Package 'regmedint'

August 11, 2021

Title Regression-Based Causal Mediation Analysis with an Interaction Term

Version 0.2.1

Description 'R' implementation of the regression-based causal mediation analysis with a treatment-mediator interaction term, as originally implemented in the 'SAS' macro by Valeri and VanderWeele (2013) <doi:10.1037/a0031034> and Valeri and VanderWeele (2015) <doi:10.1097/EDE.0000000000000253>. Linear and logistic models are supported for the mediator model. Linear, logistic, loglinear, Poisson, negative binomial, Cox, and accelerated failure time (exponential and Weibull) models are supported for the outcome model.

License GPL-2

Encoding UTF-8

LazyData true

Imports Deriv, MASS, Matrix, assertthat, sandwich, survival

Suggests boot, furrr, future, geepack, knitr, mice, mitools, modelr, purrr, rlang, rmarkdown, stringr, testthat, tidyverse, locfit

RoxygenNote 7.1.1

VignetteBuilder knitr

URL https://kaz-yos.github.io/regmedint/

BugReports https://github.com/kaz-yos/regmedint/issues

Depends R (>= 2.10)

NeedsCompilation no

Author Kazuki Yoshida [cre, aut] (<https://orcid.org/0000-0002-2030-3549>), Yi Li [ctb, aut] (<https://orcid.org/0000-0002-9359-210X>), Maya Mathur [ctb] (<https://orcid.org/0000-0001-6698-2607>)

Maintainer Kazuki Yoshida <kazukiyoshida@mail.harvard.edu>

R topics documented:

beta_hat 2
calc_myreg 3
calc_myreg_mreg_linear_yreg_linear 4
calc_myreg_mreg_linear_yreg_logistic 5
calc_myreg_mreg_logistic_yreg_linear 6
calc_myreg_mreg_logistic_yreg_logistic 7

coef.regmedint 8
coef.summary_regmedint 9
confint.regmedint 10
fit_mreg 11
fit_yreg 12
grad_prop_med_yreg_linear 13
grad_prop_med_yreg_logistic 14
new_regmedint 14
print.regmedint 16
print.summary_regmedint 17
prop_med_yreg_linear 18
prop_med_yreg_logistic 18
regmedint 19
report_missing 21
summary.regmedint 22
summary.regmedint_mod_poisson 23
theta_hat 24
validate_args 25
validate_regmedint 26
vcov.regmedint 27
vcov.regmedint_mod_poisson 28
vv2015 28

Index **30**

`beta_hat` *Create a vector of coefficients from the mediator model (mreg)*

Description

This function extracts `coef` from `mreg_fit` and pads with zeros appropriately to create a named vector consistently having the following elements: `(Intercept)` `avar` `cvar`: This part is eliminated when `cvar = NULL`. `EMM_AC_Mmodel`: This part is eliminated when `EMM_AC_Mmodel = NULL`.

Usage

```
beta_hat(mreg, mreg_fit, avar, cvar, EMM_AC_Mmodel = NULL)
```

Arguments

`mreg`	A character vector of length 1. Mediator regression type: `"linear"` or `"logistic"`.
`mreg_fit`	Model fit object for mreg (mediator model).
`avar`	A character vector of length 1. Treatment variable name.
`cvar`	A character vector of length > 0. Covariate names. Use `NULL` if there is no covariate. However, this is a highly suspicious situation. Even if `avar` is randomized, `mvar` is not. Thus, there should usually be some confounder(s) to account for the common cause structure (confounding) between `mvar` and `yvar`.
`EMM_AC_Mmodel`	A character vector of length > 0. Effect modifiers names. The C in AxC product term in mediator model. Use `NULL` if there is no covariate.

Value

A named numeric vector of coefficients.

`calc_myreg` *Return mediation analysis functions given mediator and outcome models.*

Description

This function returns functions that can be used to calculate the causal effect measures, given the mediator model fit (`mreg_fit`) and the outcome model fit (`yreg_fit`).

Usage

```
calc_myreg(
  mreg,
  mreg_fit,
  yreg,
  yreg_fit,
  avar,
  mvar,
  cvar,
  EMM_AC_Mmodel,
  EMM_AC_Ymodel,
  EMM_MC,
  interaction
)
```

Arguments

`mreg`	A character vector of length 1. Mediator regression type: `"linear"` or `"logistic"`.
`mreg_fit`	Model fit from `fit_mreg`
`yreg`	A character vector of length 1. Outcome regression type: `"linear"`, `"logistic"`, `"loglinear"`, `"poisson"`, `"negbin"`, `"survCox"`, `"survAFT_exp"`, or `"survAFT_weibull"`.
`yreg_fit`	Model fit from `fit_yreg`
`avar`	A character vector of length 1. Treatment variable name.
`mvar`	A character vector of length 1. Mediator variable name.
`cvar`	A character vector of length > 0. Covariate names. Use `NULL` if there is no covariate. However, this is a highly suspicious situation. Even if `avar` is randomized, `mvar` is not. Thus, there should usually be some confounder(s) to account for the common cause structure (confounding) between `mvar` and `yvar`.
`EMM_AC_Mmodel`	A character vector of length > 0. Effect modifiers names. The C in AxC product term in mediator model. Use `NULL` if there is no covariate.
`EMM_AC_Ymodel`	A character vector of length > 0. Effect modifiers names. The C in AxC product term in outcome model. Use `NULL` if there is no covariate.
`EMM_MC`	A character vector of length > 0. Effect modifiers names. The C in MxC product term in mediator model. Use `NULL` if there is no covariate.
`interaction`	A logical vector of length 1. Default to TRUE. Whether to include a mediator-treatment interaction term in the outcome regression model.

