Package 'multimediate'

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Title Causal Mediation Analysis in Presence of Multiple Mediators Uncausally Related

Version 0.1.4

Description Estimates key quantities in causal mediation analysis - including average causal mediation effects (indirect effects), average direct effects, total effects, and proportions mediated - in the presence of multiple uncausally related mediators. Methods are described by Jérolon et al., (2021) <doi:10.1515/ijb-2019-0088> and extended to accommodate survival outcomes as described by Domingo-Relloso et al., (2024) <doi:10.1101/2024.02.16.24302923>.

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Encoding UTF-8

LazyData true

URL https://samarafk.github.io/multimediate/

Imports rmutil, MASS, mvtnorm, stats, graphics, timereg

Suggests knitr, rmarkdown

RoxygenNote 7.3.2

NeedsCompilation no

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`data1` *Toy dataset 1*

Description

A toy dataset for causal mediation analysis with 3 uncausally related mediators.

Usage

```
data("data1")
```

Format

A data frame with 1000 observations on the following 8 variables.

`Treatment` a factor with levels `0` `1`

`C1` a factor with levels `0` `1`

`C2` a factor with levels `0` `1`

`C3` a factor with levels `0` `1`

`M1` a numeric vector

`M2` a numeric vector

`M3` a numeric vector

`Outcome` a numeric vector

Examples

```
#data(data1)
#data1$Treatment=as.factor(data1$Treatment)
#data1$C1=as.factor(data1$C1)
#data1$C2=as.factor(data1$C2)
#data1$C3=as.factor(data1$C3)
#data1$M1=as.numeric(data1$M1)
#data1$M2=as.numeric(data1$M2)
#data1$M3=as.numeric(data1$M3)
#data1$Outcome=as.numeric(data1$Outcome)
#summary(data1)

#M1reg=lm(M1~ Treatment + C1 + C2, data=data1)
#M2reg=lm(M2~ Treatment + C1 + C3, data=data1)
#M3reg=lm(M3~ Treatment + C1     , data=data1)
```

```
#Yreg=lm(Outcome~ Treatment + M1 + M2 + M3 + C1 + C2 + C3, data=data1)

#med.analysis=multimediate(lmodel.m=list(M1reg,M2reg,M3reg),
#correlated=TRUE,model.y=Yreg,treat="Treatment",
#treat.value=1,control.value=0,J=1000,conf.level=0.95)

#summary(med.analysis,opt="avg")
```

`data2` *Toy dataset 2*

Description

A toy dataset for causal mediation analysis with 3 uncausally related mediators.

Usage

```
data("data2")
```

Format

A data frame with 1000 observations on the following 8 variables.

`Treatment` a factor with levels `0` `1`

`C1` a factor with levels `0` `1`

`C2` a factor with levels `0` `1`

`C3` a factor with levels `0` `1`

`M1` a numeric vector

`M2` a numeric vector

`M3` a numeric vector

`Outcome` a factor with levels `FALSE` `TRUE`

Examples

```
#data(data2)
#data2$Treatment=as.factor(data2$Treatment)
#data2$C1=as.factor(data2$C1)
#data2$C2=as.factor(data2$C2)
#data2$C3=as.factor(data2$C3)
#data2$M1=as.numeric(data2$M1)
#data2$M2=as.numeric(data2$M2)
#data2$M3=as.numeric(data2$M3)
#data2$Outcome=as.factor(data2$Outcome)
#summary(data2)

#M1reg=lm(M1~ Treatment + C1, data=data2)
#M2reg=lm(M2~ Treatment + C2, data=data2)
```

```
#M3reg=lm(M3~ Treatment + C3, data=data2)

#Yreg=glm(Outcome~ Treatment + M1 + M2 + M3 + C1 + C2 + C3, data=data2, family = binomial("logit"))

#med.analysis=multimediate(lmodel.m=list(M1reg,M2reg,M3reg),
#correlated=TRUE,model.y=Yreg,treat="Treatment",
#treat.value=1,control.value=0,J=1000,conf.level=0.95)

# summary(med.analysis,opt="avg",logit="effects")
# summary(med.analysis,opt="avg",logit="OR")
# summary(med.analysis,opt="avg",logit="logOR")
# summary(med.analysis,opt="avg",logit="all")
```

`data3` *Toy dataset 3*

Description

A toy dataset for causal mediation analysis with 3 uncausally related mediators.

Usage

```
data("data3")
```

Format

A data frame with 1000 observations on the following 8 variables.

