# Package ‘sensmediation’

June 3, 2019

**Title**  Parametric Estimation and Sensitivity Analysis of Direct and Indirect Effects

**Version**  0.3.0

**Date**  2019-05-28

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**Description**  We implement functions to estimate and perform sensitivity analysis to unobserved confounding of direct and indirect effects introduced in Lindmark, de Luna and Eriksen (2018) <doi:10.1002/sim.7620>. The estimation and sensitivity analysis are parametric, based on probit and/or linear regression models. Sensitivity analysis is implemented for unobserved confounding of the exposure-mediator, mediator-outcome and exposure-outcome relationships.

**Depends**  R (>= 3.5.0)

**Imports**  maxLik (>= 1.3-4), mvtnorm (>= 1.0-8), stats

**License**  GPL-2

**Encoding**  UTF-8

**LazyData**  true

**RoxygenNote**  6.1.1

**Collate**  'calc.effects.R' 'coefs.sensmed.R' 'data.R'

 'mediationmethods.R' 'sensmediation.R'

**Suggests**  testthat (>= 2.1.0)

**NeedsCompilation**  no

**Repository**  CRAN

**Date/Publication**  2019-06-03 08:40:03 UTC

**R topics documented:**

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calc.effects

Function for estimation of natural direct and indirect effects and sensitivity analysis for unobserved mediator-outcome confounding

description

Function to estimate natural direct and indirect effect estimates and standard errors (using the delta method) based on parametric regression models and perform sensitivity analysis for unobserved confounding. Intended to be called through sensmediation (or more.effects), not on its own.

usage

calc.effects(ML.object, type = "my", exp.name, med.name, covariates = NULL, alt.decomposition = FALSE, exp.value = 1, control.value = 0, med.model = NULL, out.model = NULL)

arguments

ML.object object from coefs.sensmed

type the type of confounding for which the sensitivity analysis is to be performed. type = "my", the default, corresponds to unobserved mediator-outcome confounding, type = "zm" to exposure-mediator confounding and type = "zy" to exposure-outcome confounding.

exp.name A character string indicating the name of the exposure variable used in the models.

med.name A character string indicating the name of the mediator used in the models.

covariates if conditional effects are to be estimated the list of covariate values. Covariates not specified are marginalized over. For more information, see sensmediation.

alt.decomposition logical indicating whether alternative definitions of the direct and indirect effects should be used (for more information, see sensmediation).

exp.value value of the exposure variable used as the exposure condition, default is 1.
calc.effects

control.value  value of the exposure variable used as the control (unexposed) condition, default is 0.
med.model     If type = "zy", fitted glm model object representing the mediator model at the basis of the estimation.
out.model     If type = "zm", fitted glm model object representing the outcome model at the basis of the estimation.

Value

A list with elements:

effects       A list with elements NIE and NDE, row matrices with the estimated NIE and NDE (or NIE* and NDE* if alt.decomposition = TRUE) for each value of the sensitivity parameter Rho.
std.errs      A list with elements se.nie and se.nde, row matrices with the estimated standard errors for the natural direct and indirect effects for the different values of the sensitivity parameter Rho.
betas         list of the estimated mediator model parameters over Rho, with
               • beta0 Intercept
               • beta1 Exposure
               • beta2 Covariates
               • beta3 Exposure-covariate interactions
Components that are not included in the input mediator model are set to 0.

thetas        list of the estimated outcome model parameters over Rho, with
               • theta0 Intercept
               • theta1 Exposure
               • theta2 Mediator
               • theta3 Exposure-mediator interaction
               • theta4 Covariates
               • theta5 Exposure-covariate interactions
               • theta6 Mediator-covariate interactions
               • theta7 Exposure-mediator-covariate interactions
Components that are not included in the input outcome model are set to 0.

part.deriv    List with the partial derivatives of the NDE (Lambda), NIE (Gamma) and TE (Eta) wrt the mediator and outcome model parameters for each value of Rho

sigma.thetabeta a list with the joint covariance matrix of the outcome and mediator model parameters for each value of Rho. Note that the covariance matrix is constructed for all estimated parameters listed in betas and thetas but that components not included in the input mediator and outcome models are set to 0.
covariates    list of the covariate values that the effects are conditioned on.

Author(s)

Anita Lindmark
coefs.sensmed

ML estimation of regression parameters for calculation of direct and indirect effects under unobserved confounding

Description

This function gives ML estimates of the regression parameters used to calculate mediation effects and perform sensitivity analysis. The optimization is performed using `maxLik`, see Details for more information. Called by `sensmediation`.

Usage

coefs.sensmed(model.expl, model.resp, Rho, progress = TRUE, ...)

