

Package ‘mma’

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Type Package

Title Multiple Mediation Analysis

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Description Used for general multiple mediation analysis.

The analysis method is described in Yu et al. (2014) <doi:10.4172/2155-6180.1000189> ``General Multiple Mediation Analysis With an Application to Explore Racial Disparity in Breast Cancer Survival'', published on Journal of Biometrics & Biostatistics, 5(2):189; and Yu et al.(2017) <DOI:10.1016/j.sste.2017.02.001> ``Exploring racial disparity in obesity: a mediation analysis considering geo-coded environmental factors'', published on Spatial and Spatio-temporal Epidemiology, 21, 13-23.

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 mma-package

Mediation Analysis Package

Description

This package is used to identify mediators and for general mediation analysis. Mediation effect refers to the effect conveyed by intervening variables to an observed relationship between an exposure and a response variable (outcome). In this package, the exposure is called the predictor, the intervening variables are called mediators. The mediation effects include the total effect, direct effect, and indirect effect, which are defined and the statistical inferences described in Yu et al.(2014).

Details

Package: mma
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 Version: 10
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"[data.org](#)" is used to identify potential mediators. "[med](#)", and "[boot.med](#)" are used for statistical inferences on the mediation effects when the predictor is binary or continuous. "[mma](#)" is a combined function that automatically identify potential mediators, based on which to make statistical

inference on the mediation effects.

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Examples

```
data("weight_behavior")
#binary predictor
#binary y
x=weight_behavior[,c(2,4:14)]
pred=weight_behavior[,3]
y=weight_behavior[,15]
temp.b.b.glm<-mma(x,y,pred=pred,contmed=c(7:9,11:12),binmed=c(6,10),binref=c(1,1),
                 catmed=5,catref=1,predref="M",alpha=0.4,alpha2=0.4,n=2,n2=2)

temp.b.b.mart<-mma(x,y,pred=pred,contmed=c(7:9,11:12),binmed=c(6,10),binref=c(1,1),
                 catmed=5,catref=1,predref="M",alpha=0.4,alpha2=0.4,nonlinear=TRUE,n=2,n2=5)
```

```
#continuous y
x=weight_behavior[,c(2,4:14)]
pred=weight_behavior[,3]
y=weight_behavior[,1]
temp.b.c.glm<-mma(x,y,pred=pred,mediator=5:12,jointm=list(n=1,j1=7:9),
                 predref="M",alpha=0.4,alpha2=0.4,n2=20)
temp.b.c.mart<-mma(x,y,pred=pred,mediator=5:12,jointm=list(n=1,j1=7:9),
                  predref="M",alpha=0.4,alpha2=0.4,
                  n=2,nonlinear=TRUE,n2=20)
```

boot.med

Statistical Inference on Mediation Analysis with Continuous or Binary Predictor

Description

To make inferences on the mediation effects when the predictor is continuous or binary.

Usage

```
boot.med(data,x=data$x, y=data$y,dirx=data$dirx,binm=data$binm,
         contm=data$contm,catm=data$catm,jointm=data$jointm,
         cova=data$cova, margin=1,n=20,
         nonlinear=FALSE,df1=1,nu=0.001,D=3,distn=NULL,family1=data$family1,
         n2=50,w=rep(1,nrow(x)),refy=NULL,x.new=x,pred.new=dirx,
         cova.new=cova,binpred=data$binpred,type=NULL,
         w.new=NULL,all.model=FALSE,xmod=NULL,custom.function=NULL,para=FALSE)
```

Arguments

data	the list of result from data.org that organize the covariates, mediators, predictor and outcome. If data is FALSE, then need to set x, y, dirx, contm, catm, and jointm.
x	a data frame contains all mediators and covariates. Need to set up only when data is FALSE. All variables in x that are not identified as potential mediators (by mediator, contmed, binmed, catmed, or jointm) are forced in mediation analysis as covariates.
y	the vector of outcome variable. Need to set up only when data is FALSE.
dirx	the vector/matrix of predictor(s). Need to set up only when data is FALSE.
binm	the variable names or the column number of x that locates the binary mediators. Need to set up only when data is FALSE.
contm	the variable names or the column numbers of x that locate the potential continuous mediators. Need to set up only when data is FALSE.
catm	categorical mediators should be binarized and be presented as a list, where the first item is the number of categorical variables and the following items are the names or the column numbers of each binarized categorical variable in x. data.org organizes the categorical mediators in this format after they pass the mediator tests. Need to set up only when data is FALSE.

jointm	a list where the first item is the number of groups of joint mediators to be considered, and each of the following items identifies the names or the column numbers of the mediators in x for each group of joint mediators. Need to set up only when data is FALSE.
cova	The data frame of covariates to be used to predict the mediator(s). The covariates in cova cannot be potential mediators. If the covariates are for some specific potential mediators, cova\$for.m is the vector of names of potential mediators that use the covariates. Works for continuous predictors (pred) only, also the specified covariates should have no missing if only some mediators uses the covariates. Works mainly for continuous predictors (pred), also the specified covariates should have no missing if only some mediators uses the covariates.
margin	the change in predictor when calculating the mediation effects, see Yu et al. (2014).
n	the time of resampling in calculating the indirect effects, default is n=20, see Yu et al. (2014).
nonlinear	if TRUE, Multiple Additive Regression Trees (MART) will be used to fit the final full model in estimating the outcome. The default value of nonlinear is FALSE, in which case, a generalized linear model will be used to fit the final full model.
df1	if nonlinear is TRUE, natural cubic spline will be used to fit the relationship between the predictor and each mediator. The df is the degree of freedom in the ns() function, the default is 1.
nu	set the parameter "shrinkage" in gbm function if MART is to be used, by default, nu=0.001. See also help(gbm.fit).
D	set the parameter "interaction.depth" in gbm function if MART is to be used, by default, D=3. See also help(gbm.fit).
distn	the assumed distribution of the outcome if MART is used for final full model. The default value of distn is "gaussian" for continuous y, and "bernoulli" for binary y.
family1	define the conditional distribution of y given x, and the linkage function that links the mean of y with the system component if generalized linear model is used as the final full model. The default value of family1 is gaussian(link="identity") for continuous y, and binomial(link = "logit") for binary y.
n2	the number of times of bootstrap resampling. The default value is n2=50.
w	the weight for observations.
refy	if y is binary, the reference group of y.
x.new	of the same format as x, with a new set of covariates and mediators on which to calculate the mediation effects.
pred.new	a new set of predictor(s).
cova.new	a new set of covariate(s).
binpred	if TRUE, the predictor is binary.
type	the type of prediction when y is class Surv. Is "risk" if not specified.
w.new	the weights for new.x.

<code>all.model</code>	save all the fitted model from bootstrap samples if TRUE. This needs to be true to make inferences on moderation effects.
<code>xmod</code>	If there is a moderator, <code>xmod</code> gives the moderator's name in <code>cova</code> and/or <code>x</code> .
<code>custom.function</code>	a string of customer defined final model for predicting the outcome(s). The response variable should be noted as "responseY", the dataset should be noted as "dataset123". The weights for observations should be noted as "weights123". The covariates should be in <code>x</code> or <code>pred</code> . Use "~." for all variables in <code>x</code> and <code>pred</code> is allowed. The customer defined model should be able to make prediction by using "predict(object, newdata=...)", where the object is the results of the fitted model. If a specific package needs to be called to fit the model, the user should call the package first. For example, if the <code>gamlss</code> package is used to fit a piecewise polynomial with "age" to be the mediator and "race" be the predictor, we can set <code>custom.function="gamlss(responseV~b(age,df=3)+race,data=dataset123,tace=FALSE)".</code> The length of <code>custom.function</code> should be the same as the dimension of <code>y</code> . If <code>custom.function[j]</code> is NA, the usual method will be used to fit <code>y[j]</code> .
<code>para</code>	It is for binary predictors. If it is true, we would like the x-m relationship be fitted parametrically.

Details

The mediators are not tested in this function. `data.org` should be used for the tests and data organizing, and then the resulting list from `data.org` can be used directly to define the arguments in this function. `boot.med` considers all variables in `x` as mediators or covariates in the final model and all variables identified by `contm`, `binm`, `catm`, or `jointm` as mediators.

Value

Returns an `mma` object.