`Treatment` a factor with levels `0` `1`

`C1` a factor with levels `0` `1`

`C2` a factor with levels `0` `1`

`C3` a factor with levels `0` `1`

`M1` a numeric vector

`M2` a numeric vector

`M3` a numeric vector

`Outcome` a factor with levels `0` `1` `2` `3`

Examples

```
#data(data3)
#data3$Treatment=as.factor(data3$Treatment)
#data3$C1=as.factor(data3$C1)
#data3$C2=as.factor(data3$C2)
#data3$C3=as.factor(data3$C3)
#data3$M1=as.numeric(data3$M1)
#data3$M2=as.numeric(data3$M2)
#data3$M3=as.numeric(data3$M3)
```

```
#data3$Outcome=as.factor(data3$Outcome)

#summary(data3)

#M1reg=lm(M1~ Treatment + C1 + C3, data=data3)
#M2reg=lm(M2~ Treatment + C1 + C2, data=data3)
#M3reg=lm(M3~ Treatment + C2 + C3, data=data3)

#library(MASS)
#Yreg=polr(Outcome ~ Treatment + M1 + M2 + M3 + C1 + C2 + C3 , data = data3, method = "probit")

#med.analysis=multimediate(lmodel.m=list(M1reg,M2reg,M3reg),
#correlated=TRUE,model.y=Yreg,treat="Treatment",
#treat.value=1,control.value=0,J=100,conf.level=0.95)

#summary(med.analysis,opt="avg")
```

`data4` *Toy dataset 4*

Description

A toy dataset for causal mediation analysis with 3 uncausally related mediators.

Usage

```
data("data4")
```

Format

A data frame with 1000 observations on the following 8 variables.

`Treatment` a numeric vector

`C1` a factor with levels `0` `1`

`C2` a factor with levels `0` `1`

`C3` a factor with levels `0` `1`

`M1` a numeric vector

`M2` a factor with levels `0` `1`

`M3` a factor with levels `0` `1` `2` `3`

`Outcome` a numeric vector

Examples

```
#data(data4)
#data4$Treatment=as.factor(data4$Treatment)
#data4$C1=as.factor(data4$C1)
#data4$C2=as.factor(data4$C2)
#data4$C3=as.factor(data4$C3)
#data4$M1=as.numeric(data4$M1)
#data4$M3=as.factor(data4$M3)
#data4$M2=as.factor(data4$M2)
#data4$Outcome=as.numeric(data4$Outcome)
#summary(data4)

#M1reg=lm(M1~  Treatment + C1 + C2 + C3, data = data4)
#M2reg=glm(M2~ Treatment + C1 + C3, data = data4, family = binomial("probit"))
#M3reg=polr(M3~Treatment + C2 + C3     , data = data4, method = "probit")

#Yreg=lm(Outcome~ Treatment + M1 + M2 + M3 + C1 + C2 + C3, data=data4)

#med.analysis=multimediate(lmodel.m=list(M1reg,M2reg,M3reg),
#correlated=TRUE,model.y=Yreg,treat="Treatment",
#treat.value=1,control.value=0,J=1000,conf.level=0.95)

#summary(med.analysis,opt="avg")
```

`data5` *Toy dataset 5*

Description

A toy dataset for causal mediation analysis with 3 uncausally related mediators and survival outcome.

Usage

```
data("data4")
```

Format

A data frame with 3000 observations on the following 8 variables.

`Exposure` a numeric vector

`M1` a numeric vector

`M2` a numeric vector

`M3` a numeric vector

`event` event

`surv_time` time before event

Examples

```
#data(data5)
#modM1=lm(M1 ~ Exposure, data = data5)
#modM2=lm(M2 ~ Exposure, data = data5)
#modM3=lm(M3 ~ Exposure, data = data5)
#lmodel.m=list(modM1,modM2, modM3)
#model.y=aalen(Surv(surv_time, event) ~ const(Exposure) + const(M1) + const(M2)
#+ const(M3), data = data5, robust=T)
#multi.media=multimediate(lmodel.m,correlated=TRUE,model.y,treat='Exposure',
#treat.value=1,control.value=0,J=1000,conf.level=0.95,data=data5)
#summary(multi.media, opt='avg')
```

`multimediate` *multimediate*

Description

`multimediate` estimates several quantities in causal mediation analysis, including the average causal mediation effect (indirect effect), average direct effect, proportion mediated, and total effect, in the presence of multiple uncausally related mediators.