Arguments

- `model.expl`: Fitted `glm` model object. If sensitivity analysis to mediator-outcome confounding the mediator model. Otherwise the exposure model.
- `model.resp`: Fitted `glm` model object. If sensitivity analysis to exposure-mediator confounding the mediator model. Otherwise the outcome model.
- `Rho`: The sensitivity parameter vector. If `type="my"` the correlation between the error terms in the mediator and outcome models. If `type="zm"` the correlation between the error terms in the exposure and mediator models. If `type="zy"` the correlation between the error terms in the exposure and outcome models.
- `progress`: Logical, indicating whether or not the progress (i.e. the `proc.time` for each `Rho`) of the optimization will be output
- `...`: Additional arguments to be passed on to the `maxLik` function. Can be used to set the method and control arguments of the `maxLik` function.

Details

The maximization of the log-likelihood is performed using `maxLik`, the default is to use the Newton-Raphson method and an analytic gradient and Hessian.

Value

coefs.sensmed returns a list with elements:

- `call`: The matched call
- `coef`: A matrix with the estimated regression parameters for `model.resp` over the range of `Rho`. One column per value of `Rho`.
- `sigma.res.resp`: If `model.resp` is a linear regression model, the estimated standard deviation of the error term for each `Rho`.

See Also

`sensmediation`
If `model.expl` is a linear regression model, the estimated standard deviation of the error term for each Rho.

**Rho**

The sensitivity parameter vector.

**expl.coef**

A matrix with the estimated regression parameters for `model.expl` over the range of Rho. One column per value of Rho.

**model.expl**

The original fitted `glm` object of `model.expl`.

**model.resp**

The original fitted `glm` object of `model.resp`.

**X.expl**

The model matrix (see `model.matrix`) of `model.expl`.

**X.resp**

The model matrix (see `model.matrix`) of `model.resp`.

**outc.resp**

The outcome variable of `model.resp`.

**outc.expl**

The outcome variable of `model.expl`.

**sigmas**

A list with the estimated covariance matrices for the regression parameters of `model.resp` and `model.expl` over Rho.

**max.info**

Information about the maximization (whether or not the convergence was successful, message, method and number of iterations) for each Rho, see `maxLik` for more information.

**value**

The values of the loglikelihood function for the best set of regression parameters from the optimization for each Rho, see `maxLik`.

**Author(s)**

Anita Lindmark

**References**


**See Also**

`sensmediation`

**Examples**

```r
default: Not run:
# Example with data from Riksstroke (the Swedish stroke register)

data(RSdata)

# Probit mediator and outcome models:
med.model <- glm(lowered.consc ~ AF + age.cat + sex, data = RSdata,
                family = binomial(link = 'probit'))
out.model <- glm(cf NSmo ~ AF + lowered.consc + age.cat + sex, data = RSdata,
               family = binomial(link = 'probit'))

# Estimation of regression coefficients under different values of Rho
```
# Rho = correlation between error terms in mediator and outcome model:
coefs.MY <- coefs.sensmed(model.expl = m.model, model.resp = o.model, Rho = seq(0, 0.5, 0.1))
# Outcome model regression coefficients:
coefs.MY$coef

## End(Not run)

---

**effects**

*Functions to calculate natural direct and indirect effects.*

**Description**

Functions used to calculate natural direct and indirect effects based on the estimated regression parameters. Called by `calc.effects`. The functions are named according to the convention `eff."mediator model type""outcome model type"` where `b` stands for binary probit regression and `c` stands for linear regression.

**Usage**

```r
eff.bb(Rho, betas, thetas, x.med, x.out, alt.decomposition, exp.value, control.value)

eff.bc(Rho, betas, thetas, x.med, x.out, alt.decomposition, exp.value, control.value)

eff.cb(Rho, betas, thetas, sigma.eta, x.med, x.out, alt.decomposition, exp.value, control.value)

eff.cc(Rho, betas, thetas, x.med, x.out, alt.decomposition, exp.value, control.value)
```

**Arguments**

- **Rho**: The sensitivity parameter vector.
- **betas**: List of mediator regression parameters.
- **thetas**: List of outcome regression parameters.
- **x.med**: Mediator covariate matrix for which to calculate standard errors.
- **x.out**: Outcome covariate matrix for which to calculate standard errors.
- **alt.decomposition**: Logical indicating whether or not alternative definitions of the direct and indirect effects should be used.
- **exp.value**: Value of the exposure variable used as the exposure condition.
- **control.value**: Value of the exposure variable used as the control (unexposed) condition.
- **sigma.eta**: For a continuous mediator and binary outcome, matrix with the estimated residual standard deviation for the mediator model over the range of `Rho`. 

