Package ‘regmedint’

January 13, 2024

Title  Regression-Based Causal Mediation Analysis with Interaction and Effect Modification Terms

Version  1.0.1

Description  This is an extension of the regression-based causal mediation analysis first proposed by Valeri and VanderWeele (2013) <doi:10.1037/a0031034> and Valeri and VanderWeele (2015) <doi:10.1097/EDE.0000000000000253>. It supports including effect measure modification by covariates(treatment-covariate and mediator-covariate product terms in mediator and outcome regression models) as proposed by Li et al (2023) <doi:10.1097/EDE.0000000000001643>. It also accommodates the original 'SAS' macro and 'PROC CAUSALMED' procedure in 'SAS' when there is no effect measure modification. 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, testthat, tidyverse, magic, formattable, kableExtra

RoxygenNote  7.2.3

VignetteBuilder  knitr

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

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

Depends  R (>= 2.10)

NeedsCompilation  no

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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_mreg (this part is eliminated when emm_ac_mreg = NULL).

Usage

beta_hat(mreg, mreg_fit, avar, cvar, emm_ac_mreg = NULL)
calc_myreg

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 are usually some confounder(s) to account for the common cause structure (confounding) between mvar and yvar.
em_mreg A character vector of length > 0. Effect modifiers names. The covariate vector in treatment-covariate product term in the mediator model.

Value

A named numeric vector of coefficients.

calc_myreg Return mediation analysis functions given mediator and outcome models specifications.

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_mreg,
  emm_ac_yreg,
  emm_mc_yreg,
  interaction
)

Arguments

mreg A character vector of length 1. Mediator regression type: "linear" or "logistic".
mreg_fit Model fit from fit_mreg
calc_myreg_mreg_linear_yreg_linear

A character vector of length 1. Outcome regression type: "linear", "logistic", "loglinear", "poisson", "negbin", "survCox", "survAFT_exp", or "survAFT_weibull".

A character vector of length 1. Treatment variable name.

A character vector of length 1. Mediator variable name.

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 are usually some confounder(s) to account for the common cause structure (confounding) between mvar and yvar.

A character vector of length > 0. Effect modifiers names. The covariate vector in treatment-covariate product term in the mediator model.

A character vector of length > 0. Effect modifiers names. The covariate vector in treatment-covariate product term in the outcome model.

A character vector of length > 0. Effect modifiers names. The covariate vector in mediator-covariate product term in outcome model.

A logical vector of length 1. The presence of treatment-mediator interaction in the outcome model. Default to TRUE.

Value

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

Description

Construct functions for the conditional effect estimates and their standard errors in the mreg linear / yreg linear setting. Internally, this function deconstructs model objects and feeds parameter estimates 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_mreg,
  emm_ac_yreg,
  emm_mc_yreg,
  interaction
)
calc_myreg_mreg_linear_yreg_logistic

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 are usually some confounder(s) to account for the common cause structure (confounding) between `mvar` and `yvar`.
- **emm_ac_mreg**: A character vector of length > 0. Effect modifiers names. The covariate vector in treatment-covariate product term in the mediator model.
- **emm_ac_yreg**: A character vector of length > 0. Effect modifiers names. The covariate vector in treatment-covariate product term in the outcome model.
- **emm_mc_yreg**: A character vector of length > 0. Effect modifiers names. The covariate vector in mediator-covariate product term in outcome model.
- **interaction**: A logical vector of length 1. The presence of treatment-mediator interaction in the outcome model. Default to TRUE.

Value

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

Description

Construct functions for the conditional effect estimates and their standard errors in the mreg linear / yreg logistic setting. Internally, this function deconstructs model objects and feeds parameter estimates 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_mreg,
  emm_ac_yreg,
  emm_mc_yreg,
  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 are usually some confounder(s) to account for the common cause structure (confounding) between `mvar` and `yvar`.
- **emm_ac_mreg**: A character vector of length > 0. Effect modifiers names. The covariate vector in treatment-covariate product term in the mediator model.
- **emm_ac_yreg**: A character vector of length > 0. Effect modifiers names. The covariate vector in treatment-covariate product term in the outcome model.
- **emm_mc_yreg**: A character vector of length > 0. Effect modifiers names. The covariate vector in mediator-covariate product term in outcome model.
- **interaction**: A logical vector of length 1. The presence of treatment-mediator interaction in the outcome model. Default to `TRUE`.

Value

A list containing 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 deconstructs model objects and feeds parameter estimates 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_mreg,
  emm_ac_yreg,
  emm_mc_yreg,
  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 are usually some confounder(s) to account for the common cause structure (confounding) between mvar and yvar.
emm_ac_mreg A character vector of length > 0. Effect modifiers names. The covariate vector in treatment-covariate product term in the mediator model.
emm_ac_yreg A character vector of length > 0. Effect modifiers names. The covariate vector in treatment-covariate product term in the outcome model.
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 deconstructs model objects and feeds parameter estimates 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_mreg, emm_ac_yreg, emm_mc_yreg, 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.
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 are usually some confounder(s) to account for the common cause structure (confounding) between mvar and yvar.