Value

A list containing two functions. The first is for calculating point estimates. The second is for calculating the correspoding

---

`calc_myreg_mreg_linear_yreg_linear` *Create calculators for effects and se (mreg linear / yreg linear)*

Description

Construct functions for the conditional effect estimates and their standard errors in the mreg linear / yreg linear setting. Internally, this function deconstruct model objects and feed parameter estiamtes to the internal worker functions `calc_myreg_mreg_linear_yreg_linear_est` and `calc_myreg_mreg_linear_yreg_linear_se`.

Usage

```
calc_myreg_mreg_linear_yreg_linear(
  mreg,
  mreg_fit,
  yreg,
  yreg_fit,
  avar,
  mvar,
  cvar,
  EMM_AC_Mmodel,
  EMM_AC_Ymodel,
  EMM_MC,
  interaction
)
```

Arguments

`mreg`	A character vector of length 1. Mediator regression type: `"linear"` or `"logistic"`.
`mreg_fit`	Model fit from `fit_mreg`
`yreg`	A character vector of length 1. Outcome regression type: `"linear"`, `"logistic"`, `"loglinear"`, `"poisson"`, `"negbin"`, `"survCox"`, `"survAFT_exp"`, or `"survAFT_weibull"`.
`yreg_fit`	Model fit from `fit_yreg`
`avar`	A character vector of length 1. Treatment variable name.
`mvar`	A character vector of length 1. Mediator variable name.
`cvar`	A character vector of length > 0. Covariate names. Use `NULL` if there is no covariate. However, this is a highly suspicious situation. Even if `avar` is randomized, `mvar` is not. Thus, there should usually be some confounder(s) to account for the common cause structure (confounding) between `mvar` and `yvar`.
`EMM_AC_Mmodel`	A character vector of length > 0. Effect modifiers names. The C in AxC product term in mediator model. Use `NULL` if there is no covariate.
`EMM_AC_Ymodel`	A character vector of length > 0. Effect modifiers names. The C in AxC product term in outcome model. Use `NULL` if there is no covariate.

EMM_MC	A character vector of length > 0. Effect modifiers names. The C in MxC product term in mediator model. Use NULL if there is no covariate.
interaction	A logical vector of length 1. Default to TRUE. Whether to include a mediator-treatment interaction term in the outcome regression model.

Value

A list contraining a function for effect estimates and a function for corresponding standard errors.

`calc_myreg_mreg_linear_yreg_logistic`
Create calculators for effects and se (mreg linear / yreg logistic)

Description

Construct functions for the conditional effect estimates and their standard errors in the mreg linear / yreg logistic setting. Internally, this function deconstruct model objects and feed parameter estiamtes to the internal worker functions `calc_myreg_mreg_linear_yreg_logistic_est` and `calc_myreg_mreg_linear_yreg_logistic_se`.

Usage

```
calc_myreg_mreg_linear_yreg_logistic(
  mreg,
  mreg_fit,
  yreg,
  yreg_fit,
  avar,
  mvar,
  cvar,
  EMM_AC_Mmodel,
  EMM_AC_Ymodel,
  EMM_MC,
  interaction
)
```

Arguments

mreg	A character vector of length 1. Mediator regression type: "linear" or "logistic".
mreg_fit	Model fit from fit_mreg
yreg	A character vector of length 1. Outcome regression type: "linear", "logistic", "loglinear", "poisson", "negbin", "survCox", "survAFT_exp", or "survAFT_weibull".
yreg_fit	Model fit from fit_yreg
avar	A character vector of length 1. Treatment variable name.
mvar	A character vector of length 1. Mediator variable name.
cvar	A character vector of length > 0. Covariate names. Use NULL if there is no covariate. However, this is a highly suspicious situation. Even if avar is randomized, mvar is not. Thus, there should usually be some confounder(s) to account for the common cause structure (confounding) between mvar and yvar.

EMM_AC_Mmodel	A character vector of length > 0. Effect modifiers names. The C in AxC product term in mediator model. Use NULL if there is no covariate.
EMM_AC_Ymodel	A character vector of length > 0. Effect modifiers names. The C in AxC product term in outcome model. Use NULL if there is no covariate.
EMM_MC	A character vector of length > 0. Effect modifiers names. The C in MxC product term in mediator model. Use NULL if there is no covariate.
interaction	A logical vector of length 1. Default to TRUE. Whether to include a mediator-treatment interaction term in the outcome regression model.

Value

A list contraining a function for effect estimates and a function for corresponding standard errors.

`calc_myreg_mreg_logistic_yreg_linear`
Create calculators for effects and se (mreg logistic / yreg linear)

Description

Construct functions for the conditional effect estimates and their standard errors in the mreg logistic / yreg linear setting. Internally, this function deconstruct model objects and feed parameter estiamtes to the internal worker functions `calc_myreg_mreg_logistic_yreg_linear_est` and `calc_myreg_mreg_logistic_yreg_linear_se`.