---
Analytic gradients of the loglikelihood functions for ML estimation of regression parameters

Description

Implementation of the analytic gradients of the loglikelihood functions for ML estimation of regression parameters for different combinations of exposure, mediator and outcome models. The functions are named according to the convention \texttt{grr."model.exp1 type"."model.resp type"}

Usage

\begin{verbatim}
grr.bb(par, Rho, X.exp1 = X.exp1, X.resp = X.resp, 
  outc.resp = outc.resp, outc.exp1 = outc.exp1)

grr.bc(par, Rho, X.exp1 = X.exp1, X.resp = X.resp, 
  outc.resp = outc.resp, outc.exp1 = outc.exp1)

grr.cb(par, Rho, X.exp1 = X.exp1, X.resp = X.resp, 
  outc.resp = outc.resp, outc.exp1 = outc.exp1)

grr.cc(par, Rho, X.exp1 = X.exp1, X.resp = X.resp, 
  outc.resp = outc.resp, outc.exp1 = outc.exp1)
\end{verbatim}

Arguments

\begin{itemize}
  \item \texttt{par} \hspace{1cm} Vector of parameter values.  
  \item \texttt{Rho} \hspace{1cm} The value of the sensitivity parameter.  
  \item \texttt{X.exp1} \hspace{1cm} The model matrix (see \texttt{model.matrix}) of \texttt{model.exp1}  
  \item \texttt{X.resp} \hspace{1cm} The model matrix (see \texttt{model.matrix}) of \texttt{model.resp}  
  \item \texttt{outc.exp1} \hspace{1cm} The outcome of \texttt{model.exp1}, a column matrix.  
  \item \texttt{outc.resp} \hspace{1cm} The outcome of \texttt{model.resp}, a vector.  
\end{itemize}

See Also

\begin{itemize}
  \item \texttt{coefs.sensmed} 
  \item \texttt{maxLik}
\end{itemize}
hess

Analytic Hessians of the loglikelihood functions for ML estimation of regression parameters

Description

Implementation of the analytic Hessians of the loglikelihood functions for ML estimation of regression parameters for different combinations of exposure, mediator and outcome models. The functions are named according to the convention hess."model.expl type""model.resp type" where b stands for binary probit regression and c stands for linear regression.

Usage

hess.bb(par, Rho, X.expl = X.expl, X.resp = X.resp, outc.resp = outc.resp, outc.expl = outc.expl)

hess.bc(par, Rho, X.expl = X.expl, X.resp = X.resp, outc.resp = outc.resp, outc.expl = outc.expl)

hess.cb(par, Rho, X.expl = X.expl, X.resp = X.resp, outc.resp = outc.resp, outc.expl = outc.expl)

hess.cc(par, Rho, X.expl = X.expl, X.resp = X.resp, outc.resp = outc.resp, outc.expl = outc.expl)

Arguments

par  Vector of parameter values.
Rho  The value of the sensitivity parameter.
X.expl  The model matrix (see model.matrix) of model.expl
X.resp  The model matrix (see model.matrix) of model.resp
outc.resp  The outcome of model.resp, a vector.
outc.expl  The outcome of model.expl, a column matrix.

See Also

coeffs.sensmed, maxLik
LogL

Implementation of loglikelihood functions for ML estimation of regression parameters

Description

Implementation of loglikelihood functions for ML estimation of regression parameters for different combinations of exposure, mediator and outcome models. The functions are named according to the convention LogL."model.expl type"."model.resp type" where b stands for binary probit regression and c stands for linear regression.

Usage

LogL.bb(par, Rho, X.expl = X.expl, X.resp = X.resp,
         outc.resp = outc.resp, outc.expl = outc.expl)

LogL.bc(par, Rho, X.expl = X.expl, X.resp = X.resp,
         outc.resp = outc.resp, outc.expl = outc.expl)

LogL.cb(par, Rho, X.expl = X.expl, X.resp = X.resp,
         outc.resp = outc.resp, outc.expl = outc.expl)

LogL.cc(par, Rho, X.expl = X.expl, X.resp = X.resp,
         outc.resp = outc.resp, outc.expl = outc.expl)

Arguments

par Vector of parameter values.
Rho The value of the sensitivity parameter.
X.expl The model matrix (see model.matrix) of model.expl
X.resp The model matrix (see model.matrix) of model.resp
outc.resp The outcome of model.resp, a vector.
outc.expl The outcome of model.expl, a column matrix.

