Package ‘genius’

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Title G-Estimation under No-Interaction with Unmeasured Selection

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Description This package implements the MR GENIUS estimator.

Depends R (>= 3.4.1)

License GPL-3

Encoding UTF-8

LazyData true

RoxygenNote 6.0.1

Imports gmm (>= 1.6-1),
BB

Suggests knitr,
rmarkdown

VignetteBuilder knitr

R topics documented:

`genius_addY` *MR GENIUS under additive outcome model*

Description

Implements MR GENIUS under an additive outcome model.

Usage

```
genius_addY(Y, A, G, formula = A ~ G, alpha = 0.05, lower = -10,
  upper = 10)
```

Arguments

`Y`	A numeric vector of outcomes.
`A`	A numeric vector of exposures (binary values should be coded in 0/1).
`G`	A numeric matrix of instruments; each column stores values for one instrument (a numeric vector if only a single instrument is available).
`formula`	An object of class "formula" describing the linear predictor of the model for $E(A\|G)$ (default A G, main effects of all available instruments).
`alpha`	Significance level for confidence interval (default value=0.05).
`lower`	The lower end point of the causal effect interval to be searched (default value=-10).
`upper`	The upper end point of the causal effect interval to be searched (default value=10).

Details

This function implements the estimators given in equations (6) and (12) of Tchetgen Tchetgen et al (2017) for single and multiple instruments, respectively. The term $E(A|G)$ is modelled under the logit and identity links for binary and continuous exposure respectively, with a default linear predictor consisting of the main effects of all available instruments.

Value

A "genius" object containing the following items:

`beta.est`	The point estimate of the causal effect (on the additive scale) of the exposure on the outcome.
`beta.var`	The corresponding estimated variance.
`ci`	The corresponding Wald-type confidence interval at specified significance level.
`pval`	The p-value for two-sided Wald test of null causal effect (on the additive scale) of the exposure on the outcome.

References

Tchetgen Tchetgen, E., Sun, B. and Walter, S. (2017). The GENIUS Approach to Robust Mendelian Randomization Inference. arXiv e-prints.

Examples

```
# the following packages are needed to simulate data
library("msm")
library("MASS")
expit <- function(x) {
   exp(x)/(1+exp(x))
}

### example with binary exposure, all instruments invalid ###
# true causal effect, beta = 1.0
# Number of instruments, nIV = 10
# Y: vector of outcomes
# A: vector of exposures
# G: matrix of instruments, one column per instrument

nIV=10; N=5000; beta=1;
```

```
phi=rep(-0.02,nIV); gamma=rep(-0.15,nIV); alpha=rep(-0.5,nIV);
Gn = mvrnorm(N,rep(0,nIV),diag(rep(1,nIV)))

G  = (Gn>0)*1;
U= as.vector(phi%*%t(G))+ rtnorm(n=N,mean=0.35,lower=0.2,upper=0.5);
A = rbinom(N,1,expit(as.vector(gamma%*%t(G)))+U-0.35-as.vector(phi%*%t(G)));
Y = as.vector(alpha%*%t(G)) + beta*A + U + rnorm(N);

genius_addY(Y,A,G);

### specify a more richly parameterized linear predictor for the model
### of E[A|G] containing all main effects and pairwise interactions of
### instruments

colnames(G)=paste("g",1:10,sep="")

genius_addY(Y,A,G,A~(g1+g2+g3+g4+g5+g6+g7+g8+g9+g10)^2);

### example with continous exposure, all instruments invalid ###

nIV=10; N=500; beta=1;
phi=rep(-0.5,nIV); gamma=rep(-2,nIV); alpha=rep(-0.5,nIV);
lambda0=1; lambda1=rep(0.5,nIV);
Gn = mvrnorm(N,rep(0,nIV),diag(rep(1,nIV)))

G  = (Gn>0)*1;
U = as.vector(phi%*%t(G))+rnorm(N);
A = as.vector(gamma%*%t(G)) +U + rnorm(N,mean=0,sd=abs(lambda0+as.vector(lambda1%*%t(G))));
Y = as.vector(alpha%*%t(G)) + beta*A + U + rnorm(N);

genius_addY(Y,A,G);
```

`genius_mulA` *MR GENIUS under multiplicative exposure model*

Description

Implements MR GENIUS under a multiplicative exposure model.