<code>estimation</code>	list the estimation of <code>ie</code> (indirect effect), <code>te</code> (total effect), and <code>de</code> (direct effect from the predictor) separately.
<code>bootsresults</code>	a list where the first item, <code>ie</code> , is a matrix of <code>n2</code> rows where each column gives the estimated indirect effect from the corresponding mediator (identified by the column name) from the <code>n2</code> bootstrap samples; the second item, <code>te</code> , is a vector of estimated total effects from the bootstrap sample; and the 3rd item, <code>de</code> , is a vector of estimated direct effect of the predictor from the bootstrap sample.
<code>model</code>	a list where the first item, <code>MART</code> , is TRUE if <code>mart</code> is fitted for the final model; the second item, <code>Survival</code> , is TRUE if a survival model is fitted; the third item, <code>type</code> , is the type of prediction when a survival model is fitted; the fourth item, <code>model</code> , is the fitted final full model where <code>y</code> is the outcome and all predictor, covariates, and mediators are the explanatory variables; and the fourth item, <code>best.iter</code> is the number of best iterations if <code>MART</code> is used to fit the final model.
<code>data</code>	a list that contains all the used data: <code>x=x</code> , <code>y=y</code> , <code>dirx=dirx</code> , <code>binm=binm</code> , <code>contm=contm</code> , <code>catm=catm</code> , <code>jointm=jointm</code> , <code>binpred=FALSE</code> .
<code>boot.detail</code>	a list that contains the mediation effects on each row of <code>new.x</code> : <code>new.x=new.x</code> , <code>te1</code> , <code>de1</code> , <code>ie1</code> .

all_model	a list with all fitted models from bootstrap samples if all.model is TRUE.
all_iter	if all.model is TRUE, a matrix with all fitted best iterations if MART is used. Each row is from one bootstrap sample.
all_boot	if all.model is TRUE, a matrix with all bootstrap samples. Each row is one bootstrap sample.

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See Also

"[med](#)" just estimate the mediation effects.

Examples

```
data("weight_behavior")
##binary x
#binary y
x=weight_behavior[,c(2,4:14)]
pred=weight_behavior[,3]
y=weight_behavior[,15]
data.bin<-data.org(x,y,pred=pred,contmed=c(7:9,11:12),binmed=c(6,10),binref=c(1,1),
                  catmed=5,catref=1,predref="M",alpha=0.4,alpha2=0.4)
temp1<-boot.med(data=data.bin,n=2,n2=4)
temp2<-boot.med(data=data.bin,n=2,n2=4,nu=0.05,nonlinear=TRUE)

#continuous y
x=weight_behavior[,c(2,4:14)]
pred=weight_behavior[,3]
y=weight_behavior[,1]
```

```

data.cont<-data.org(x,y,pred=pred,mediator=5:12,jointm=list(n=1,j1=7:9),
                  predref="M",alpha=0.4,alpha2=0.4)
temp3<-boot.med(data=data.cont,n=2,n2=4)
temp4<-boot.med(data=data.cont,n=2,n2=4,nu=0.05, nonlinear=TRUE)

##Surv class outcome (survival analysis)

data(cgd1)      #a dataset in the survival package
x=cgd1[,c(4:5,7:12)]
pred=cgd1[,6]
status<-ifelse(is.na(cgd1$etime1),0,1)
y=Surv(cgd1$futime,status)
#for continuous predictor
data.surv.contx<-data.org(x,y,pred=pred,mediator=1:ncol(x),
                        alpha=0.5,alpha2=0.5)
temp9.contx<-boot.med(data=data.surv.contx,n=1,n2=2, type="lp")
temp10.contx<-boot.med(data=data.surv.contx,nonlinear=TRUE,n=1,n2=2)

#for binary predictor

x=cgd1[,c(5:12)]
pred=cgd1[,4]
data.surv.binx<-data.org(x,y,pred=pred,mediator=1:ncol(x),
                        alpha=0.4,alpha2=0.4)
temp9.binx<-boot.med(data=data.surv.binx,n=1,n2=2, type="lp")
summary(temp9.binx)
temp10.binx<-boot.med(data=data.surv.binx,nonlinear=TRUE,n=1,n2=2)

```

boot.mod

*Statistical Inference on Mediation Analysis with Continuous or Binary
Predictor at different level of the moderator*

Description

To make inferences on the mediation effects when the predictor is continuous or binary at different level of the moderator.

Usage

```

boot.mod(mma1,vari,continuous.resolution=10,
        w=NULL,n=20,
        x.new=NULL,w.new=NULL,pred.new=NULL,cova.new=NULL,xj=1,margin=1,
        xmod=vari,df1=1,para=FALSE)

```


Arguments

mma1	the mma project generated from the function mma or boot.med.
vari	The name of the moderator. The moderator should be included in the original data as a covariate for the response(in x) and/or for mediators (in cov).
continuous.resolution	The number of equally space points (for continuous moderator) or levels (for categorical moderator) at which to evaluate mediation effects separately. If the moderator is categorical, continuous.resolution=10 implies using all individual levels.
w	the weight for observations.
n	the time of resampling in calculating the indirect effects, default is n=20, see Yu et al. (2014).
x.new	of the same format as x, with a new set of covariates and mediators on which to calculate the mediation effects.
w.new	the weights for new.x.
pred.new	a new set of predictor(s).
cova.new	a new set of covariate for mediator(s).
xj	the inference of mediation effects at different levels of moderator is made on the xjth predictor.
margin	the change in predictor when calculating the mediation effects, see Yu et al. (2014).
xmod	If there is a moderator, xmod gives the moderator's name in cov and/or x.
df1	if nonlinear is TRUE, natural cubic spline will be used to fit the relationship between the predictor and each mediator. The df is the degree of freedom in the ns() function, the default is 1.
para	It is for binary predictors. If it is true, we would like the x-m relationship be fitted parametrically.

Details

calculate the mediation effects from the xjth predictor to the response variable(s) at each level of the mediator.

Value

Returns an mma.mod object, which is similar to the mma object. Instead of calculating mediation effects for each predictor, the function returns the mediation effects of the xjth predictor at each level of the moderator.

Author(s)

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See Also

"[med](#)" just estimate the mediation effects.

Examples

```
#binary x and categorical moderator
#linear model
data("weight_behavior")
pred=weight_behavior[,3]
x=weight_behavior[,c(2,4:14)]
inter=form.interaction(x,pred,inter.cov=c("race"),predref="M")
x=cbind(x,inter)
y=weight_behavior[,15]
head(x)
data.bin<-data.org(x,y,pred=pred,contmed=c(7:9,11:12),binmed=c(6,10),
                  binref=c(1,1),catmed=5,catref=1,predref="M",alpha=0.4,alpha2=0.4)
temp1<-boot.med(data=data.bin,n=2,n2=4,all.model=TRUE)
temp1.mode=boot.mod(temp1,vari="race",continuous.resolution=10)
plot2.mma(temp1.mode,vari="exercises",moderator="race")
plot2.mma(temp1.mode,vari="sports",moderator="race")

#nonlinear model
x=weight_behavior[,c(2,4:14)]
pred=weight_behavior[,3]
y=weight_behavior[,15]
data.bin<-data.org(x,y,pred=pred,contmed=c(7:9,11:12),binmed=c(6,10),binref=c(1,1),
                  catmed=5,catref=1,predref="M",alpha=0.4,alpha2=0.4)
temp2<-boot.med(data=data.bin,n=2,n2=4,nu=0.05,nonlinear=TRUE,all.model=TRUE)
temp2.mode=boot.mod(temp2,vari="race",continuous.resolution=10)
plot2.mma(temp2.mode,vari="exercises",moderator="race")
plot2.mma(temp2.mode,vari="sports",moderator="race")
```

```

#binary x and continuou moderator
x=weight_behavior[,c(2,4:14)]
pred=weight_behavior[,3]
y=weight_behavior[,1]
inter=form.interaction(x,pred,inter.cov=c("age"),predref="M")
x=cbind(x,inter)
head(x)
data.cont<-data.org(x,y,pred=pred,contmed=c(7:9,11:12),binmed=c(6,10),
                    binref=c(1,1),catmed=5,catref=1,predref="M",alpha=0.4,alpha2=0.4)
temp3<-boot.med(data=data.cont,n=2,n2=4,all.model=TRUE)
temp3.mode=boot.mod(temp3,vari="age",continuous.resolution=2)
summary(temp3.mode)

plot2.mma(temp3.mode,vari="exercises",moderator="age")
plot2.mma(temp3.mode,vari="sports",moderator="age")

x=weight_behavior[,c(2,4:14)]
pred=weight_behavior[,3]
y=weight_behavior[,1]
data.cont<-data.org(x,y,pred=pred,mediator=5:12,jointm=list(n=1,j1=7:9),
                    predref="M",alpha=0.4,alpha2=0.4)
temp4<-boot.med(data=data.cont,n=2,n2=4,nu=0.05,nonlinear=TRUE,all.model=TRUE)
temp4.mode=boot.mod(temp4,vari="age",continuous.resolution=2,n=20)
summary(temp4.mode)
summary(temp4.mode,bymed=TRUE)

```

cgd1

cgd1 Data Set

Description

This database was obtained from the survival package containing a time-to-event data.

Usage

```
data(weight_behavior)
```

Format

The data set contains many variables.

Examples

```
data(cgd1)
names(cgd1)
```

Description

Do a preliminary data analysis to identify potential mediators and covariates. Each variable listed in `jointm` is forced in the final estimation model as a mediator. Also organize the data into a format that can be directly used for the mediation analysis functions.