See Also

coefs.sensmed, maxLik
ML

*Functions for ML estimation of regression parameters for sensitivity analysis*

**Description**

Functions for ML estimation of regression parameters for sensitivity analysis for different combinations of exposure, mediator and outcome models. The functions are named according to the convention `ML."model.expl type""model.resp type"` where `b` stands for binary probit regression and `c` stands for linear regression. The optimization is performed using `maxLik`. The functions are intended to be called through `coefsNsensmed`, not on their own.

**Usage**

- `ML.bb(model.expl, model.resp, Rho, progress = TRUE, ...)`
- `ML.bc(model.expl, model.resp, Rho, progress = TRUE, ...)`
- `ML.cb(model.expl, model.resp, Rho, progress = TRUE, ...)`
- `ML.cc(model.expl, model.resp, Rho, progress = TRUE, ...)`

**Arguments**

- `model.expl` Fitted `glm` model object (probit or linear). If sensitivity analysis to mediator-outcome confounding the mediator model. Otherwise the exposure model.
- `model.resp` Fitted `glm` model object (probit or linear). If sensitivity analysis to exposure-mediator confounding the mediator model. Otherwise the outcome model.
- `Rho` The sensitivity parameter vector. If `type="my"` the correlation between the error terms in the mediator and outcome models. If `type="zm"` the correlation between the error terms in the exposure and mediator models. If `type="zy"` the correlation between the error terms in the exposure and outcome models.
- `progress` Logical, indicating whether or not the progress (i.e. the `proc.time` for each `Rho`) of the optimization will be output
- `...` Additional arguments to be passed on to the `maxLik` function. Can be used to set the method and control arguments of the `maxLik` function.

**Value**

A list with elements:

- `coef` A matrix with the estimated regression parameters for `model.resp` over the range of `Rho`. One column per value of `Rho`.
- `Rho` The sensitivity parameter vector.
- `expl.coef` A matrix with the estimated regression parameters for `model.expl` over the range of `Rho`. One column per value of `Rho`. 
more.effects

model.expl the original fitted glm object of model.expl.
model.resp the original fitted glm object of model.resp.
X.expl The model matrix (see model.matrix) of model.expl
X.resp The model matrix (see model.matrix) of model.resp
outc.resp The outcome variable of model.resp.
outc.expl The outcome variable of model.expl.
sigma.res.expl If model.expl is linear, a column matrix with the estimated residual standard
deviation for model.expl over the range of Rho.
sigma.res.resp If model.resp is linear, a column matrix with the estimated residual standard
deviation for model.resp over the range of Rho.
value The values of the -loglikelihood function for the best set of regression parameters
from the optimization for each Rho.
sigmas A list with the covariance matrices for the model parameters in model.expl and
model.resp for each Rho.
max.info Information about the maximization (whether or not the convergence was successful, message, method and number of iterations) for each Rho, see maxLik
for more information.

Author(s)
Anita Lindmark

See Also
doefs.sensmed, maxLik

Description
Takes an "effectsMed" object and estimates additional natural direct and indirect effects, with a
sensitivity analysis using the same sensitivity parameter as in the original analysis, without having to redo the optimization to find the estimated regression coefficients. The effects to be estimated are regulated through the arguments covariates, alt.decomposition, exp.value and control.value as described in the documentation for sensmediation. The confidence level used is regulated through the argument conf.level.

Usage
more.effects(sensmed.object, conf.level = 0.95, covariates = NULL,
alt.decomposition = FALSE, exp.value = NULL, control.value = NULL)
Arguments

sensmed.object  an object of class "effectsMed" for which additional effects are to be calculated.
conf.level      the confidence level to be used for confidence intervals and uncertainty intervals.
covariates      if conditional effects are to be estimated the list of covariate values (see sensmediation). Covariates not specified are marginalized over.
alternative     logical indicating whether alternative definitions of the direct and indirect effects should be used (see sensmediation).
exp.value        value of the exposure variable used as the exposure condition, default is to take the value stored in sensmed.object.
control.value    value of the exposure variable used as the control (unexposed) condition, default is to take the value stored in sensmed.object.

Value

more.effects returns an object of class "effectsMed", see the documentation for sensmediation for information.