A character vector of length > 0. Effect modifiers names. The covariate vector in treatment-covariate product term in the mediator model.

A character vector of length > 0. Effect modifiers names. The covariate vector in treatment-covariate product term in the outcome model.

A character vector of length > 0. Effect modifiers names. The covariate vector in mediator-covariate product term in outcome model.

A logical vector of length 1. The presence of treatment-mediator interaction in the outcome model. Default to TRUE.

Value

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

description

Extract point estimates.

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 1

a1

A numeric vector of length 1

m_cde

A numeric vector of length 1 The 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 of the same length as cvar. 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

```r
library(regmedint)
data(vv2015)
regmedint_obj <- regmedint(data = vv2015,
  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**

```r
## 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 parameter 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.
confint.regmedint

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 1
a1 A numeric vector of length 1
m_cde A numeric vector of length 1 The 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 of the same length as cvar. 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 = TRUE)

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**

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

**Arguments**

- `mreg` A character vector of length 1. Mediator regression type: "linear" or "logistic".
- `data` Data frame containing the following 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 are usually some confounder(s) to account for the common cause structure (confounding) between `mvar` and `yvar`.
- `emm_ac_mreg` A character vector of length > 0. Effect modifiers names. The covariate vector in treatment-covariate product term in the mediator model.

**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

```r
fit_yreg(
  yreg,
  data,
  yvar,
  avar,
  mvar,
  cvar,
  emm_ac_yreg = NULL,
  emm_mc_yreg = NULL,
  eventvar,
  interaction
)
```

Arguments

- `data`: Data frame containing the following relevant variables.
- `yvar`: A character vector of length 1. Outcome variable name. It should be the time variable for the survival outcome.
- `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 are usually some confounder(s) to account for the common cause structure (confounding) between mvar and yvar.
- `emm_ac_yreg`: A character vector of length > 0. Effect modifiers names. The covariate vector in treatment-covariate product term in the outcome model.
- `emm_mc_yreg`: A character vector of length > 0. Effect modifiers names. The covariate vector in mediator-covariate product term in outcome model.
- `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. The presence of treatment-mediator interaction in the outcome model. Default to TRUE.

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 one 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

<table>
<thead>
<tr>
<th>Argument</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>pnde</td>
<td>A numeric vector of length one. Pure natural direct effect.</td>
</tr>
<tr>
<td>tnie</td>
<td>A numeric vector of length one. Total natural indirect effect.</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Argument</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>pnde</td>
<td>A numeric vector of length one. Pure natural direct effect.</td>
</tr>
<tr>
<td>tnie</td>
<td>A numeric vector of length one. Total natural indirect effect.</td>
</tr>
</tbody>
</table>
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 validating the arguments.

Usage

```r
new_regmedint(
  data,
  yvar,
  avar,
  mvar,
  cvar,
  emm_ac_mreg,
  emm_ac_yreg,
  emm_mc_yreg,
  eventvar,
  a0,
  a1,
  m_cde,
  c_cond,
  yreg,
  mreg,
  interaction,
  casecontrol
)
```

Arguments

data      Data frame containing the following relevant variables.
yvar      A character vector of length 1. Outcome variable name. It should be the time variable for the survival outcome.
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 are usually some confounder(s) to account for the common cause structure (confounding) between mvar and yvar.
emm_ac_mreg  A character vector of length > 0. Effect modifiers names. The covariate vector in treatment-covariate product term in the mediator model.

emm_ac_yreg  A character vector of length > 0. Effect modifiers names. The covariate vector in treatment-covariate product term in the outcome model.

emm_mc_yreg  A character vector of length > 0. Effect modifiers names. The covariate vector in mediator-covariate product term in outcome model.

eventvar  An 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. The 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 levels at which natural direct and indirect 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. The presence of treatment-mediator interaction in the outcome model. Default to TRUE.

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,
)
print.regmedint

args_mreg_fit = list(),
args_yreg_fit = list(),
...
)

Arguments

  x  An object of the regmedint class.
  a0  A numeric vector of length 1
  a1  A numeric vector of length 1
  m_cde  A numeric vector of length 1 The mediator value at which the controlled direct
          effect (CDE) conditional on the adjustment covariates is evaluated. If not pro-
          vided, the default value supplied to the call to regmedint will be used. Only the
          CDE is affected.
  c_cond  A numeric vector of the same length as cvar. 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)

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,
prop_med_yreg_logistic

```
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.
**Description**

The package is an R implementation of regression-based closed-form causal mediation as originally described in Valeri & VanderWeele 2013 and Valeri & VanderWeele 2015 [https://www.hsph.harvard.edu/tyler-vanderweele/tools-and-tutorials/](https://www.hsph.harvard.edu/tyler-vanderweele/tools-and-tutorials/). The earlier version is a sister program of the SAS macro. The current extended version (version 1.0 and later) supports effect modification by covariates (treatment-covariate and mediator-covariate product terms) in mediator and outcome models.

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

**Usage**