Usage

```
data.org(x,y,pred,mediator=NULL,contmed=NULL,binmed=NULL,binref=NULL,catmed=NULL,
        catref=NULL,jointm=NULL,refy=rep(NA,ncol(data.frame(y))),
        family1=as.list(rep(NA,ncol(data.frame(y)))),
        predref=rep(NA,ncol(data.frame(pred))),alpha=0.1,alpha2=0.1,
        testtype=1, w=NULL,cova=NULL)
```

Arguments

<code>x</code>	a data frame contains the predictor, all potential mediators and covariates. Note that <code>x</code> has to be a data frame. All variables in <code>x</code> that are not identified as potential mediators (by <code>mediator</code> , <code>contmed</code> , <code>binmed</code> , <code>catmed</code> , or <code>jointm</code>) are forced in mediation analysis as covariates.
<code>y</code>	the vector of outcome variable. The outcome can be binary, continuous, or of "Surv" class (see survival package for help).
<code>pred</code>	the column or matrix of predictor(s): the predictor is the exposure variable, it can be a binary or multi-categorical factor or one/a few continuous variable(s).
<code>mediator</code>	the list of mediators (column numbers in <code>x</code> or by variable names). The mediators to be checked can be identified by "contmed", "binmed" and "catmed", or by this argument, "mediator", where binary and categorical mediators in <code>x</code> are identified as factors or characters, the reference group is the first level of the factor or factorized character. If a mediator has only two unique values, the mediator is identified as binary. If the reference groups need to be changed, the binary or categorical mediators can be listed in <code>binmed</code> or <code>catmed</code> , and the corresponding reference group in <code>binref</code> or <code>catref</code> .
<code>contmed</code>	a vector of variable names or column numbers that locate the potential continuous mediators in <code>x</code> .
<code>binmed</code>	a vector of column numbers that locate the potential binary mediators in <code>x</code> .
<code>binref</code>	the defined reference groups of the binary potential mediators in <code>binmed</code> . The first levels of the mediators if is null.
<code>catmed</code>	a vector of variable names or column numbers that locate the potential categorical mediators in <code>x</code> . The first levels of the mediators if is null.
<code>catref</code>	the defined reference groups of the categorical potential mediators in <code>catmed</code> .

jointm	a list that identifies the mediators that need to be considered jointly, where the first item indicates the number of groups of mediators to be considered jointly, and each of the following items identifies the variable names or column numbers of the mediators in x for each group of joint mediators.
refy	if y is binary, the reference group of y. The default is the first level of <code>as.factor(y)</code> . y for the reference group is assigned as 0.
family1	define the conditional distribution of y given x, and the linkage function that links the mean of y with the system component in generalized linear model. The default value of family1 is <code>binomial(link = "logit")</code> for binary y, and <code>gaussian(link="identity")</code> for continuous y.
predref	if the predictor is categorical, identify the reference group of the predictor. The default is the first level of the predictor. The value of the predictor is 0 for the reference group.
alpha	the significance level at which to test if the potential mediators (identified by <code>contmed</code> , <code>binmed</code> , and <code>catmed</code>) can be used as a covariate or mediator in estimating y when all variables in x are included in the model. The default value is <code>alpha=0.1</code>
alpha2	the significant level at which to test if a potential mediator is related with the predictor. The default value is <code>alpha2=0.1</code> .
testtype	if the testtype is 1 (by default), covariates/mediators are identified using full model; if the testtype is 2, covariates/mediators are tested one by one in models with the predictor only.
w	the weight for data analysis, by default is <code>rep(1,length(y))</code> .
cova	The data frame of covariates to be used to predict the mediator(s). The covariates in cova cannot be potential mediators. If the covariates are for some specific potential mediators, <code>cova\$for.m</code> is the vector of names of potential mediators that use the covariates. Works for continuous predictors (<code>pred</code>) only, also the specified covariates should have no missing if only some mediators uses the covariates.

Value

`data.org` returns a list with the organized data and identifiers of the potential mediators in the organized data set. The list has two components, `bin.results` if there is binary or categorical exposure(s), `cont.results` if there is continuous exposures.

x	the organized data frame that include all potential mediators and covariates that should be used to estimate the outcome.
dirx	the vector/matrix of predictor(s)/exposure variable(s).
contm	the column numbers of x that locate the potential continuous mediators.
binm	when the predictor is continuous, <code>binm</code> gives the column numbers of x that locate the potential binary mediators.
catm	when the predictor is binary, <code>catm</code> gives the column numbers of x that locate the potential binary or categorical mediators; when the predictor is continuous, <code>catm</code> gives a list where the first item is the number of potential categorical mediators, and the following items give the column numbers of each binarized categorical mediator in x.

jointm	a list where the first item is the number of groups of joint mediators, and each of the following items identifies the column numbers of the mediators in the newly organized x for each group of joint mediators.
y	the vector/matrix of outcome(s).
y_type	the variable type of outcome(s): 1 is continuous, 2 is binary, 3 is reserved for multi-categorical (no 3 would show in y_type, since all categorical responses are binarized), and 4 is survival.
fullmodel	a list with each item the full linear model fitted with all potential mediators and covariates for each response.
rela	p-values of tests on the relationship between the predictor(s) and each potential mediator.
P1	If testtype=2, P1 gives the p-value of the corresponding variables in predicting the outcome(s) when only the variable and predictor are covariates in the model.
binpred	The column numbers of binary predictors in pred.
contpred	The column numbers of continuous predictors in pred.
catpred	A list with each item includes the column numbers of a categorical predictor in pred.

Note

All other variables in x but not identified by mediator, contmed, binmed, or catmed are forced in the final model as covariates. Compared with data.org, joint mediators are considered in this function. Every variable in the jointm should be listed in contmed, binmed, or catmed, and these variables are forced to be included as mediators for further mediation analysis. A variables can be included in more than one groups of joint mediators in jointm.

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See Also

"[data.org](#)" that does not consider joint mediators, which can be added freely in the mediation analysis functions later.

Examples

```
data("weight_behavior")
#binary predictor
#binary y
x=weight_behavior[,c(2,4:14)]
pred=weight_behavior[,3]
y=weight_behavior[,15]
data.b.b.2.1<-data.org(x,y,mediator=5:12,jointm=list(n=1,j1=c(5,7,9)),
                    pred=pred,predref="M", alpha=0.4,alpha2=0.4)
summary(data.b.b.2.1)
#Or you can specify the potential mediators and change the reference
#group for binary or categorical mediators. In the following code,
#potential continuous mediators are columns 8,9,10,12, and 13 of x,
#binary mediators are columns 7 and 11, and categorical mediator is
#column 6 of x with 1 to be the reference group for all categorical
#and binary mediators.
data.b.b.2<-data.org(x,y,pred=pred,contmed=c(7:9,11:12),binmed=c(6,10),
                    binref=c(1,1),catmed=5,catref=1,jointm=list(n=1,j1=c(5,7,9)),
                    predref="M",alpha=0.4,alpha2=0.4)
summary(data.b.b.2)
#use the mediator argument instead of contmet, binmed and catmed

#multivariate predictor

x=weight_behavior[,c(2:3,5:14)]
pred=weight_behavior[,4]
y=weight_behavior[,15]
data.b.b.2.3<-data.org(x,y,mediator=5:12,jointm=list(n=1,j1=c(5,7,9)),
                    pred=pred,predref="OTHER", alpha=0.4,alpha2=0.4)
summary(data.b.b.2.3)

#multivariate responses
x=weight_behavior[,c(2:3,5:14)]
pred=weight_behavior[,4]
y=weight_behavior[,c(1,15)]
data.b.b.2.4<-data.org(x,y,mediator=5:12,jointm=list(n=1,j1=c(5,7,9)),
                    pred=pred,predref="OTHER", alpha=0.4,alpha2=0.4)
summary(data.b.b.2.4)

#continuous y
x=weight_behavior[,c(2,4:14)]
pred=weight_behavior[,3]
```

```

y=weight_behavior[,1]
data.b.c.2<-data.org(x,y,pred=pred,mediator=5:12,jointm=list(n=1,j1=7:9),
  predref="M",alpha=0.4,alpha2=0.4)
summary(data.b.c.2)

#continuous predictor
#binary y
x=weight_behavior[,3:14]
pred=weight_behavior[,2]
y=weight_behavior[,15]
data.c.b.2<-data.org(x,y,pred=pred,mediator=5:12,catref=1,
  jointm=list(n=2,j1=7:9,j2=c(5,7)),alpha=0.4,alpha2=0.4)
summary(data.c.b.2)

#multivariate predictors
x=weight_behavior[,c(3:12,14)]
pred=weight_behavior[,c(2,13)]
y=weight_behavior[,15]
data.c.b.2.2<-data.org(x,y,pred=pred,mediator=5:11,catref=1,
  jointm=list(n=2,j1=7:9,j2=c(5,7)),alpha=0.4,alpha2=0.4)
summary(data.c.b.2.2)

#continuous y
x=weight_behavior[,3:14]
pred=weight_behavior[,2]
y=weight_behavior[,1]
data.c.c.2<-data.org(x,y,pred=pred,contmed=c(7:9,11:12),binmed=c(6,10),
  binref=c(1,1),catmed=5,catref=1,jointm=list(n=2,j1=7:9,j2=c(5,7)),
  alpha=0.4,alpha2=0.4)
summary(data.c.c.2)

#multivariate responses
x=weight_behavior[,c(2:3,5:14)]
pred=weight_behavior[,4]
y=weight_behavior[,c(1,15)]
data.b.c.2.4<-data.org(x,y,mediator=5:12,jointm=list(n=1,j1=c(5,7,9)),
  pred=pred,predref="OTHER", alpha=0.4,alpha2=0.4)
summary(data.b.c.2.4)

#
x=weight_behavior[,c(3:12,14)]
pred=weight_behavior[,c(2,13)]
y=weight_behavior[,c(1,15)]
data.c.c.2.2<-data.org(x,y,pred=pred,mediator=5:11,catref=1,
  jointm=list(n=2,j1=7:9,j2=c(5,7)),alpha=0.4,alpha2=0.4)
summary(data.c.c.2.2)

#Surv class outcome (survival analysis)
data(cgd1)      #a dataset in the survival package
x=cgd1[,c(4:5,7:12)]
pred=cgd1[,6]
status<-ifelse(is.na(cgd1$etime1),0,1)
y=Surv(cgd1$futime,status)