Author(s)

Anita Lindmark

See Also

sensmediation

Examples

## Not run:

# Example with data from Riksstroke (the Swedish stroke register)

data(RSdata)

# Probit mediator and outcome models:
med.model <- glm(lowered.consc ~ AF + age.cat + sex, data = RSdata, family = binomial(link = 'probit'))
out.model <- glm(cf.3mo ~ AF + lowered.consc + age.cat + sex, data = RSdata, family = binomial(link = 'probit'))

# First we estimate marginal NIE, NDE with sensitivity analyses to mediator-outcome confounding:
sensmed <- sensmediation(med.model, out.model, exp.name = "AF!", med.name = "lowered.consc", Rho = seq(0, 0.5, 0.1))

# Then we also estimate NIE, NDE conditional on male sex without reestimating the regression coefficients:
sensmed.cond <- more.effects(sensmed.object = sensmed, covariates = list(sex = 1))
summary(sensmed.cond)
partdevs

plot(sensmed.cond)

## End(Not run)

---

**partdevs**

*Implementations of the partial derivatives (gradients) of the expressions for the direct, indirect and total effects. Used to calculate standard errors (delta method).*

---

**Description**

Functions implementing the partial derivatives (gradients) of the expressions for the direct, indirect and total effects. These are then used to calculate standard errors of the effects using the delta method. Called by the `stderrs` functions. The functions are named according to the convention `partdevs"mediator model type""outcome model type"` where `b` stands for binary probit regression and `c` stands for linear regression.

**Usage**

```r
partdevs.bb(beta0, beta1, beta2, beta3, theta0, theta1, theta2, theta3, theta4, theta5, theta6, theta7, x.med, x.out, t.de, t.ie, exp.value, control.value)

partdevs.bc(beta0, beta1, beta2, beta3, theta2, theta3, theta4, theta5, theta6, theta7, x.med, x.out, t.de, t.ie, exp.value, control.value)

partdevs.cb(beta0, beta1, beta2, beta3, theta0, theta1, theta2, theta3, theta4, theta5, theta6, theta7, sigma.eta, x.med, x.out, t.de, t.ie, exp.value, control.value)

partdevs.cc(beta0, beta1, beta2, beta3, theta2, theta3, theta6, theta7, exp.value, control.value, x.med, x.out, t.de, t.ie)
```

**Arguments**

- `beta0, beta1` Vectors of mediator regression parameters (intercept and exposure) over Rho
- `beta2, beta3` Matrices of mediator regression parameters (covariate main effects and exposure-covariate interactions) over Rho
- `theta0, theta1, theta2, theta3` Vectors of outcome regression parameters (intercept, exposure, mediator, exposure-mediator interaction) over Rho
- `theta4, theta5, theta6, theta7` Matrices of outcome regression parameters (covariate main effects, exposure-covariate, mediator-covariate and exposure-mediator-covariate interactions) over Rho
- `x.med` Mediator covariate matrix for which to calculate standard errors
plot.effectsMed  

Plot function for objects of class "effectsMed"

Description

Plots the estimated natural indirect or direct effects with confidence intervals over the range of the sensitivity parameter \( \rho \).

Usage

```r
## S3 method for class 'effectsMed'
plot(x, effect = "indirect", xlab = NULL, ylab = NULL, xlim = NULL, ylim = NULL, main = NULL, lwd = graphics::par("lwd"), ...)
```

Arguments

- `x`: object of class "effectsMed"
- `effect`: which effect to plot results for ("indirect" or "direct")
- `xlab`: a title for the x axis, see `title`. Default is \( \text{expression}(\rho) \).
- `ylab`: a title for the y axis, see `title`. Default is \( \text{NIE} \) if alt.decomposition = TRUE or \( \text{NDE} \) (NDE*)
- `xlim`: the x limits (x1, x2) of the plot, see `plot.default`. Default is \( \text{c}(\text{min}(x$\rho), \text{max}(x$\rho)) \)
- `ylim`: the y limits of the plot. Default is \( \text{c}(\text{min}(x$\text{CI}\_\text{nie}[,1]), \text{max}(x$\text{CI}\_\text{nie}[,2])) \)
- `main`: a main title for the plot, see `title`
- `lwd`: line widths for the lines of the plot, see `par`
- `...`: additional graphical parameters to be passed to plotting functions, see `par`
RSdata

Example data for the functions in sensmediation

Description

The data are a subsample of 1000 observations from Riksstroke, the Swedish Stroke Register. The original data consisted of over 50 000 patients with first time ischemic stroke during the years 2009-2012. The data are limited to patients over the age of 44 and its purpose is to illustrate the functioning of the functions in the package.

Usage

data(RSdata)

Format

A data frame with 1000 observations on the following 5 variables.

cf_3mo  Outcome: case fatality within 3 months after stroke, 1 = deceased, 0 = not deceased.
lowered_consc  Mediator: level of consciousness upon arrival to hospital. 1 = lowered consciousness, 0 = fully alert.
AF  Exposure: atrial fibrillation. Factor with levels, "1" = atrial fibrillation, "0" = no atrial fibrillation.
age_cat  Age at time of stroke. Factor with levels, "45-69", "70-79", "80-89" and "90-".
sex  Factor with levels, "1" = male, "0" = female

Examples

data(RSdata)

sensmediation

Estimate natural direct and indirect effects based on parametric regression models and perform sensitivity analysis

Description

Function to estimate the natural direct and indirect effects based on parametric regression models. Standard errors for the effects are calculated using the delta method. The function also gives sensitivity analysis results for unobserved confounding. Implements methods introduced in Lindmark, de Luna and Eriksson (2018).
Usage

sensmediation(med.model, out.model, exp.model = NULL, exp.name = NULL,
med.name = NULL, type = "my", Rho = 0, progress = TRUE,
conf.level = 0.95, covariates = NULL, alt.decomposition = FALSE,
control.value = 0, exp.value = 1, covariance = NULL,
med.full = NULL, out.full = NULL, all.interactions = NULL, ...)