```r
regmedint(
  data,
  yvar,
  avar,
  mvar,
  cvar,
  emm_ac_mreg = NULL,
  emm_ac_yreg = NULL,
  emm_mc_yreg = NULL,
  eventvar = NULL,
  a0,
  a1,
  m_cde,
  c_cond,
  mreg,
  yreg,
  interaction = TRUE,
  casecontrol = FALSE,
  na_omit = FALSE
)
```

**Arguments**

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

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 are usually some confounder(s) to account for the common cause structure (confounding) between mvar and yvar.

emm_ac_mreg A character vector of length > 0. Effect modifiers names. The covariate vector in treatment-covariate product term in the mediator model.

emm_ac_yreg A character vector of length > 0. Effect modifiers names. The covariate vector in treatment-covariate product term in the outcome model.

emm_mc_yreg A character vector of length > 0. Effect modifiers names. The covariate vector in mediator-covariate product term in outcome model.

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. The 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 levels at which natural direct and indirect 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. The presence of treatment-mediator interaction in the outcome model. Default to TRUE.

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 remove NAs in the 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
Examples

```r
library(regmedint)
data(vv2015)
regmedint_obj1 <- regmedint(data = vv2015,
  yvar = "y",
  avar = "x",
  mvar = "m",
  cvar = c("c"),
  eventvar = "event",
  a0 = 0,
  a1 = 1,
  m_cde = 1,
  c_cond = 3,
  mreg = "logistic",
  yreg = "survAFT_weibull",
  interaction = TRUE,
  casecontrol = FALSE)
summary(regmedint_obj1)

regmedint_obj2 <- regmedint(data = vv2015,
  yvar = "y",
  avar = "x",
  mvar = "m",
  cvar = c("c"),
  emm_ac_mreg = c("c"),
  emm_ac_yreg = c("c"),
  emm_mc_yreg = c("c"),
  eventvar = "event",
  a0 = 0,
  a1 = 1,
  m_cde = 1,
  c_cond = 3,
  mreg = "logistic",
  yreg = "survAFT_weibull",
  interaction = TRUE,
  casecontrol = FALSE)
summary(regmedint_obj2)
```
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 following relevant variables.
yvar         A character vector of length 1. Outcome variable name. It should be the time variable for the survival outcome.
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 are usually 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

```r
# 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 1
- **a1**: A numeric vector of length 1
- **m_cde**: A numeric vector of length 1 The 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 of the same length as `cvar`. 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 `yreg_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

```r
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**

```r
## 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`
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_yreg (this part is eliminated when emm_ac_yreg = NULL), emm_mc_yreg (this part is eliminated when emm_mc_yreg = NULL).

Usage

theta_hat(
  yreg,
  yreg_fit,
  avar,
  mvar,
  cvar,
  emm_ac_yreg = NULL,
  emm_mc_yreg = 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 are usually some confounder(s) to account for the common cause structure (confounding) between mvar and yvar.
emm_ac_yreg A character vector of length > 0. Effect modifiers names. The covariate vector in treatment-covariate product term in the outcome model.
emm_mc_yreg A character vector of length > 0. Effect modifiers names. The covariate vector in mediator-covariate product term in outcome model.
interaction A logical vector of length 1. The presence of treatment-mediator interaction in the outcome model. Default to TRUE.

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**

```r
validate_args(data,
              yvar,
              avar,
              mvar,
              cvar,
              emm_ac_mreg,
              emm_ac_yreg,
              emm_mc_yreg,
              eventvar,
              a0,
              a1,
              m_cde,
              c_cond,
              mreg,
              yreg,
              interaction,
              casecontrol)
```

**Arguments**

- `data`  Data frame containing the following relevant variables.
- `yvar`  A character vector of length 1. Outcome variable name. It should be the time variable for the survival outcome.
- `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 are usually some confounder(s) to account for the common cause structure (confounding) between `mvar` and `yvar`.
- `emm_ac_mreg`  A character vector of length > 0. Effect modifiers names. The covariate vector in treatment-covariate product term in the mediator model.
- `emm_ac_yreg`  A character vector of length > 0. Effect modifiers names. The covariate vector in treatment-covariate product term in the outcome model.
emmc_yreg  A character vector of length > 0. Effect modifers names. The covariate vector in mediator-covariate product term in outcome model.

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. The 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 levels at which natural direct and indirect 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. The presence of treatment-mediator interaction in the outcome model. Default to TRUE.

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

```r
# 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 1
- `a1`: A numeric vector of length 1
- `m_cde`: A numeric vector of length 1 The 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 of the same length as `cvar`. 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-diagonals are NA since these are not estimated.

Examples

```r
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
```
```r
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**

```r
## 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**


**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/
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