```



```

#for continuous predictor
#all other variables are considered as potential mediator
data.surv.contx<-data.org(x,y,pred=pred,mediator=(1:ncol(x)),
                        alpha=0.5,alpha2=0.5)
summary(data.surv.contx)

#for binary predictor
x=cgd1[,c(5:12)]
pred=cgd1[,4]
data.surv.binx<-data.org(x,y,pred=pred,mediator=(1:ncol(x)),
                        alpha=0.4,alpha2=0.4)
summary(data.surv.binx)

```

form.interaction *Create interaction terms of predictor(s) and potential moderator(s).*

Description

Create interaction terms of predictor(S) and potential moderator(s). Mainly for linear models.

Usage

```
form.interaction(x,pred,inter.cov,predref=NULL,kx=NULL)
```

Arguments

x	As the x in data.org.
pred	The predictor(s) that might have interaction effect with the potential moderators.
inter.cov	The vector of names of potential moderators, which are included in x as covariates.
predref	The reference group of the predictor if the predictor is categorical.
kx	The interaction is with the kx-th predictor(s). kx can be a vector. If kx is null, the interaction is with each predictor.

Details

form.interaction is used to create interaction terms between predictor(s) and potential moderator(s). The created interaction terms should be used as covariates in linear mediation analysis. The function is not needed for nonlinear mediation method.

Value

Return a matrix with the interaction terms `pred*inter.cov`.

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See Also

["test.moderation"](#), ["moderate"](#)

Examples

```
data("weight_behavior")
pred=data.frame(weight_behavior[,3])
names(pred)="pred"
x=weight_behavior[,c(2,4:14)]
inter=form.interaction(x,pred,inter.cov=c("sports","sweat"),predref=NULL)
x=cbind(x,inter)
head(x)
```

 med

Mediation Analysis with Binary or Continuous Predictor

Description

To estimate the mediation effects when the predictor is binary or continuous.

Usage

```
med(data, x=data$bin.results$x, y=data$bin.results$y, dirx=data$bin.results$dirx,
     binm=data$bin.results$binm, contm = data$bin.results$contm,
     catm = data$bin.results$catm, jointm = data$bin.results$jointm,
     cova=data$bin.results$cova, allm = c(contm, catm),
     margin=1, n=20, nonlinear=FALSE, df1=1, nu=0.001, D=3, distn=NULL,
     family1=data$bin.results$family1, refy=rep(0, ncol(y)),
     binpred=data$bin.results$binpred, x.new=x, pred.new=dirx,
     cova.new=cova, type=NULL, w=NULL, w.new=NULL, xmod=NULL,
     custom.function=NULL, para=FALSE)
```

Arguments

data	the list of result from data.org that organize the covariates, mediators, predictor and outcome. If data is FALSE, then need to set x1, y1, dirx, contm, catm, and jointm.
x	a data frame contains all mediators and covariates. Need to set up only when data is FALSE. All variables in x that are not identified as potential mediators (by mediator, contmed, binmed, catmed, or jointm) are forced in mediation analysis as covariates.
y	the vector of outcome variable. Need to set up only when data is FALSE.
dirx	the vector or matrix of predictor(s). The reference group is set to be 0. Need to set up only when data is FALSE.
binm	the variable names or the column number of x that locates the binary mediators. Need to set up only when data is FALSE.

contm	the variable names or the column numbers of x that locate the potential continuous mediators. Need to set up only when data is FALSE.
catm	categorical mediators should be binarized and be presented as a list, where the first item is the number of categorical variables and the following items are the names or the column numbers of each binarized categorical variable in x. data.org organizes the categorical mediators in this format after they pass the mediator tests. Need to set up only when data is FALSE.
jointm	a list where the first item is the number of groups of joint mediators to be considered, and each of the following items identifies the names or the column numbers of the mediators in x for each group of joint mediators. Need to set up only when data is FALSE.
cova	The data frame of covariates to be used to predict the mediator(s). The covariates in cova cannot be potential mediators. If the covariates are for some specific potential mediators, cova\$for.m is the vector of names of potential mediators that use the covariates. Works for continuous predictors (pred) only, also the specified covariates should have no missing if only some mediators uses the covariates. Need to set up only when data is FALSE.
allm	the column numbers of all mediators. Need to set up only when data is FALSE. The default value of allm is c(contm,catm).
margin	the change in predictor when calculating the mediation effects, see Yu et al. (2014).
n	the time of resampling in calculating the indirect effects, default is n=20, see Yu et al. (2014).
nonlinear	if TRUE, Multiple Additive Regression Trees (MART) will be used to fit the final full model in estimating the outcome. The default value of nonlinear is FALSE, in which case, a generalized linear model will be used to fit the final full model.
df1	if nonlinear is TRUE, natural cubic spline will be used to fit the relationship between the predictor and each mediator. The df is the degree of freedom in the ns() function, the default is 1.
nu	set the parameter "shrinkage" in gbm function if MART is to be used, by default, nu=0.001. See also help(gbm.fit).
D	set the parameter "interaction.depth" in gbm function if MART is to be used, by default, D=3. See also help(gbm.fit).
distn	the assumed distribution(s) of the outcome(s) if MART is used for final full model. The default value of distn is "gaussian" for continuous y, "bernoulli" for binary y and coxph for "Surv" class outcome.
family1	a list with the ith item define the conditional distribution of y[,i] given x, and the linkage function that links the mean of y with the system component if generalized linear model is used as the final full model. The default value of family1 is gaussian(link="identity") for continuous y[,i], and binomial(link = "logit") for binary y[,i].
refy	if y is binary, the reference group of y.
binpred	if TRUE, the predict variable is binary.

<code>x.new</code>	A new set of covariates, of the same format as <code>x</code> (after <code>data.org</code>), on which to calculate the mediation effects. For continuous predictor only. If is <code>NULL</code> , the mediation effects will be calculated based on the original data set.
<code>pred.new</code>	A new set of predictor(s), of the same format as <code>pred</code> (after <code>data.org</code>), on which to calculate the mediation effects. For continuous predictor only.
<code>cova.new</code>	A new set of covariate(s) to estimate mediators, of the same format as <code>cova</code> .
<code>type</code>	the type of prediction when <code>y</code> is class <code>Surv</code> . By default, <code>type</code> is "risk".
<code>w</code>	the weight for each case in <code>x</code> .
<code>w.new</code>	the weight for each case in <code>x.new</code> .
<code>xmod</code>	If there is a moderator, <code>xmod</code> gives the moderator's name in <code>cova</code> and/or <code>x</code> .
<code>custom.function</code>	a string of customer defined final model for predicting the outcome(s). The response variable should be noted as "responseY", the dataset should be noted as "dataset123". The weights for observations should be noted as "weights123". The covariates should be in <code>x</code> or <code>pred</code> . Use "~." for all variables in <code>x</code> and <code>pred</code> is allowed. The customer defined model should be able to make prediction by using "predict(object, newdata=...)", where the object is the results of the fitted model. If a specific package needs to be called to fit the model, the user should call the package first. For example, if the <code>gamlss</code> package is used to fit a piecewise polynomial with "age" to be the mediator and "race" be the predictor, we can set <code>custom.function="gamlss(responseV~b(age,df=3)+race,data=dataset123,tace=FALSE)".</code> The length of <code>custom.function</code> should be the same as the dimension of <code>y</code> . If <code>custom.function[j]</code> is <code>NA</code> , the usual method will be used to fit <code>y[j]</code> .
<code>para</code>	It is for binary predictors. If it is true, we would like the x-m relationship be fitted parametrically.