Usage

```
calc_myreg_mreg_logistic_yreg_linear(
  mreg,
  mreg_fit,
  yreg,
  yreg_fit,
  avar,
  mvar,
  cvar,
  EMM_AC_Mmodel,
  EMM_AC_Ymodel,
  EMM_MC,
  interaction
)
```

Arguments

mreg	A character vector of length 1. Mediator regression type: `"linear"` or `"logistic"`.
mreg_fit	Model fit from `fit_mreg`
yreg	A character vector of length 1. Outcome regression type: `"linear"`, `"logistic"`, `"loglinear"`, `"poisson"`, `"negbin"`, `"survCox"`, `"survAFT_exp"`, or `"survAFT_weibull"`.
yreg_fit	Model fit from `fit_yreg`
avar	A character vector of length 1. Treatment variable name.
mvar	A character vector of length 1. Mediator variable name.

cvar	A character vector of length > 0. Covariate names. Use NULL if there is no covariate. However, this is a highly suspicious situation. Even if avar is randomized, mvar is not. Thus, there should usually be some confounder(s) to account for the common cause structure (confounding) between mvar and yvar.
EMM_AC_Mmodel	A character vector of length > 0. Effect modifiers names. The C in AxC product term in mediator model. Use NULL if there is no covariate.
EMM_AC_Ymodel	A character vector of length > 0. Effect modifiers names. The C in AxC product term in outcome model. Use NULL if there is no covariate.
EMM_MC	A character vector of length > 0. Effect modifiers names. The C in MxC product term in mediator model. Use NULL if there is no covariate.
interaction	A logical vector of length 1. Default to TRUE. Whether to include a mediator-treatment interaction term in the outcome regression model.

Value

A list contraining a function for effect estimates and a function for corresponding standard errors.

`calc_myreg_mreg_logistic_yreg_logistic`
Create calculators for effects and se (mreg logistic / yreg logistic)

Description

Construct functions for the conditional effect estimates and their standard errors in the mreg logistic / yreg logistic setting. Internally, this function deconstruct model objects and feed parameter estiamtes to the internal worker functions `calc_myreg_mreg_logistic_yreg_logistic_est` and `calc_myreg_mreg_logistic_yreg_logistic_se`.

Usage

```
calc_myreg_mreg_logistic_yreg_logistic(
  mreg,
  mreg_fit,
  yreg,
  yreg_fit,
  avar,
  mvar,
  cvar,
  EMM_AC_Mmodel,
  EMM_AC_Ymodel,
  EMM_MC,
  interaction
)
```

Arguments

mreg	A character vector of length 1. Mediator regression type: `"linear"` or `"logistic"`.
mreg_fit	Model fit from `fit_mreg`
yreg	A character vector of length 1. Outcome regression type: `"linear"`, `"logistic"`, `"loglinear"`, `"poisson"`, `"negbin"`, `"survCox"`, `"survAFT_exp"`, or `"survAFT_weibull"`.

yreg_fit	Model fit from fit_yreg
avar	A character vector of length 1. Treatment variable name.
mvar	A character vector of length 1. Mediator variable name.
cvar	A character vector of length > 0. Covariate names. Use NULL if there is no covariate. However, this is a highly suspicious situation. Even if avar is randomized, mvar is not. Thus, there should usually be some confounder(s) to account for the common cause structure (confounding) between mvar and yvar.
EMM_AC_Mmodel	A character vector of length > 0. Effect modifiers names. The C in AxC product term in mediator model. Use NULL if there is no covariate.
EMM_AC_Ymodel	A character vector of length > 0. Effect modifiers names. The C in AxC product term in outcome model. Use NULL if there is no covariate.
EMM_MC	A character vector of length > 0. Effect modifiers names. The C in MxC product term in mediator model. Use NULL if there is no covariate.
interaction	A logical vector of length 1. Default to TRUE. Whether to include a mediator-treatment interaction term in the outcome regression model.

Value

A list contraining a function for effect estimates and a function for corresponding standard errors.

---

coef.regmedint *Extract point estimates.*

Description

Extract point estimates evaluated at a0, a1, m_cde, and c_cond.

Usage

```
## S3 method for class 'regmedint'
coef(object, a0 = NULL, a1 = NULL, m_cde = NULL, c_cond = NULL, ...)
```

Arguments

object	An object of the regmedint class.
a0	A numeric vector of length one.
a1	A numeric vector of length one.
m_cde	A numeric vector of length one. A mediator value at which the controlled direct effect (CDE) conditional on the adjustment covariates is evaluated. If not provided, the default value supplied to the call to regmedint will be used. Only the CDE is affected.
c_cond	A numeric vector as long as the number of adjustment covariates. A set of covariate values at which the conditional natural effects are evaluated.
...	For compatibility with the generic. Ignored.

Value

A numeric vector of point estimates.

Examples

```
library(regmedint)
data(vv2015)
regmedint_obj <- regmedint(data = vv2015,
                           ## Variables
                           yvar = "y",
                           avar = "x",
                           mvar = "m",
                           cvar = c("c"),
                           eventvar = "event",
                           ## Values at which effects are evaluated
                           a0 = 0,
                           a1 = 1,
                           m_cde = 1,
                           c_cond = 0.5,
                           ## Model types
                           mreg = "logistic",
                           yreg = "survAFT_weibull",
                           ## Additional specification
                           interaction = TRUE,
                           casecontrol = FALSE)
coef(regmedint_obj)
## Evaluate at different values
coef(regmedint_obj, m_cde = 0, c_cond = 1)
```

---

coef.summary_regmedint

Extract the result matrix from a summary_regmedint object.

Description

Extract the result matrix from a summary_regmedint object.

Usage

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

Arguments

object	An object with a class of summary_regmedint.
...	For compatibility with the generic.

Value

A matrix populated with results.

Examples

```
library(regmedint)
data(vv2015)
regmedint_obj <- regmedint(data = vv2015,
                           ## Variables
                           yvar = "y",
                           avar = "x",
                           mvar = "m",
                           cvar = c("c"),
                           eventvar = "event",
                           ## Values at which effects are evaluated
                           a0 = 0,
                           a1 = 1,
                           m_cde = 1,
                           c_cond = 0.5,
                           ## Model types
                           mreg = "logistic",
                           yreg = "survAFT_weibull",
                           ## Additional specification
                           interaction = TRUE,
                           casecontrol = FALSE)
coef(summary(regmedint_obj))
```

`confint.regmedint` *Confidence intervals for mediation prameter estimates.*

Description

Construct Wald approximate confidence intervals for the quantities of interest.