Usage

```
multimediate(
  lmodel.m,
  correlated = FALSE,
  model.y,
  treat,
  treat.value = 1,
  control.value = 0,
  J = 1000,
  conf.level = 0.95,
  fun = mean,
  data = NULL,
  peryr = 1e+05,
  verbose = TRUE
)
```

Arguments

`lmodel.m`	list of fitted models object for mediators. Can be of class 'lm', 'polr','glm'.
`correlated`	a logical value. if 'FALSE' a identity matrix is used for the matrix of correlation of mediators; if 'TRUE' matrix of correlation is estimated. Default is 'FALSE'.
`model.y`	a fitted model object for the outcome. Can be of class 'lm', 'polr','glm' or 'aalen'.

treat	a character string indicating the name of the treatment variable used in the models. The treatment can be either binary (integer or a two-valued factor) or continuous (numeric).
treat.value	value of the treatment variable used as the treatment condition. Default is 1.
control.value	value of the treatment variable used as the control condition. Default is 0.
J	number of Monte Carlo draws for quasi-Bayesian approximation.
conf.level	level of the returned two-sided confidence intervals. Default is to return the 2.5 and 97.5 percentiles of the simulated quantities.
fun	the function used to compute the point estimate of the effects of interest from its empirical distribution. The function mean or median can be used. Default is the function mean.
data	dataset with all variables used in the mediator and outcome models
peryr	the number of person-years to multiply the additive estimator to obtain results in scale of cases per person-years (only applicable to the survival outcome)
verbose	Logical. If 'TRUE' (default), messages and a progress bar are displayed during execution.

Details

For binary outcomes, it also estimates average causal mediation effects on the odds ratio (OR) and log-odds (logOR) scales.

For survival outcomes, `multimediate` additionally estimates average causal mediation effects on cases per person-year scale.

Value

multimediate returns an object of class `mm`, a list that contains at least the components listed below. The function `summary` (i.e., `summary.mm`) can be used to obtain a table of the results.

- `model.y`: the fitted outcome model.
- `model.m`: a list of fitted mediator models, one for each mediator.
- `treatment`: a character string indicating the name of the treatment variable used in the models.
- `treat.value`: value of the treatment variable used as the treatment condition.
- `control.value`: value of the treatment variable used as the control condition.
- `sims`: the number of Monte Carlo draws for quasi-Bayesian approximation.

References

Jérolon, A., Baglietto, L., Birmelé, E., Alarcon, F., & Perduca, V. (2021). Causal mediation analysis in presence of multiple mediators uncausally related. *The International Journal of Biostatistics*, 17(2), 191–221. doi:10.1515/ijb-2019-0088

Domingo-Relloso A, Jerolon A, Tellez-Plaza M, Bermudez JD. Causal mediation for uncausally related mediators in the context of survival analysis. medRxiv [Preprint]. 2024 Feb 18:2024.02.16.24302923. doi: 10.1101/2024.02.16.24302923

Examples

```
# Load example data
data(data1)
summary(data1)

# Fit mediator models
M1reg <- lm(M1 ~ Treatment + C1 + C2, data = data1)
M2reg <- lm(M2 ~ Treatment + C1 + C3, data = data1)
M3reg <- lm(M3 ~ Treatment + C1, data = data1)

# Fit outcome model
Yreg <- lm(Outcome ~ Treatment + M1 + M2 + M3 + C1 + C2 + C3, data = data1)

# Perform multiple mediation analysis (may take some time)

med.analysis <- multimediate(
  lmodel.m = list(M1reg, M2reg, M3reg),
  correlated = TRUE,
  model.y = Yreg,
  treat = "Treatment",
  treat.value = 1,
  control.value = 0,
  J = 250,
  conf.level = 0.95,
  verbose = FALSE
)

summary(med.analysis, opt = "avg")
```

`summary.mm` *summary.mm*

Description

`summary.mm` is used to display the results of the mediation analyzes done with `multimediate`.

Usage

```
## S3 method for class 'mm'
summary(object, opt = "navg", logit = "all", ...)
```

Arguments

`object`	element of the class `mm`.
`opt`	a character string indicating the details of the analysis "navg" for the average causal effects for t=0,1 and "avg" for the average causal effects.

`logit`	a character string indicating, when the outcome is binary, the scale of the average causal effects. "effects" for average causal effects, " OR" average causal effects on OR scale, "logOR" average causal effects on logOR scale and "all" for all scale.
`...`	additional arguments affecting the summary produced

Value

table summarizing the causal analysis

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