Details

The mediators are not tested in this function. `data.org` should be used first for the tests and data organizing, and then the resulting list from `data.org` can be used directly to define the arguments in this function. `med` considers all variables in `x` as mediators or covariates in the final model and all variables identified by `contm`, `binm`, `catm`, or `jointm` as mediators.

Value

The result is an `med` object with the item `a.bin` for results of binary or categorical exposure(s) and the item `a.cont` for continuous exposure(s):

<code>denm</code>	a matrix where each column gives the estimated direct effect not from the corresponding mediator (identified by the column name), see Yu et al. (2014) for the definition, and each row corresponding to the results from one resampling for binary predictor or the results on a row of <code>x.new</code> for continuous predictor.
<code>ie</code>	a matrix where each column gives the estimated indirect effect from the corresponding mediator (identified by the column name) and each row corresponding to the results from one resampling for binary predictor or the results on a row of <code>x.new</code> for continuous predictor.

te a vector of the estimated total effect on x.new.

model a list, where the first item, MART, is TRUE if a mart is fitted as the final model; the second item, Survival is T if a survival model is fit; the third item, type, is the type of prediction when a survival model is fitted; the fourth item, full.model, is the fitted final full model where y is the outcome and all predictor, covariates, and mediators are the explanatory variables; and the fifth item, best.iter, is the number of best iterations if MART is used to fit the final model, is NULL if the final model is a generalized linear model.

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See Also

"boot.med" to make inferences on the estimated mediation effects using bootstrap method.

Examples

```
data("weight_behavior")
##binary x
#binary y
x=weight_behavior[,c(2,4:14)]
pred=weight_behavior[,3]
y=weight_behavior[,15]
data.bin<-data.org(x,y,pred=pred,contmed=c(7:9,11:12),binmed=c(6,10),
  binref=c(1,1),catmed=5,catref=1,predref="M",alpha=0.4,alpha2=0.4)
```

```

temp1<-med(data=data.bin,n=2)
#or use self-defined final function
temp1<-med(data=data.bin,n=2,custom.function =
  'glm(responseY~.,data=dataset123,family="quasibinomial",
  weights=weights123)')
temp2<-med(data=data.bin,n=2,nonlinear=TRUE)

#multiple predictors (categorical and continuous predictors)
x=weight_behavior[,c(3,5:14)]
pred=weight_behavior[,c(2,4)]
y=weight_behavior[,15]
data.b.b.2.3<-data.org(x,y,mediator=4:11,jointm=list(n=1,j1=c(5,7,9)),
  pred=pred,predref="OTHER", alpha=0.4,alpha2=0.4)
temp1.2<-med(data.b.b.2.3,n=2)
temp2.2<-med(data.b.b.2.3,n=2,nonlinear=TRUE)

#multivariate responses
x=weight_behavior[,c(2:3,5:14)]
pred=weight_behavior[,4]
y=weight_behavior[,c(1,15)]
data.b.b.2.4<-data.org(x,y,mediator=5:12,jointm=list(n=1,j1=c(5,7,9)),
  pred=pred,predref="OTHER", alpha=0.4,alpha2=0.4)
temp1.3<-med(data.b.b.2.4,n=2)
#or use the self defined function
temp1.3<-med(data.b.b.2.4,n=2,custom.function =c('glm(responseY~.,
  data=dataset123,family="gaussian",weights=weights123)',
  'glm(responseY~.,data=dataset123,family="quasibinomial",
  weights=weights123)'))
temp2.3<-med(data.b.b.2.4,n=2,nonlinear=TRUE)

#continuous y
x=weight_behavior[,c(2,4:14)]
pred=weight_behavior[,3]
y=weight_behavior[,1]
data.cont<-data.org(x,y,pred=pred,mediator=5:12,jointm=list(n=1,j1=7:9),
  predref="M",alpha=0.4,alpha2=0.4)
temp3<-med(data=data.cont,n=2)
temp4<-med(data=data.cont,n=2,nonlinear=TRUE)

##continuous x
#binary y
x=weight_behavior[,3:14]
pred=weight_behavior[,2]
y=weight_behavior[,15]
data.contx<-data.org(x,y,pred=pred,mediator=4:10,alpha=0.4,alpha2=0.4)
temp5<-med(data=data.contx,n=2)
#or use the self defined function
temp5<-med(data=data.contx,n=2,custom.function ='glm(responseY~.,
  data=dataset123,family="quasibinomial",weights=weights123)')
temp6<-med(data=data.contx,n=2,nonlinear=TRUE,nu=0.05)

#continuous y

```

```

x=weight_behavior[,3:14]
y=weight_behavior[,1]
pred=weight_behavior[,2]
data.contx<-data.org(x,y,pred=pred,contmed=c(11:12),binmed=c(6,10),
                    binref=c(1,1),catmed=5,catref=1,
                    alpha=0.4,alpha2=0.4)

temp7<-med(data=data.contx,n=2)
temp8<-med(data=data.contx,n=2,nonlinear=TRUE,nu=0.05)

##Surv class outcome (survival analysis)
data(cgd1)      #a dataset in the survival package
x=cgd1[,c(4:5,7:12)]
pred=cgd1[,6]
status<-ifelse(is.na(cgd1$time1),0,1)
y=Surv(cgd1$time, status)
#for continuous predictor
data.surv.contx<-data.org(x,y,pred=pred,mediator=1:ncol(x),
                        alpha=0.5,alpha2=0.5)
temp9.contx<-med(data=data.surv.contx,n=2,type="lp")

#close to mart results when use type="lp"
temp9.contx
temp10.contx<-med(data=data.surv.contx,n=2,nonlinear=TRUE)
#results in the linear part unit
temp10.contx

#for binary predictor
x=cgd1[,c(5:12)]
pred=cgd1[,4]
data.surv.binx<-data.org(x,y,pred=pred,mediator=1:ncol(x),
                        alpha=0.4,alpha2=0.4)
temp9.binx<-med(data=data.surv.binx,n=2,type="lp")
temp9.binx
temp10.binx<-med(data=data.surv.binx,n=2,nonlinear=TRUE)
temp10.binx

```

Description

Test for mediators and do statistical inferences on the identified mediation effects.

Usage

```

mma(x,y,pred,mediator=NULL, contmed=NULL,binmed=NULL,binref=NULL,catmed=NULL,
    catref=NULL, jointm=NULL, covs=NULL, refy=rep(NA,ncol(data.frame(y))),
    predref=rep(NA,ncol(data.frame(pred))),alpha=0.1,alpha2=0.1, margin=1, n=20,
    nonlinear=FALSE,df1=1,nu=0.001,D=3,distn=NULL,

```

```
family1=as.list(rep(NA,ncol(data.frame(y))))),n2=50,w=rep(1,nrow(x)),
testtype=1, x.new=NULL, pred.new=NULL, cova.new=NULL, type=NULL,w.new=NULL,
all.model=FALSE,xmod=NULL,custom.function = NULL,para=FALSE)
```

Arguments

x	a data frame contains the predictor, all potential mediators and covariates. All variables in x that are not identified as potential mediators (by mediator, contmed, binmed, catmed, or jointm) are forced in mediation analysis as covariates.
y	the vector of outcome variable.
pred	the vector/matrix of the predictor(s).
mediator	the list of mediators (column numbers in x or by variable names). The mediators to be checked can be identified by "contmed", "binmed" and "catmed", or by this argument, "mediator", where binary and categorical mediators in x are identified by factors, the reference group is the first level of the factor.
contmed	a vector of column numbers that locate the potential continuous mediators in x.
binmed	a vector of column numbers that locate the potential binary mediators in x.
binref	the defined reference groups of the binary potential mediators in binmed.
catmed	a vector of column numbers that locate the potential categorical mediators in x.
catref	the defined reference groups of the categorical potential mediators in catmed.
jointm	a list that identifies the mediators that need to be considered jointly, where the first item indicates the number of groups of mediators to be considered jointly, and each of the following items identifies the column numbers of the mediators in x for each group of joint mediators.
cova	The data frame of covariates to be used to predict the mediator(s). The covariates in cova cannot be potential mediators. If the covariates are for some specific potential mediators, cova\$for.m is the vector of names of potential mediators that use the covariates. Works for continuous predictors (pred) only, also the specified covariates should have no missing if only some mediators uses the covariates. Works mainly for continuous predictors (pred), also the specified covariates should have no missing if only some mediators uses the covariates.
refy	if y is binary, the reference group of y. By default, the reference group will be the first level of as.factor(y).
predref	if predictor is binary, identify the reference group of the binary predictor. By default, the reference group will be the first level of the predictor.
alpha	the significance level at which to test if the potential mediators (identified by contmed, binmed, and catmed) can be used as a covariate or mediator in estimating y when all variables in x are included in the model. The default value is alpha=0.1
alpha2	the significant level at which to test if a potential mediator is related with the predictor. The default value is alpha2=0.1.
margin	if binpred is FALSE, define the change in predictor when calculating the mediation effects, see Yu et al. (2014).