Arguments

med.model  Fitted \texttt{glm} model object representing the mediator model at the basis of the estimation (see Details for more information).

out.model  Fitted \texttt{glm} model object representing the outcome model at the basis of the estimation (see Details for more information).

exp.model  Fitted \texttt{glm} model object representing the exposure model. Should be provided if type="zm" or type="zy".

exp.name  A character string indicating the name of the exposure variable used in the models. Needs to match the name of the exposure found in the output from the fitted glm-models (this is especially important to check for exposures of class \texttt{factor}).

med.name  A character string indicating the name of the mediator used in the models. Needs to match the name of the mediator found in the output from the outcome glm-model (this is especially important to check for mediators of class \texttt{factor}).

type  the type of confounding for which the sensitivity analysis is to be performed. type="my", the default, corresponds to unobserved mediator-outcome confounding, type="zm" to exposure-mediator confounding and type="zy" to exposure-outcome confounding.

Rho  The sensitivity parameter vector. If type="my" the correlation between the error terms in the mediator and outcome models. If type="zm" the correlation between the error terms in the exposure and mediator models. If type="zy" the correlation between the error terms in the exposure and outcome models.

progress  Logical, indicating whether or not the progress (i.e. the \texttt{proc.time} for each Rho) of the optimization will be output.

conf.level  the confidence level to be used for confidence intervals and uncertainty intervals.

covariates  if conditional effects are to be estimated the named list of covariate values (see Details). Covariates not specified are marginalized over.

alt.decomposition  logical indicating whether or not alternative definitions of the direct and indirect effects should be used (see Details).

control.value  value of the exposure variable used as the control (unexposed) condition, default is 0.

exp.value  value of the exposure variable used as the exposure condition, default is 1.

covariance, med.full, out.full, all.interactions  arguments used in previous versions of the package that are now deprecated.

...  Additional arguments to be passed on to the \texttt{maxLik} function. Can be used to set the method and control arguments of the \texttt{maxLik} function (see \texttt{coefs.sensmed}).
Details

To obtain the ML estimates of the regression parameters used to calculate mediation effects and perform sensitivity analysis sensmediation calls `coefs.sensmed`. The maximization of the log-likelihood is performed using `maxLik`, the default is to use the Newton-Raphson method and an analytic gradient and Hessian.

The mediator and outcome models (and exposure model for type = "zm" or "zy") should be fitted using `glm` and can be of two types, probit models (family = `binomial(link = 'probit')`) for binary mediators or outcomes (exposures) and linear regression models (family = `gaussian`) for continuous mediators or outcomes (exposures). The outcome model may contain exposure-mediator, exposure-covariate, mediator-covariate and exposure-mediator-covariate interactions. The mediator model may contain exposure-covariate interactions. All models may also contain interactions between covariates. Note, however that interactions may not be included in a model without also including the main effects of the interacting variables. That is, interactions should be specified either as `X1*X2` or `X1 + X2 + X1:X2`, not as `X1:X2` alone.

To obtain results conditional on specific covariate values, these values should be provided through the `covariates` argument as a named list (see Examples). The effects will be averaged over covariates not specified in the list.

The total effect can be decomposed into a direct and indirect effect in different ways. Let z be the exposure value and z* the control (unexposed) value. The default is to give the decomposition into the "pure direct effect" $E(Y(z, M(z*))) - E(Y(z*, M(z*)))$ (here denoted NDE) and the "total indirect effect" $E(Y(z, M(z))) - E(Y(z, M(z*)))$ (denoted NIE). Setting `alt.decomposition = TRUE` instead gives the decomposition into the "total direct effect" $E(Y(z, M(z))) - E(Y(z*, M(z)))$ (here denoted NDE*) and "pure indirect effect" $E(Y(z*, M(z))) - E(Y(z*, M(z*)))$ (denoted NIE*).

Standard errors for the effects are calculated using the delta method. Confidence intervals (CI) for (and p-values for tests of) the natural direct and indirect effects for each value of the sensitivity parameter are constructed based on a normal approximation. Uncertainty intervals (UI) are constructed as the union of all CIs over the sensitivity parameter vector.

