.
q_learners	A Stack object, or other learner class (inheriting from Lrnr_base), containing instantiated learners from <b>sl3</b> ; used to fit a model for a nuisance regression of the intermediate confounder, conditioning on the treatment and potential baseline covariates.
r_learners	A Stack object, or other learner class (inheriting from Lrnr_base), containing instantiated learners from <b>sl3</b> ; used to fit a model for a nuisance regression of the intermediate confounder, conditioning on the mediators, the treatment, and potential baseline confounders.
u_learners	A Stack object, or other learner class (inheriting from Lrnr_base), containing instantiated learners from <b>sl3</b> ; used to fit a pseudo-outcome regression required for in the efficient influence function.
v_learners	A Stack object, or other learner class (inheriting from Lrnr_base), containing instantiated learners from <b>sl3</b> ; used to fit a pseudo-outcome regression required for in the efficient influence function.
d_learners	A Stack object, or other learner class (inheriting from Lrnr_base), containing instantiated learners from <b>sl3</b> ; used to fit an initial efficient influence function regression when computing the efficient influence function in a two-phase sampling design.

estimator	The desired estimator of the direct or indirect effect (or contrast-specific param- eter) to be computed. Both an efficient one-step estimator using cross-fitting and a cross-validated targeted minimum loss estimator (TMLE) are available. The default is the TML estimator.
estimator_args	A list of extra arguments to be passed (via) to the function call for the specified estimator. The default is chosen so as to allow the number of folds used to compute the one-step or TML estimators to be easily adjusted. In the case of the TML estimator, the number of update (fluctuation) iterations is limited, and a tolerance is included for the updates introduced by tilting (fluctuation) models.
g_bounds	A numeric vector containing two values, the first being the minimum allowable estimated propensity score value and the second being the maximum allowable for estimated propensity scores. Defaults to $c(0.001, 0.999)$ .

# Examples

```
# here, we show one-step and TML estimates of the interventional direct
# effect; the indirect effect can be evaluated by a straightforward change
# to the penultimate argument. the natural direct and indirect effects can
# be evaluated by omitting the argument Z (inappropriate in this example).
# create data: covariates W, exposure A, post-exposure-confounder Z,
#
               mediator M, outcome Y
n_obs <- 200
w_1 <- rbinom(n_obs, 1, prob = 0.6)</pre>
w_2 <- rbinom(n_obs, 1, prob = 0.3)</pre>
w <- as.data.frame(cbind(w_1, w_2))</pre>
a <- as.numeric(rbinom(n_obs, 1, plogis(rowSums(w) - 2)))</pre>
z <- rbinom(n_obs, 1, plogis(rowMeans(-log(2) + w - a) + 0.2))</pre>
m_1 <- rbinom(n_obs, 1, plogis(rowSums(log(3) * w + a - z)))</pre>
m_2 <- rbinom(n_obs, 1, plogis(rowSums(w - a - z)))</pre>
m <- as.data.frame(cbind(m_1, m_2))</pre>
y <- rbinom(n_obs, 1, plogis(1 / (rowSums(w) - z + a + rowSums(m))))</pre>
# one-step estimate of the interventional direct effect
os_de <- medoutcon(</pre>
  W = w, A = a, Z = z, M = m, Y = y,
 effect = "direct",
  estimator = "onestep"
)
# TML estimate of the interventional direct effect
# NOTE: improved variance estimate and de-biasing from targeting procedure
tmle_de <- medoutcon(</pre>
  W = w, A = a, Z = z, M = m, Y = y,
  effect = "direct",
  estimator = "tmle"
)
```

print.medoutcon

Print method for natural/interventional (in)direct effect estimate objects

# Description

The print method for objects of class medoutcon.

#### Usage

## S3 method for class 'medoutcon'
print(x, ...)

# Arguments

х	An object of class medoutcon.
	Other options (not currently used).

summary.medoutcon Summary for natural/interventional (in)direct effect estimate objects

# Description

Print a convenient summary for objects of S3 class medoutcon.

#### Usage

## S3 method for class 'medoutcon'
summary(object, ..., ci\_level = 0.95)

object	An object of class medoutcon, as produced by invoking medoutcon.
	Other arguments. Not currently used.
ci_level	A numeric indicating the level of the confidence interval to be computed.

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