n	the time of resampling in calculating the indirect effects, default is n=20, see Yu et al. (2014).
nonlinear	if TRUE, Multiple Additive Regression Trees (MART) will be used to fit the final full model in estimating the outcome. The default value of nonlinear is FALSE, in which case, a generalized linear model will be used to fit the final full model.
df1	if nonlinear is TRUE, natural cubic spline will be used to fit the relationship between the continuous predictor and each mediator. The df is the degree of freedom in the ns() function, the default is 1.
nu	set the parameter "interaction.depth" in gbm function if MART is to be used, by default, nu=0.001. See also help(gbm.fit).
D	set the parameter "shrinkage" in gbm function if MART is to be used, by default, D=3. See also help(gbm.fit).
distn	the assumed distribution of the outcome if MART is used for final full model. The default value of distn is "bernoulli" for binary y, and "gaussian" for continuous y.
family1	define the conditional distribution of y given x, and the linkage function that links the mean of y with the system component if generalized linear model is used as the final full model. The default value of family1 is binomial(link = "logit") for binary y, gaussian(link="identity") for continuous y.
n2	the number of times of bootstrap resampling. The default value is n2=50.
w	the weight for each observation.
testtype	if the testtype is 1 (by default), covariates/mediators are identified using full model; if the testtype is 2, covariates/mediators are tested one by one in models with the predictor only.
x.new	A new set of predictor and corresponding covariates, of the same format as x (after data.org), on which to calculate the mediation effects. For continuous predictor only. If is NULL, the mediation effects will be calculated based on the original data set.
pred.new	A new set of predictor(s), of the same format as x (after data.org), on which to calculate the mediation effects. For continuous predictor only.
cova.new	a new set of covariate(s).
type	the type of prediction when y is class Surv. Is "risk" if not specified.
w.new	the weights for new.x.
all.model	save all the fitted model from bootstrap samples if TRUE. This needs to be true to make inferences on moderation effects.
xmod	If there is a moderator, xmod gives the moderator's name in cova and/or x.
custom.function	a string of customer defined final model for predicting the outcome(s). The response variable should be noted as "responseY", the dataset should be noted as "dataset123". The weights for observations should be noted as "weights123". The covariates should be in x or pred. Use "~." for all variables in x and pred is allowed. The customer defined model should be able to make prediction by

using "predict(object, newdata=...)", where the object is the results of the fitted model. If a specific package needs to be called to fit the model, the user should call the package first. For example, if the gamlss package is used to fit a piecewise polynomial with "age" to be the mediator and "race" be the predictor, we can set custom.function="gamlss(responseV~b(age,df=3)+race,data=dataset123,tace=FALSE)". The length of custom.function should be the same as the dimension of y. If custom.function[j] is NA, the usual method will be used to fit y[j].

para It is for binary predictors. If it is true, we would like the x-m relationship be fitted parametrically.

Details

mma first tests if the potential mediators defined by binm, contm, and catm should be treated as mediators or covariates (if none, the variable will be deleted from further analysis). All variables identified by jointm are treated as mediators. All other variables in x that are not tested are treated as covariates. Then mma does the mediation effects estimation and inference on the selected variables.

Value

Returns an mma object.

estimation	list the estimation of ie (indirect effect), te (total effect), and de (direct effect from the predictor) separately.
bootsresults	a list where the first item, ie, is a matrix of n2 rows where each column gives the estimated indirect effect from the corresponding mediator (identified by the column name) from the n2 bootstrap samples; the second item, te, is a vector of estimated total effects from the bootstrap sample; and the 3rd item, de, is a vector of estimated direct effect of the predictor from the bootstrap sample.
model	a list where the first item, MART, is T if mart is fitted for the final model; the second item, Survival, is T if a survival model is fitted; the third item, type, is the type of prediction when a survival model is fitted; the fourth item, model, is the fitted final full model where y is the outcome and all predictor, covariates, and mediators are the explanatory variables; and the fourth item, best.iter is the number of best iterations if MART is used to fit the final model.
data	a list that contains all the used data: x=x, y=y, dirx=dirx, binm=binm, contm=contm, catm=catm, jointm=jointm, binpred=FALSE.
boot.detail	for continuous predictor only: a list that contains the mediation effects on each row of new.pred: new.pred=new.pred, te1, de1, ie1.
all_model	a list with all fitted models from bootstrap samples if all.model is TRUE.
all_iter	if all.model is TRUE, a matrix with all fitted best iterations if MART is used. Each row is from one bootstrap sample.
all_boot	if all.model is TRUE, a matrix with all bootstrap samples. Each row is one bootstrap sample.

Author(s)

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References

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- Yu, Q., Wu, X., Li, B., and Scribner, R. (2018). <doi:10.1002/sim.7977>. "Multiple Mediation Analysis with Survival Outcomes – With an Application to Explore Racial Disparity in Breast Cancer Survival," *Statistics in Medicine*.
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See Also

"[data.org](#)" is for mediator tests, and "[med](#)" , and "[boot.med](#)" for mediation analysis and inferences.

Examples

```
data("weight_behavior")
#binary predictor
#binary y
x=weight_behavior[,c(2,4:14)]
pred=weight_behavior[,3]
y=weight_behavior[,15]
temp.b.b.glm<-mma(x,y,pred=pred,contmed=c(7:9,11:12),binmed=c(6,10),binref=c(1,1),
                 catmed=5,catref=1,predref="M",alpha=0.4,alpha2=0.4,n=2,n2=2)

temp.b.b.mart<-mma(x,y,pred=pred,contmed=c(7:9,11:12),binmed=c(6,10),binref=c(1,1),
                 catmed=5,catref=1,predref="M",alpha=0.4,alpha2=0.4,nonlinear=TRUE,n=2,n2=5)
#continuous y
x=weight_behavior[,c(2,4:14)]
pred=weight_behavior[,3]
y=data.frame(weight_behavior[,1])
colnames(y)="bmi"
temp.b.c.glm<-mma(x,y,pred=pred,mediator=5:12,jointm=list(n=1,j1=7:9),
                 predref="M",alpha=0.4,alpha2=0.4,n2=20)
```

```

temp.b.c.mart<-mma(x,y,pred=pred,mediator=5:12,jointm=list(n=1,j1=7:9),
                  predref="M",alpha=0.4,alpha2=0.4,
                  n=2,nonlinear=TRUE,n2=20)

##Surv class outcome (survival analysis)
data(cgd1)      #a dataset in the survival package
x=cgd1[,c(4:5,7:12)]
pred=cgd1[,6]
status<-ifelse(is.na(cgd1$time1),0,1)
y=Surv(cgd1$time1,status)
#for continuous predictor
temp.cox.contx<-mma(x,y,pred=pred,mediator=1:ncol(x),
                   alpha=0.5,alpha2=0.5,n=1,n2=2,type="lp")
summary(temp.cox.contx)
temp.surv.mart.contx<-mma(x,y,pred=pred,mediator=1:ncol(x),
                          alpha=0.5,alpha2=0.5,nonlinear=TRUE,n2=2)

#for binary predictor
x=cgd1[,c(5:12)]
pred=cgd1[,4]
temp.cox.binx<-mma(x,y,pred=pred,mediator=1:ncol(x),
                  alpha=0.4,alpha2=0.4,n=1,n2=2,type="lp")
summary(temp.cox.binx)

```

moderate

Calculate and plot the direct effect of the selected exposure variable at each level of the moderator.

Description

Calculate and plot the direct effect of the selected exposure variable at each level of the moderator.

Usage

```
moderate(med1,vari,j=1,kx=1,continuous.resolution=100,plot=TRUE)
```

Arguments

med1	The med object from the med function.
vari	The name of the moderator.
j	The jth response if the response is multiple.
kx	The moderate effect is with the kx-th predictor(s).
continuous.resolution	The number of equally space points at which to evaluate continuous predictors.
plot	Plot the direct effect at each level of the moderator if ture.

Details

Calculate and plot the direct effect of the selected exposure variable at each level of the moderator base on the result from the [med](#) function.

Value

The [moderate](#) returns a list where the item result is a data frame with two or three elements

moderator	the moderator levels.
x	the level of the exposure variable – available only for continuous exposure and moderate with nonlinear method.
de	the direct effect at the corresponding moderator (and exposure) level(s).