Value

`sensmediation` returns an object of class "effectsMed".

The function `summary` (`summary.effectsMed`) gives a summary of the results in the form of a table with the estimated effects and results of the sensitivity analysis. The function `plot` (`plot.effectsMed`) plots the estimated natural indirect or direct effects with confidence intervals over the range of the sensitivity parameter.

call
Rho
`The matched call`

`The sensitivity parameter vector.`

`type`
`character, the type of confounding the sensitivity analysis is performed for.`

`coefs.sensmed`
`a list with the output from coefs.sensmed`

`NIE`
`matrix with the estimated NIEs (or NIE*s if alt.decomposition=TRUE) over the range of the sensitivity parameter Rho.`

`NDE`
`matrix with the estimated NDEs (or NDE*s if alt.decomposition=TRUE) over the range of the sensitivity parameter Rho.`
stderrs: list with the standard errors of the NIE (NIE*), NDE (NDE*) and total effect over the range of the sensitivity parameter Rho.

CI: a list with the confidence intervals of the NIE (NIE*), NDE (NDE*) and total effect over the range of the sensitivity parameter Rho.

UI: matrix with the uncertainty intervals for the NIE (NIE*) and NDE (NDE*) over the range of the sensitivity parameter Rho.

conf.level: numeric, the confidence level used for confidence intervals and uncertainty intervals.

covariates: list of the covariate values that the effects are conditioned on.

exp.name: character vector containing the name of the exposure variable.

med.name: character vector containing the name of the mediator variable.

exp.value: value of the exposure variable used as the exposure condition.

control.value: value of the exposure variable used as the control (unexposed) condition.

alt.decomposition: logical, indicating whether the alternative definitions of the direct and indirect effects have been used.

med.model: the mediator model input.

out.model: the outcome model input.

betas: list of the estimated mediator model parameters over Rho, with
- beta0 Intercept
- beta1 Exposure
- beta2 Covariates
- beta3 Exposure-covariate interactions
Components that are not included in the input mediator model are set to 0.

thetas: list of the estimated outcome model parameters over Rho, with
- theta0 Intercept
- theta1 Exposure
- theta2 Mediator
- theta3 Exposure-mediator interaction
- theta4 Covariates
- theta5 Exposure-covariate interactions
- theta6 Mediator-covariate interactions
- theta7 Exposure-mediator-covariate interactions
Components that are not included in the input outcome model are set to 0.

part.deriv: List with the partial derivatives of the NDE (Lambda), NIE (Gamma) and TE (Eta) wrt the mediator and outcome model parameters for each value of Rho. See partdevs.

sigma.thetabeta: a list with the joint covariance matrix of the outcome and mediator model parameters for each value of Rho. Note that the covariance matrix is constructed for all estimated parameters listed in betas and thetas but that components not included in the input mediator and outcome models are set to 0.
Author(s)
Anita Lindmark

References

See Also
more.effects which can be used to calculate additional direct and indirect effects with sensitivity analysis using the same sensitivity parameter without running the optimization again.

Examples

# Example with data from Riksstroke (the Swedish stroke register)

data(RSdata)

# Probit mediator and outcome models:
m.model <- glm(lowered.consc ~ AF + age.cat + sex, data = RSdata, family = binomial(link = 'probit'))
o.model <- glm(cf.3mo ~ AF + lowered.consc + age.cat + sex, data = RSdata, family = binomial(link = 'probit'))

# Estimation of NIE, NDE and sensitivity analyses to mediator-outcome confounding:
# (note that the name of the exposure is "AF1" to match the name in coef(out.model))
sensmed <- sensmediation(m.model, o.model, exp.name = "AF1", med.name = "lowered.consc",
                         Rho = c(0, .1)))
summary(sensmed)
plot(sensmed)

# Not run:
## Conditional effects and sensitivity analysis to mediator-outcome confounding using
## more.effects():
sensmed.cond <- more.effects(sensmed.object = sensmed, covariates = list(sex = 1, age.cat = "70-79"))
summary(sensmed.cond)

## End(Not run)

## Not run:
## Sensitivity analysis to exposure-mediator confounding:
e.model <- glm(AF ~ age.cat + sex, data = RSdata, family = binomial(link = 'probit'))
sensmed.zm <- sensmediation(med.model = m.model, out.model = o.model, exp.model = e.model, type = "zm", Rho = seq(0, .5, .1), exp.name = "AF1", med.name = "lowered.consc")
stderrs

summary(sensmed.zm)