Usage

```
## S3 method for class 'regmedint'
confint(
  object,
  parm = NULL,
  level = 0.95,
  a0 = NULL,
  a1 = NULL,
  m_cde = NULL,
  c_cond = NULL,
  ...
)
```

Arguments

`object`	An object of the `regmedint` class.
`parm`	For compatibility with generic. Ignored.
`level`	A numeric vector of length one. Requested confidence level. Defaults to 0.95.
`a0`	A numeric vector of length one.

a1	A numeric vector of length one.
m_cde	A numeric vector of length one. A mediator value at which the controlled direct effect (CDE) conditional on the adjustment covariates is evaluated. If not provided, the default value supplied to the call to regmedint will be used. Only the CDE is affected.
c_cond	A numeric vector as long as the number of adjustment covariates. A set of covariate values at which the conditional natural effects are evaluated.
...	For compatibility with generic.

Value

A numeric matrix of the lower limit and upper limit.

Examples

```
library(regmedint)
data(vv2015)
regmedint_obj <- regmedint(data = vv2015,
                           ## Variables
                           yvar = "y",
                           avar = "x",
                           mvar = "m",
                           cvar = c("c"),
                           eventvar = "event",
                           ## Values at which effects are evaluated
                           a0 = 0,
                           a1 = 1,
                           m_cde = 1,
                           c_cond = 0.5,
                           ## Model types
                           mreg = "logistic",
                           yreg = "survAFT_weibull",
                           ## Additional specification
                           interaction = TRUE,
                           casecontrol = FALSE)
confint(regmedint_obj)
## Evaluate at different values
confint(regmedint_obj, m_cde = 0, c_cond = 1)
## Change confidence level
confint(regmedint_obj, m_cde = 0, c_cond = 1, level = 0.99)
```

---

fit_mreg *Fit a model for the mediator given the treatment and covariates.*

Description

lm is called if mreg = "linear". glm is called with family = binomial() if mreg = "logistic".

Usage

```
fit_mreg(mreg, data, avar, mvar, cvar, EMM_AC_Mmodel = NULL)
```

Arguments

mreg	A character vector of length 1. Mediator regression type: "linear" or "logistic".
data	Data frame containing the relevant variables.
avar	A character vector of length 1. Treatment variable name.
mvar	A character vector of length 1. Mediator variable name.
cvar	A character vector of length > 0. Covariate names. Use NULL if there is no covariate. However, this is a highly suspicious situation. Even if avar is randomized, mvar is not. Thus, there should usually be some confounder(s) to account for the common cause structure (confounding) between mvar and yvar.
EMM_AC_Mmodel	A character vector of length > 0. Effect modifiers names. The C in AxC product term in mediator model. Use NULL if there is no covariate.

Value

A regression object of class lm (linear) or glm (logistic)

---

fit_yreg *Fit a model for the outcome given the treatment, mediator, and covariates.*

Description

The outcome model type yreg can be one of the following "linear", "logistic", "loglinear" (implemented as modified Poisson), "poisson", "negbin", "survCox", "survAFT_exp", or "survAFT_weibull".

Usage

```
fit_yreg(
  yreg,
  data,
  yvar,
  avar,
  mvar,
  cvar,
  EMM_AC_Ymodel = NULL,
  EMM_MC = NULL,
  eventvar,
  interaction
)
```

Arguments

yreg	A character vector of length 1. Outcome regression type: "linear", "logistic", "loglinear", "poisson", "negbin", "survCox", "survAFT_exp", or "survAFT_weibull".
data	Data frame containing the relevant variables.
yvar	A character vector of length 1. Outcome variable name. It should be the time variable for survival outcomes.
avar	A character vector of length 1. Treatment variable name.

mvar	A character vector of length 1. Mediator variable name.
cvar	A character vector of length > 0. Covariate names. Use NULL if there is no covariate. However, this is a highly suspicious situation. Even if avar is randomized, mvar is not. Thus, there should usually be some confounder(s) to account for the common cause structure (confounding) between mvar and yvar.
EMM_AC_Ymodel	A character vector of length > 0. Effect modifiers names. The C in AxC product term in outcome model. Use NULL if there is no covariate.
EMM_MC	A character vector of length > 0. Effect modifiers names. The C in MxC product term in mediator model. Use NULL if there is no covariate.
eventvar	An character vector of length 1. Only required for survival outcome regression models. Note that the coding is 1 for event and 0 for censoring, following the R survival package convention.
interaction	A logical vector of length 1. Default to TRUE. Whether to include a mediator-treatment interaction term in the outcome regression model.

Details

The outcome regression functions to be called are the following:

- "linear" lm
- "logistic" glm
- "loglinear" glm (modified Poisson)
- "poisson" glm
- "negbin" glm.nb
- "survCox" coxph
- "survAFT_exp" survreg
- "survAFT_weibull" survreg

Value

Model fit object from on of the above regression functions.

---

grad_prop_med_yreg_linear

Calculate the gradient of the proportion mediated for yreg linear.

Description

Calculate the gradient of the proportion mediated for yreg linear case.

Usage

```
grad_prop_med_yreg_linear(pnde, tnie)
```

Arguments

pnde	A numeric vector of length one. Pure natural direct effect.
tnie	A numeric vector of length one. Total natural indirect effect.

Value

A numeric vector of length two. Gradient of the proportion mediated with respect to pnde and tnie.

---

grad_prop_med_yreg_logistic *Calculate the gradient of the proportion mediated for yreg logistic.*

Description

Calculate the gradient of the proportion mediated for yreg logistic case.