Author(s)

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See Also

["form.interaction"](#), ["test.moderation"](#)

Examples

```
#nonlinear model
data("weight_behavior")
x=weight_behavior[,c(2,4:14)]
pred=weight_behavior[,3]
y=weight_behavior[,15]
data.bin<-data.org(x,y,pred=pred,contmed=c(7:9,11:12),binmed=c(6,10),
  binref=c(1,1),catmed=5,catref=1,predref="M",alpha=0.4,alpha2=0.4)
temp2<-med(data=data.bin,n=2,nonlinear=TRUE)
result1=moderate(temp2,vari="race")
result2=moderate(temp2,vari="age")
```

plot.med

Plot the mediation effect on the fitted med object

Description

Plot the marginal effect of the selected variable on the outcome, and the marginal effect of the predictor on the selected variable.

Usage

```
## S3 method for class 'med'
plot(x,...,vari,xlim=NULL)
```

Arguments

<code>x</code>	a med object created initially call to <code>med</code> , <code>med.binx</code> , or <code>med.contx</code> .
<code>vari</code>	an indices or the name of the variable to plot.
<code>xlim</code>	the range of the variable to be plotted.
<code>...</code>	other arguments passed to the plot function.

Details

`plot.med` plots the marginal effect of the selected variable on the outcome, and the marginal effect of the predictor on the selected variable. If the predictor is binary, draw a histogram or boxplot of the marginal density of the variable at each different value of the predictor.

Value

No return value, called for graphs

Author(s)

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References

Yu, Q., Fan, Y., and Wu, X. (2014) <doi:10.4172/2155-6180.1000189>. "General Multiple Mediation Analysis With an Application to Explore Racial Disparity in Breast Cancer Survival," *Journal of Biometrics & Biostatistics*,5(2): 189.

See Also

["med"](#)

Examples

```
data("weight_behavior")
x=weight_behavior[,c(2,4:14)]
pred=weight_behavior[,3]
y=weight_behavior[,15]
data.bin<-data.org(x,y,pred=pred,contmed=c(7:9,11:12),binmed=c(6,10),
  binref=c(1,1),catmed=5,catref=1,predref="M",alpha=0.4,alpha2=0.4)
temp1<-med(data=data.bin,n=2)
temp2<-med(data=data.bin,n=2,nonlinear=TRUE)
plot(temp1,data.bin,vari="exercises",xlim=c(0,50))
plot(temp2,data.bin,vari="sports")
```

plot.mma	<i>Relative effects plot of the fitted mma object</i>
----------	---

Description

Plot the marginal effect of the selected variable on the outcome, and the marginal effect of the predictor on the selected variable.

Usage

```
## S3 method for class 'mma'
plot(x, ..., vari, xlim=NULL, alpha=0.95,
      quantile=FALSE)
```

Arguments

x	a mma object created initially call to mma, boot.met.binx, or boot.met.contx.
vari	an indices or the name of the variable to plot.
xlim	the range of the variable to be plotted.
alpha	for continuous predictor only, to draw the alpha confidence interval of the indirect effect.
quantile	for continuous predictor only, if true to draw the alpha confidence interval of the indirect effect based on quantile, otherwise, based on the normal approximation.
...	other arguments passed to the plot function.

Details

plot.mma plots the marginal effect of the selected variable on the outcome, and the marginal effect of the predictor on the selected variable. If the predictor is binary, draw a histogram or boxplot of the marginal density of the variable at each different value of the predictor.

Value

No return value, called for drawing graphs

Author(s)

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References

Yu, Q., Fan, Y., and Wu, X. (2014) <doi:10.4172/2155-6180.1000189>. "General Multiple Mediation Analysis With an Application to Explore Racial Disparity in Breast Cancer Survival," *Journal of Biometrics & Biostatistics*,5(2): 189.

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See Also

"mma", "boot.med"

Examples

```
data("weight_behavior")
x=weight_behavior[,c(2,4:14)]
pred=weight_behavior[,3]
y=weight_behavior[,15]
temp.b.b.glm<-mma(x,y,pred=pred,contmed=c(7:9,11:12),binmed=c(6,10),binref=c(1,1),
                 catmed=5,catref=1,predref="M",alpha=0.4,alpha2=0.4,n=2,n2=2)
plot(temp.b.b.glm,vari="exercises",xlim=c(0,50))
plot(temp.b.b.glm,vari="sports")
```

plot2.mma

Relative effects plot of the fitted mma object with moderator

Description

Plot the marginal effect of the selected variable on the outcome, and the marginal effect of the predictor on the selected variable, at each level of the moderator.

Usage

```
plot2.mma(x, ..., vari, xlim=NULL, alpha=0.95, quantile=FALSE, moderator, xj=1)
```

Arguments

x	a mma object created initially call to boot.mod.
vari	an indices or the name of the variable to plot.
xlim	the range of the variable to be plotted.
alpha	for continuous predictor only, to draw the alpha confidence interval of the indirect effect.

quantile	for continuous predictor only, if true to draw the alpha confidence interval of the indirect effect based on quantile, otherwise, based on the normal approximation.
...	other arguments passed to the plot function.
moderator	the name of the moderator.
xj	the moderation effect on the xjth predictor.

Details

plot2.mma plots the marginal effect of the selected variable on the outcome, and the marginal effect of the predictor on the selected variable, at each level of the moderator. If the predictor is binary, draw a histogram or boxplot of the marginal density of the variable at each different value of the predictor.

Value

No return value, called for graphs

Author(s)

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References

- Yu, Q., Fan, Y., and Wu, X. (2014) <doi:10.4172/2155-6180.1000189>. "General Multiple Mediation Analysis With an Application to Explore Racial Disparity in Breast Cancer Survival," *Journal of Biometrics & Biostatistics*,5(2): 189.
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See Also

["boot.mod"](#)

Examples

#see boot.mod menu.

`print.med`*Print an med object*

Description

Print the estimation of mediation effects from an med object: from functions med.

Usage

```
## S3 method for class 'med'  
print(x, ..., digit=4)
```

Arguments

<code>x</code>	a med object created initially call to med.
<code>...</code>	other arguments passed to the print function.
<code>digit</code>	the number of digits to keep at printing.

Value

No return value, called for graphs

Author(s)

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References

Yu, Q., Fan, Y., and Wu, X. (2014) <doi:10.4172/2155-6180.1000189>. "General Multiple Mediation Analysis With an Application to Explore Racial Disparity in Breast Cancer Survival," *Journal of Biometrics & Biostatistics*,5(2): 189.

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See Also

["med"](#)

Examples

```

data("weight_behavior")
##binary x
#binary y
x=weight_behavior[,c(2,4:14)]
pred=weight_behavior[,3]
y=weight_behavior[,15]
data.bin<-data.org(x,y,pred=pred,contmed=c(7:9,11:12),binmed=c(6,10),
                  binref=c(1,1),catmed=5,catref=1,predref="M",alpha=0.4,alpha2=0.4)
temp1<-med(data=data.bin,n=2)
temp2<-med(data=data.bin,n=2,nonlinear=TRUE)
temp1
print(temp2,digit=5)

```

print.mma	<i>Print a mma object</i>
-----------	---------------------------

Description

Print the estimation of mediation effects from an mma object.

Usage

```

## S3 method for class 'mma'
print(x,...,digit=3)

```

Arguments

x	a mma object created initially call to mma, boot.med.binx, or boot.med.contx.
...	other arguments passed to the print function.
digit	the number of decimal digits to keep.

Value

Return a LIST

ie	estimation of the indirect effects from the mma object.
te	estimation of the total effect from the mma object.
de	estimation of the direct effect from the mma object.

Author(s)

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References

- Yu, Q., Fan, Y., and Wu, X. (2014) <doi:10.4172/2155-6180.1000189>. "General Multiple Mediation Analysis With an Application to Explore Racial Disparity in Breast Cancer Survival," *Journal of Biometrics & Biostatistics*,5(2): 189.
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See Also

"mma", "boot.med"

Examples

```
data("weight_behavior")
x=weight_behavior[,c(2,4:14)]
pred=weight_behavior[,3]
y=weight_behavior[,15]
temp.b.b.glm<-mma(x,y,pred=pred,contmed=c(7:9,11:12),binmed=c(6,10),binref=c(1,1),
                 catmed=5,catref=1,predref="M",alpha=0.4,alpha2=0.4,n=2,n2=2)
print(temp.b.b.glm,digit=8)
```

summary.med_iden

Summary method for class "med_iden".

Description

Compute the estimations, standard deviations and confidence intervals of the mediation effects.

Usage

```
## S3 method for class 'med_iden'
summary(object,...,only=FALSE)
## S3 method for class 'summary.med_iden'
print(x,...)
```

Arguments

object	a med_iden object created initially call to data.org.
x	a summary.med_iden object created initially call to summary.med_iden
...	other arguments passed to the print function.
only	if only=T, show test results for selected covariates and mediators only.

Details

summary.med_iden gives a list of identified mediators, covariates and the test results.