## End(Not run)

## Not run:
# Additional effects using more.effects:
# Results with conf.level = 0.99:
sensmed.zm.99 <- more.effects(sensmed.object = sensmed.zm, conf.level = 0.99)
summary(sensmed.zm.99)

## End(Not run)

## Not run:
# Examples with simulated data, continuous exposure:

require(mvtnorm)

n <- 1000
set.seed(102677)

x <- rnorm(n)
z <- -0.5 + 0.1*x + rnorm(n)
R <- 0.5
Sigma <- cbind(c(1,R), c(R,1))
epsilon <- rmvnorm(n, sigma = Sigma)
m <- -1.2 + 0.8*z + 0.13*x + epsilon[,1]
y <- -1 + 0.05*z + 3*m + 0.5*x + epsilon[,2]

# Models:
z.model <- glm(z ~ x)
m.model <- glm(m ~ z + x)
y.model <- glm(y ~ z + m + x)

## Estimation of NIE, NDE. Note that the exposure condition is 2
## so effects are calculated for a 2 unit increase of the exposure:
eff.contz <- sensmediation(med.model = m.model, out.model = y.model,
                           exp.name = "z", med.name = "m", control.value = 0, exp.value = 2)
summary(eff.contz)

## End(Not run)

stderrs

Functions to calculate standard errors of the direct, indirect and total
effects using the delta method.

Description

Functions used to calculate standard errors of the direct, indirect and total effects using the delta
method. Called by calc.effects. The functions are named according to the convention stderr."mediator model type"."outcome model type".
where b stands for binary probit regression and c stands for linear regression.

Usage

```r
stderr.bb(Rho, betas, thetas, sigma.pars, x.med, x.out, alt.decomposition, exp.value, control.value)
```

```r
stderr.bc(Rho, betas, thetas, sigma.pars, x.med, x.out, alt.decomposition, exp.value, control.value)
```

```r
stderr.cb(Rho, betas, thetas, sigma.eta, sigma.pars, x.med, x.out, alt.decomposition, exp.value, control.value)
```

```r
stderr.cc(Rho, betas, thetas, sigma.pars, x.med, x.out, alt.decomposition, exp.value, control.value)
```

Arguments

- `Rho` The sensitivity parameter vector.
- `betas` List of mediator regression parameters
- `thetas` List of outcome regression parameters
- `sigma.pars` List of covariance matrices for the mediator and outcome regression parameters
- `x.med` Mediator covariate matrix for which to calculate standard errors
- `x.out` Outcome covariate matrix for which to calculate standard errors
- `alt.decomposition` logical indicating whether or not alternative definitions of the direct and indirect effects should be used.
- `exp.value` value of the exposure variable used as the exposure condition.
- `control.value` value of the exposure variable used as the control (unexposed) condition.
- `sigma.eta` For a continuous mediator and binary outcome, matrix with the estimated residual standard deviation for the mediator model over the range of Rho.

Description

Summary function for objects of class "effectsMed"

Usage

```r
## S3 method for class 'effectsMed'
summary(object, non.sign = FALSE, ...)
```

```r
## S3 method for class 'summaryeffectsMed'
print(x, digits = max(3,getOption("digits") - 3), ...)```
Arguments

- **object**: object of class "effectsMed"
- **non.sign**: logical indicating whether sensitivity analysis results should be printed for non-significant effects.
- **x**: object of class "summaryeffectsMed"
- **digits**: number of digits to be printed.

Value

A list with values:

- **call**: The matched call
- **Rho**: The sensitivity parameter vector.
- **type**: character, the type of confounding the sensitivity analysis is performed for.
- **conf.level**: numeric, the confidence level used for confidence intervals and uncertainty intervals.
- **UI**: matrix with the uncertainty intervals for the NIE (NIE*) and NDE (NDE*) over the range of the sensitivity parameter Rho.
- **covariates**: list of the covariate values that the effects are conditioned on.
- **exp.name**: character vector containing the name of the exposure.
- **med.name**: character vector containing the name of the mediator.
- **alt.decomposition**: logical, indicating whether the alternative definitions of the direct and indirect effects have been used.
- **non.sign**: logical indicating whether sensitivity analysis results are printed for non-significant effects.
- **effects**: Results of the mediation analysis. Estimated NIE and NDE with confidence intervals and p-values for Rho = 0
- **ns.nie**: values of Rho with estimated NIEs and confidence intervals where the NIE is not significant.
- **ns.nde**: values of Rho with estimated NDEs and confidence intervals where the NDE is not significant.
- **rev.nie**: values of Rho with estimated NIEs and confidence intervals where the NIE is reversed.
- **rev.nde**: values of Rho with estimated NDEs and confidence intervals where the NDE is reversed.
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