Usage

```
grad_prop_med_yreg_logistic(pnde, tnie)
```

Arguments

pnde	A numeric vector of length one. Pure natural direct effect.
tnie	A numeric vector of length one. Total natural indirect effect.

Value

A numeric vector of length two. Gradient of the proportion mediated with respect to pnde and tnie.

---

new_regmedint *Low level constructor for a regmedint S3 class object.*

Description

This is not a user function and meant to be executed within the regmedint function after validatingthe arguments.

Usage

```
new_regmedint(
  data,
  yvar,
  avar,
  mvar,
  cvar,
  EMM_AC_Mmodel,
  EMM_AC_Ymodel,
  EMM_MC,
  eventvar,
  a0,
  a1,
  m_cde,
  c_cond,
  yreg,
```

```
  mreg,
  interaction,
  casecontrol
)
```

Arguments

data	Data frame containing the relevant variables.
yvar	A character vector of length 1. Outcome variable name. It should be the time variable for survival outcomes.
avar	A character vector of length 1. Treatment variable name.
mvar	A character vector of length 1. Mediator variable name.
cvar	A character vector of length > 0. Covariate names. Use NULL if there is no covariate. However, this is a highly suspicious situation. Even if avar is randomized, mvar is not. Thus, there should usually be some confounder(s) to account for the common cause structure (confounding) between mvar and yvar.
EMM_AC_Mmodel	A character vector of length > 0. Effect modifiers names. The C in AxC product term in mediator model. Use NULL if there is no covariate.
EMM_AC_Ymodel	A character vector of length > 0. Effect modifiers names. The C in AxC product term in outcome model. Use NULL if there is no covariate.
EMM_MC	A character vector of length > 0. Effect modifiers names. The C in MxC product term in mediator model. Use NULL if there is no covariate.
eventvar	An character vector of length 1. Only required for survival outcome regression models. Note that the coding is 1 for event and 0 for censoring, following the R survival package convention.
a0	A numeric vector of length 1. Reference level of treatment variable that is considered "untreated" or "unexposed".
a1	A numeric vector of length 1.
m_cde	A numeric vector of length 1. Mediator level at which controlled direct effect is evaluated at.
c_cond	A numeric vector of the same length as cvar. Covariate vector at which conditional effects are evaluated at.
yreg	A character vector of length 1. Outcome regression type: "linear", "logistic", "loglinear", "poisson", "negbin", "survCox", "survAFT_exp", or "survAFT_weibull".
mreg	A character vector of length 1. Mediator regression type: "linear" or "logistic".
interaction	A logical vector of length 1. Default to TRUE. Whether to include a mediator-treatment interaction term in the outcome regression model.
casecontrol	A logical vector of length 1. Default to FALSE. Whether data comes from a case-control study.

Value

A regmedint object.

`print.regmedint` *print method for regmedint object*

Description

Print the `mreg_fit`, `yreg_fit`, and the mediation analysis effect estimates.

Usage

```
## S3 method for class 'regmedint'
print(
  x,
  a0 = NULL,
  a1 = NULL,
  m_cde = NULL,
  c_cond = NULL,
  args_mreg_fit = list(),
  args_yreg_fit = list(),
  ...
)
```

Arguments

`x`	An object of the `regmedint` class.
`a0`	A numeric vector of length one.
`a1`	A numeric vector of length one.
`m_cde`	A numeric vector of length one. A mediator value at which the controlled direct effect (CDE) conditional on the adjustment covariates is evaluated. If not provided, the default value supplied to the call to `regmedint` will be used. Only the CDE is affected.
`c_cond`	A numeric vector as long as the number of adjustment covariates. A set of covariate values at which the conditional natural effects are evaluated.
`args_mreg_fit`	A named list of argument to be passed to the method for the `mreg_fit` object.
`args_yreg_fit`	A named list of argument to be passed to the method for the `mreg_fit` object.
`...`	For compatibility with the generic. Ignored.

Value

Invisibly return the `regmedint` class object as is.

Examples

```
library(regmedint)
data(vv2015)
regmedint_obj <- regmedint(data = vv2015,
                           ## Variables
                           yvar = "y",
                           avar = "x",
                           mvar = "m",
                           cvar = c("c"),
```

```
                            eventvar = "event",
                            ## Values at which effects are evaluated
                            a0 = 0,
                            a1 = 1,
                            m_cde = 1,
                            c_cond = 0.5,
                            ## Model types
                            mreg = "logistic",
                            yreg = "survAFT_weibull",
                            ## Additional specification
                            interaction = TRUE,
                            casecontrol = FALSE)
## Implicit printing
regmedint_obj
## Explicit printing
print(regmedint_obj)
## Evaluate at different values
print(regmedint_obj, m_cde = 0, c_cond = 1)
```

`print.summary_regmedint` *Print method for summary objects from* `summary.regmedint`

Description

Print results contained in a `summary_regmedint` object with additional explanation regarding the evaluation settings.

Usage

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

Arguments

`x`	An object of the class `summary_regmedint`.
`...`	For compatibility with the generic function.

Value

Invisibly return the first argument.

Examples

```
library(regmedint)
data(vv2015)
regmedint_obj <- regmedint(data = vv2015,
                            ## Variables
                            yvar = "y",
                            avar = "x",
                            mvar = "m",
                            cvar = c("c"),
```

```
                            eventvar = "event",
                            ## Values at which effects are evaluated
                            a0 = 0,
                            a1 = 1,
                            m_cde = 1,
                            c_cond = 0.5,
                            ## Model types
                            mreg = "logistic",
                            yreg = "survAFT_weibull",
                            ## Additional specification
                            interaction = TRUE,
                            casecontrol = FALSE)
## Implicit printing
summary(regmedint_obj)
## Explicit printing
print(summary(regmedint_obj))
```

`prop_med_yreg_linear` *Calculate the proportion mediated for yreg linear.*

Description

Calculate the proportion mediated on the mean difference scale.