Value

The function summary.med_iden return a list of covariates and mediators as identified by a series tests.

mediator	variable names of the identified mediators, either significant in both full model and in relate to the predictor, or being a member of the pre-identified joint mediators.
covariate	variable names of covariates: being significant in the full model but not significantly relate with the predictor.
tests	statistical test results.
results	the original object.

Author(s)

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References

- Yu, Q., Fan, Y., and Wu, X. (2014) <doi:10.4172/2155-6180.1000189>. "General Multiple Mediation Analysis With an Application to Explore Racial Disparity in Breast Cancer Survival," *Journal of Biometrics & Biostatistics*,5(2): 189.
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- Yu, Q., Medeiros, KL, Wu, X., and Jensen, R. (2018). <doi:10.1007/s11336-018-9612-2>. "Explore Ethnic Disparities in Anxiety and Depression Among Cancer Survivors Using Nonlinear Mediation Analysis," *Psychometrika*, 83(4), 991-1006.

See Also

"mma", "boot.med"

Examples

```

data("weight_behavior")
x=weight_behavior[,c(2,4:14)]
pred=weight_behavior[,3]
y=weight_behavior[,15]
data.b.b.2<-data.org(x,y,mediator=5:12,jointm=list(n=1,j1=c(5,7,9)),
                    pred=pred,predref="M", alpha=0.4,alpha2=0.4)
summary(data.b.b.2)

```

summary.mma

*Summary of an mma project***Description**

Compute the estimations, standard deviations and confidence intervals of the mediation effects.

Usage

```

## S3 method for class 'mma'
summary(object,..., alpha=0.05, plot=TRUE, RE=FALSE,
        quant=FALSE,ball.use=FALSE,bymed=FALSE)
## S3 method for class 'summary.mma'
print(x,...,digit=3)

```

Arguments

object	a mma object created initially call to mma, boot.met.binx, or boot.met.contx.
x	a summary.mma object created initially call to summary.mma.
...	other arguments passed to the print function.
alpha	the alpha level for confidence interval.
plot	default is TRUE, if ture, draw a barplot of the mediation effects with confidence intervals.
RE	default is FALSE, if ture, show the inferences on relative mediation effects.
quant	default is TRUE, if ture and ball.use is FALSE, draw the confidence intervals of relative effects using quantile.
ball.use	default is TRUE, if ture, draw the confidence intervals of relative effects using the confidence ball. If both quant and ball.use are false, draw the confidence intervals based on the standard deviatons from bootstrap estimates.
digit	the number of decimal digits to keep.
bymed	if true, show results by each mediator.

Details

summary.mma gives a list of the estimations and summary statistics based on the bootstrap results. If plot=T, draw a barplot of the relative effects of the direct effect of the predictor and indirect effects of the mediators. Relative effects is defined as the (in)direct effect divided by the total effect. The plot is arranged in order from the largest to the smallest relative effect.

Value

The function `summary.mma` return a list. The first item, `results`, is the list for mediation effects, and the second item, `re`, is the list for relative effects. Under them, `results` have the items `ie`, `te` and `de`; `re` has the items `ie` and `de`. In each of the items, `est` is the estimation of the corresponding (relative) mediation effects based on the whole data, `mean` is the average estimated (relative) effects from the bootstrap samples, `sd` is the standard deviation of the estimates from the bootstrap sample. `upbd` and `lwbd` are the upper and lower bound of the confidence interval of the estimation using parametric method from the bootstrap sample, `upbd_q` and `lwbd_q` are the corresponding quantiles of the estimation from the bootstrap sample.

`ie` a matrix of statistics inference on the (relative) indirect effects from the `mma` object. `est` is the estimate using the full sample. `mean` is the estimate that average over the bootstrap estimates. `sd` is the standard deviation of the bootstrap estimates. `upbd` and `lwbd` are the confidence bounds based on `sd`. `upbd_q` and `lwbd_q` are the confidence bounds based on quantiles of the bootstrap estimates. `upbd_b` and `lwbd_b` are confidence ball bounds based on bootstrap estimates.

`te` statistics inference on the total effects from the `mma` object.

`de` statistics inference on the (relative) direct effects from the `mma` object.

If `plot=T`, draw a barplot of the relative mediation effects.

Author(s)

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References

- Yu, Q., Fan, Y., and Wu, X. (2014) <doi:10.4172/2155-6180.1000189>. "General Multiple Mediation Analysis With an Application to Explore Racial Disparity in Breast Cancer Survival," *Journal of Biometrics & Biostatistics*,5(2): 189.
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See Also

"mma", "boot.med"

Examples

```

data("weight_behavior")
x=weight_behavior[,c(2,4:14)]
pred=weight_behavior[,3]
y=weight_behavior[,15]
temp.b.b.glm<-mma(x,y,pred=pred,contmed=c(7:9,11:12),binmed=c(6,10),binref=c(1,1),
                 catmed=5,catref=1,predref="M",alpha=0.4,alpha2=0.4,n=2,n2=2)
summary(temp.b.b.glm, RE=TRUE, ball.use=FALSE)
summary(temp.b.b.glm, ball.use=FALSE)

```

test.moderation	<i>Test for moderation effects.</i>
-----------------	-------------------------------------

Description

Used on a med object, test if there are moderation effects.

Usage

```
test.moderation(med1, vari, j=1, kx=NULL)
```

Arguments

med1	a med object created initially call to med.
vari	If med1 was from generalized linear method, vari is the vector of names of potential moderation effects – the interaction terms formed by the potential moderator(s) times the predictor(s). Those interaction terms have to be included in mediation analysis as covariates. If med1 was formed by nonlinear method, vari is the vector of names of potential moderators, which have been included in mediation analysis as covariates.
j	To check the moderation effect on the jth response.
kx	The moderation effect is with the kx-th predictor(s). kx can be a vector. If kx is null, the moderation effect is with each predictor.

Details

test.moderation is used to test whether direct moderation effect is significant based on the med object from med function (mediation analysis). If generalized linear models were used for mediation analysis, the moderation effects (formed by the interactions of potential moderators and predictor) should be included in the mediation analysis as covariates. The function test.moderation will give the significance levels of these interaction terms. If nonlinear models were used for mediation analysis, the potential moderators (but not the interaction terms) should have been included in mediation analysis as covariates. The function test.moderation will give not only significance levels of their interaction with the predictor(s) in generalized linear model, but also the H-statistics by Friedman and Popescue (2008).

Value

No return value, called for test results.

Author(s)

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References

- Yu, Q., Fan, Y., and Wu, X. (2014) <doi:10.4172/2155-6180.1000189>. "General Multiple Mediation Analysis With an Application to Explore Racial Disparity in Breast Cancer Survival," *Journal of Biometrics & Biostatistics*,5(2): 189.
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See Also

["med"](#)., ["moderate"](#)

Examples

```
data("weight_behavior")
x=weight_behavior[,c(2,4:14)]
pred=weight_behavior[,3]
y=weight_behavior[,15]
data.bin<-data.org(x,y,pred=pred,contmed=c(7:9,11:12),binmed=c(6,10),
                 binref=c(1,1),catmed=5,catref=1,predref="M",alpha=0.4,alpha2=0.4)
temp2<-med(data=data.bin,n=2,nonlinear=TRUE)
a=test.moderation(temp2,c("sports","sweat"),j=1,kx=NULL)

x=cbind(x,form.interaction(x,pred,inter.cov=c("sports","sweat"),predref=NULL))

data.bin<-data.org(x,y,pred=pred,contmed=c(7:9,11),binmed=c(6,10),
                 binref=c(1,1),catmed=5,catref=1,predref="M",alpha=0.4,alpha2=0.4)
temp1<-med(data=data.bin,n=2)
a=test.moderation(temp1,c("sports","sweat"),j=1,kx=NULL)
```

`weight_behavior`*Weight_Behavior Data Set*

Description

This database was obtained from the Louisiana State University Health Sciences Center, New Orleans, by Dr. Richard Scribner. He explored the relationship between BMI and kids behavior through a survey at children, teachers and parents in Grenada in 2014. This data set includes 691 observations and 15 variables.

Usage

```
data(weight_behavior)
```

Format

The data set contains the following variables:

bmi - body mass index, calculated by $\text{weight}(\text{kg})/\text{height}(\text{cm})^2$, numeric

age - children's age in years at the time of survey, numeric

sex - sex of the children, factor

race - race of the children, factor

numpeople - number of people in family, numeric

car - the number of cars in family, numeric

gotosch - the method used to go to school, factor

snack - eat snack or not in a day, binary

tvhours - number of hours watching TV per week, numeric

cmphours - number of hours using computer per week, numeric

cellhours - number of hours playing with cell phones per week, numeric

sports - join in a sport team or not, 1: yes; and 2: no

exercises - number of hours of exercises per week, numeric

sweat - number of hours of sweating activities per week, numeric

overweigh - the child is overweighed or not, binary

Examples

```
data(weight_behavior)
names(weight_behavior)
```

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