Usage

```
prop_med_yreg_linear(pnde, tnie)
```

Arguments

pnde	Pure natural direct effect.
tnie	Total natural indirect effect.

Value

Proportion mediated value.

`prop_med_yreg_logistic` *Calculate the proportion mediated for yreg logistic.*

Description

Calculate the approximate proportion mediated on the risk difference scale.

Usage

```
prop_med_yreg_logistic(pnde, tnie)
```

Arguments

pnde	Pure natural direct effect on the log scale.
tnie	Total natural indirect effect on the log scale.

Value

Proportion mediated value.

---

regmedint *regmedint: A package for regression-based causal mediation analysis*

Description

The package is a simple R implementation of the SAS macro as described in Valeri & VanderWeele 2013 and Valeri & VanderWeele 2015 https://www.hsph.harvard.edu/tyler-vanderweele/tools-and-tutorials/.

This is a user-interface for regression-based causal mediation analysis as described in Valeri & VanderWeele 2013 and Valeri & VanderWeele 2015.

Usage

```
regmedint(
  data,
  yvar,
  avar,
  mvar,
  cvar,
  EMM_AC_Mmodel = NULL,
  EMM_AC_Ymodel = NULL,
  EMM_MC = NULL,
  eventvar = NULL,
  a0,
  a1,
  m_cde,
  c_cond,
  mreg,
  yreg,
  interaction = TRUE,
  casecontrol = FALSE,
  na_omit = FALSE
)
```

Arguments

data	Data frame containing the relevant variables.
yvar	A character vector of length 1. Outcome variable name. It should be the time variable for survival outcomes.
avar	A character vector of length 1. Treatment variable name.
mvar	A character vector of length 1. Mediator variable name.

cvar	A character vector of length > 0. Covariate names. Use NULL if there is no covariate. However, this is a highly suspicious situation. Even if avar is randomized, mvar is not. Thus, there should usually be some confounder(s) to account for the common cause structure (confounding) between mvar and yvar.
EMM_AC_Mmodel	A character vector of length > 0. Effect modifiers names. The C in AxC product term in mediator model. Use NULL if there is no covariate.
EMM_AC_Ymodel	A character vector of length > 0. Effect modifiers names. The C in AxC product term in outcome model. Use NULL if there is no covariate.
EMM_MC	A character vector of length > 0. Effect modifiers names. The C in MxC product term in mediator model. Use NULL if there is no covariate.
eventvar	An character vector of length 1. Only required for survival outcome regression models. Note that the coding is 1 for event and 0 for censoring, following the R survival package convention.
a0	A numeric vector of length 1. Reference level of treatment variable that is considered "untreated" or "unexposed".
a1	A numeric vector of length 1.
m_cde	A numeric vector of length 1. Mediator level at which controlled direct effect is evaluated at.
c_cond	A numeric vector of the same length as cvar. Covariate vector at which conditional effects are evaluated at.
mreg	A character vector of length 1. Mediator regression type: "linear" or "logistic".
yreg	A character vector of length 1. Outcome regression type: "linear", "logistic", "loglinear", "poisson", "negbin", "survCox", "survAFT_exp", or "survAFT_weibull".
interaction	A logical vector of length 1. Default to TRUE. Whether to include a mediator-treatment interaction term in the outcome regression model.
casecontrol	A logical vector of length 1. Default to FALSE. Whether data comes from a case-control study.
na_omit	A logical vector of length 1. Default to FALSE. Whether to use na.omit() function in stats package to remove NAs in columns of interest before fitting the models.

Value

regmedint object, which is a list containing the mediator regression object, the outcome regression object, and the regression-based mediation results.

Fitting models

Use the regmedint function to fit models and set up regression-based causal mediation analysis.

Examining results

Several methods are available to examine the regmedint object. print summary coef confint FIXME: Document once implemented.

Examples

```
library(regmedint)
data(vv2015)
regmedint_obj <- regmedint(data = vv2015,
                           ## Variables
                           yvar = "y",
                           avar = "x",
                           mvar = "m",
                           cvar = c("c"),
                           eventvar = "event",
                           ## Values at which effects are evaluated
                           a0 = 0,
                           a1 = 1,
                           m_cde = 1,
                           c_cond = 0.5,
                           ## Model types
                           mreg = "logistic",
                           yreg = "survAFT_weibull",
                           ## Additional specification
                           interaction = TRUE,
                           casecontrol = FALSE)
summary(regmedint_obj)
```

---

report_missing *Report variables with missing data*

Description

Report the number of missing observations for each variables of interest relevant for the analysis

Usage

```
report_missing(data, yvar, avar, mvar, cvar, eventvar)
```

Arguments

data	Data frame containing the relevant variables.
yvar	A character vector of length 1. Outcome variable name. It should be the time variable for survival outcomes.
avar	A character vector of length 1. Treatment variable name.
mvar	A character vector of length 1. Mediator variable name.
cvar	A character vector of length > 0. Covariate names. Use NULL if there is no covariate. However, this is a highly suspicious situation. Even if avar is randomized, mvar is not. Thus, there should usually be some confounder(s) to account for the common cause structure (confounding) between mvar and yvar.
eventvar	An character vector of length 1. Only required for survival outcome regression models. Note that the coding is 1 for event and 0 for censoring, following the R survival package convention.

Value

No return value, called for side effects.

summary.regmedint *summary method for regmedint object*

Description

Summarize the mreg_fit, yreg_fit, and the mediation analysis effect estimates.

Usage

```
## S3 method for class 'regmedint'
summary(
  object,
  a0 = NULL,
  a1 = NULL,
  m_cde = NULL,
  c_cond = NULL,
  args_mreg_fit = list(),
  args_yreg_fit = list(),
  exponentiate = FALSE,
  level = 0.95,
  ...
)
```

Arguments

object	An object of the regmedint class.
a0	A numeric vector of length one.
a1	A numeric vector of length one.
m_cde	A numeric vector of length one. A mediator value at which the controlled direct effect (CDE) conditional on the adjustment covariates is evaluated. If not provided, the default value supplied to the call to regmedint will be used. Only the CDE is affected.
c_cond	A numeric vector as long as the number of adjustment covariates. A set of covariate values at which the conditional natural effects are evaluated.
args_mreg_fit	A named list of argument to be passed to the method for the mreg_fit object.
args_yreg_fit	A named list of argument to be passed to the method for the mreg_fit object.
exponentiate	Whether to add exponentiated point and confidence limit estimates. When yreg = "linear", it is ignored.
level	Confidence level for the confidence intervals.
...	For compatibility with the generic. Ignored.

Value

A summary_regmedint object, which is a list containing the summary objects of the mreg_fit and the yreg_fit as well as the mediation analysis results.

Examples

```
library(regmedint)
data(vv2015)
regmedint_obj <- regmedint(data = vv2015,
                           ## Variables
                           yvar = "y",
                           avar = "x",
                           mvar = "m",
                           cvar = c("c"),
                           eventvar = "event",
                           ## Values at which effects are evaluated
                           a0 = 0,
                           a1 = 1,
                           m_cde = 1,
                           c_cond = 0.5,
                           ## Model types
                           mreg = "logistic",
                           yreg = "survAFT_weibull",
                           ## Additional specification
                           interaction = TRUE,
                           casecontrol = FALSE)
## Detailed result with summary
summary(regmedint_obj)
## Add exponentiate results for non-linear outcome models
summary(regmedint_obj, exponentiate = TRUE)
## Evaluate at different values
summary(regmedint_obj, m_cde = 0, c_cond = 1)
## Change confidence level
summary(regmedint_obj, m_cde = 0, c_cond = 1, level = 0.99)
```

---

summary.regmedint_mod_poisson

Summary with robust sandwich variance estimator for modified Poisson

---

Description

This is a version of `summary.glm` modified to use the robust variance estimator `sandwich`.

Usage

```
## S3 method for class 'regmedint_mod_poisson'
summary(object, ...)
```

Arguments

`object`	A model object of the class `regmedint_mod_poisson`
`...`	For compatibility with the generic.

Value

An object of the class `summary.glm`

theta_hat *Create a vector of coefficients from the outcome model (yreg)*

Description

This function extracts coef from yreg_fit and 3s with zeros appropriately to create a named vector consistently having the following elements: (Intercept): A zero element is added for yreg = "survCox" for which no intercept is estimated (the baseline hazard is left unspecified). avar mvar avar:mvar: A zero element is added when interaction = FALSE. cvar: This part is eliminated when cvar = NULL. EMM_AC_Ymodel: This part is eliminated when EMM_AC_Ymodel = NULL. EMM_MC: This part is eliminated when EMM_MC = NULL.

Usage

```
theta_hat(
  yreg,
  yreg_fit,
  avar,
  mvar,
  cvar,
  EMM_AC_Ymodel = NULL,
  EMM_MC = NULL,
  interaction
)
```

Arguments

yreg	A character vector of length 1. Outcome regression type: "linear", "logistic", "loglinear", "poisson", "negbin", "survCox", "survAFT_exp", or "survAFT_weibull".
yreg_fit	Model fit object for yreg (outcome model).
avar	A character vector of length 1. Treatment variable name.
mvar	A character vector of length 1. Mediator variable name.
cvar	A character vector of length > 0. Covariate names. Use NULL if there is no covariate. However, this is a highly suspicious situation. Even if avar is randomized, mvar is not. Thus, there should usually be some confounder(s) to account for the common cause structure (confounding) between mvar and yvar.
EMM_AC_Ymodel	A character vector of length > 0. Effect modifiers names. The C in AxC product term in outcome model. Use NULL if there is no covariate.
EMM_MC	A character vector of length > 0. Effect modifiers names. The C in MxC product term in mediator model. Use NULL if there is no covariate.
interaction	A logical vector of length 1. Default to TRUE. Whether to include a mediator-treatment interaction term in the outcome regression model.

Value

A named numeric vector of coefficients.

validate_args *Validate arguments to regmedint before passing to other functions*

Description

Internal functions (usually) do not validate arguments, thus, we need to make sure informative errors are raised when the arguments are not safe for subsequent computation.

Usage

```
validate_args(
  data,
  yvar,
  avar,
  mvar,
  cvar,
  EMM_AC_Mmodel,
  EMM_AC_Ymodel,
  EMM_MC,
  eventvar,
  a0,
  a1,
  m_cde,
  c_cond,
  mreg,
  yreg,
  interaction,
  casecontrol
)
```

Arguments

data	Data frame containing the relevant variables.
yvar	A character vector of length 1. Outcome variable name. It should be the time variable for survival outcomes.
avar	A character vector of length 1. Treatment variable name.
mvar	A character vector of length 1. Mediator variable name.
cvar	A character vector of length > 0. Covariate names. Use NULL if there is no covariate. However, this is a highly suspicious situation. Even if avar is randomized, mvar is not. Thus, there should usually be some confounder(s) to account for the common cause structure (confounding) between mvar and yvar.
EMM_AC_Mmodel	A character vector of length > 0. Effect modifiers names. The C in AxC product term in mediator model. Use NULL if there is no covariate.
EMM_AC_Ymodel	A character vector of length > 0. Effect modifiers names. The C in AxC product term in outcome model. Use NULL if there is no covariate.
EMM_MC	A character vector of length > 0. Effect modifiers names. The C in MxC product term in mediator model. Use NULL if there is no covariate.

eventvar	An character vector of length 1. Only required for survival outcome regression models. Note that the coding is 1 for event and 0 for censoring, following the R survival package convention.
a0	A numeric vector of length 1. Reference level of treatment variable that is considered "untreated" or "unexposed".
a1	A numeric vector of length 1.
m_cde	A numeric vector of length 1. Mediator level at which controlled direct effect is evaluated at.
c_cond	A numeric vector of the same length as cvar. Covariate vector at which conditional effects are evaluated at.
mreg	A character vector of length 1. Mediator regression type: "linear" or "logistic".
yreg	A character vector of length 1. Outcome regression type: "linear", "logistic", "loglinear", "poisson", "negbin", "survCox", "survAFT_exp", or "survAFT_weibull".
interaction	A logical vector of length 1. Default to TRUE. Whether to include a mediator-treatment interaction term in the outcome regression model.
casecontrol	A logical vector of length 1. Default to FALSE. Whether data comes from a case-control study.

Value

No return value, called for side effects.

---

validate_regmedint *Validate soundness of a regmedint object.*

Description

Check the structure of a proposed regmedint object for soundness.

Usage

```
validate_regmedint(x)
```

Arguments

x	A regmedint object.

Value

No return value, called for side effects.

vcov.regmedint *Extract variance estimates in the vcov form.*

Description

Extract variance estimates evaluated at a0, a1, m_cde, and c_cond.

Usage

```
## S3 method for class 'regmedint'
vcov(object, a0 = NULL, a1 = NULL, m_cde = NULL, c_cond = NULL, ...)
```

Arguments

object	An object of the regmedint class.
a0	A numeric vector of length one.
a1	A numeric vector of length one.
m_cde	A numeric vector of length one. A mediator value at which the controlled direct effect (CDE) conditional on the adjustment covariates is evaluated. If not provided, the default value supplied to the call to regmedint will be used. Only the CDE is affected.
c_cond	A numeric vector as long as the number of adjustment covariates. A set of covariate values at which the conditional natural effects are evaluated.
...	For compatibility with the generic. Ignored.

Value

A numeric matrix with the diagonals populated with variance estimates. Off-diagnonals are NA since these are not estimated.

Examples

```
library(regmedint)
data(vv2015)
regmedint_obj <- regmedint(data = vv2015,
                           ## Variables
                           yvar = "y",
                           avar = "x",
                           mvar = "m",
                           cvar = c("c"),
                           eventvar = "event",
                           ## Values at which effects are evaluated
                           a0 = 0,
                           a1 = 1,
                           m_cde = 1,
                           c_cond = 0.5,
                           ## Model types
                           mreg = "logistic",
                           yreg = "survAFT_weibull",
                           ## Additional specification
                           interaction = TRUE,
```

```
                            casecontrol = FALSE)
vcov(regmedint_obj)
## Evaluate at different values
vcov(regmedint_obj, m_cde = 0, c_cond = 1)
```

`vcov.regmedint_mod_poisson` *Robust sandwich variance estimator for modified Poisson*

Description

Provide robust sandwich variance-covariance estimate using `sandwich`.

Usage

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

Arguments

`object`	A model object of the class `regmedint_mod_poisson`
`...`	For compatibility with the generic.

Value

A variance-covariance matrix using the `sandwich`.

`vv2015` *Example dataset from Valeri and VanderWeele 2015.*

Description

An example dataset from Valeri and VanderWeele (2015) <doi:10.1097/EDE.0000000000000253>.

Usage

```
vv2015
```

Format

A tibble with 100 rows and 7 variables:

id Positive integer id.

x Binary treatment assignment variable.

m Binary mediator variable.

y Time to event outcome variable.

cens Binary censoring indicator. Censored is 1.

c Continuous confounder variable.

event Binary event indicator. Event is 1.

Source

https://www.hsph.harvard.edu/tyler-vanderweele/tools-and-tutorials/

Index

∗ **datasets**
vv2015, 28

beta_hat, 2

calc_myreg, 3
calc_myreg_mreg_linear_yreg_linear, 4
calc_myreg_mreg_linear_yreg_logistic, 5
calc_myreg_mreg_logistic_yreg_linear, 6
calc_myreg_mreg_logistic_yreg_logistic, 7
coef, *2*, *24*
coef.regmedint, 8
coef.summary_regmedint, 9
confint.regmedint, 10
coxph, *13*

fit_mreg, *3–7*, 11
fit_yreg, *3–6*, *8*, 12

glm, *11*, *13*
glm.nb, *13*
grad_prop_med_yreg_linear, 13
grad_prop_med_yreg_logistic, 14

lm, *11*, *13*

new_regmedint, 14

print.regmedint, 16
print.summary_regmedint, 17
prop_med_yreg_linear, 18
prop_med_yreg_logistic, 18

regmedint, *8*, *10, 11*, *16*, 19, *22*, *27*
report_missing, 21

sandwich, *23*, *28*
summary.glm, *23*
summary.regmedint, *17*, 22
summary.regmedint_mod_poisson, 23
survreg, *13*

theta_hat, 24

validate_args, 25
validate_regmedint, 26
vcov.regmedint, 27
vcov.regmedint_mod_poisson, 28
vv2015, 28