Usage

```
genius_mulA(Y, A, G, alpha = 0.05, lower = -10, upper = 10)
```

Arguments

`Y`	A numeric vector of outcomes.
`A`	A numeric vector of exposures (binary values should be coded in 0/1).
`G`	A numeric matrix of instruments; each column stores values for one instrument (a numeric vector if only a single instrument is available).
`alpha`	Significance level for confidence interval (default value=0.05).
`lower`	The lower end point of the causal effect interval to be searched (default value=-10).
`upper`	The upper end point of the causal effect interval to be searched (default value=10).

Details

This function implements the estimator given in Lemma 3 of Tchetgen Tchetgen et al (2017), under a multiplicative exposure model. By default, the log ratio term in equation (9) is modelled as a linear combination of the main effects of all available instruments.

Value

A "genius" object containing the following items:

`beta.est`	The point estimate of the causal effect (on the additive scale) of the exposure on the outcome.
`beta.var`	The corresponding estimated variance.
`ci`	The corresponding Wald-type confidence interval at specified significance level.
`pval`	The p-value for two-sided Wald test of null causal effect (on the additive scale) of the exposure on the outcome.

References

Tchetgen Tchetgen, E., Sun, B. and Walter, S. (2017). The GENIUS Approach to Robust Mendelian Randomization Inference. arXiv e-prints.

Examples

```
#the following package is needed to simulate data
library("MASS")
nIV=10; N=2000; beta=0.5;
gamma=rep(0.5,nIV); alpha=rep(0.5,nIV);phi=rep(0.05,nIV);
Gn = mvrnorm(N,rep(0,nIV),diag(rep(1,nIV)))
G  = (Gn>0)*1;
U = as.vector(phi%*%t(G))+rnorm(N);
#exposure generated from negative binomial distribution
A = rnbinom(N,size=10,mu = exp(as.vector(gamma%*%t(G)) +0.1*U))
Y = as.vector(alpha%*%t(G)) + beta*A + U + rnorm(N);

genius_mulA(Y,A,G);
```

`genius_mulY` *MR GENIUS under multiplicative outcome model*

Description

Implements MR GENIUS under a multiplicative outcome model.

Usage

```
genius_mulY(Y, A, G, formula = A ~ G, alpha = 0.05, lower = -10,
  upper = 10)
```

Arguments

Y	A numeric vector of outcomes.
A	A numeric vector of exposures (binary values should be coded in 0/1).
G	A numeric matrix of instruments; each column stores values for one instrument (a numeric vector if only a single instrument is available).
formula	An object of class "formula" describing the linear predictor of the model for $E(A\|G)$ (default A G, main effects of all available instruments).
alpha	Significance level for confidence interval (default value=0.05).
lower	The lower end point of the causal effect interval to be searched (default value=-10).
upper	The upper end point of the causal effect interval to be searched (default value=10).

Details

This function implements MR GENIUS as the solution to the empirical version of equation (14) in Tchetgen Tchetgen et al (2017). The term $E(A|G)$ is modelled under the logit and identity links for binary and continuous exposure respectively, with a default linear predictor consisting of the main effects of all available instruments.

Value

A "genius" object containing the following items:

beta.est	The point estimate of the causal effect (on the multiplicative scale) of the exposure on the outcome.
beta.var	The corresponding estimated variance.
ci	The corresponding Wald-type confidence interval at specified significance level.
pval	The p-value for two-sided Wald test of null causal effect (on the multiplicative scale) of the exposure on the outcome.

References

Tchetgen Tchetgen, E., Sun, B. and Walter, S. (2017). The GENIUS Approach to Robust Mendelian Randomization Inference. arXiv e-prints.

Examples

```
#the following packages are needed to simulate data
library("msm")
library("MASS")

### examples under multiplicative outcome model, all instruments invalid ###
# true causal effect, beta = 1.5
# Number of instruments, nIV = 10
# Y: vector of outcomes
# A: vector of exposures
# G: matrix of instruments, one column per instrument

### binary exposure
nIV=10; N=2000; beta=1.5;
phi=rep(-0.02,nIV); gamma=rep(-0.15,nIV); alpha=rep(-0.5,nIV);
Gn = mvrnorm(N,rep(0,nIV),diag(rep(1,nIV)))
```

```
G  = (Gn>0)*1;
U= as.vector(phi%*%t(G))+ rtnorm(n=N,mean=0.35,lower=0.2,upper=0.5);
A = rbinom(N,1,expit(as.vector(gamma%*%t(G)))+U-0.35-as.vector(phi%*%t(G)));
Y = exp(beta*A)*(as.vector(alpha%*%t(G)) + U) + rnorm(N);

genius_mulY(Y,A,G);

### specify a more richly parameterized linear predictor for the model of E[A|G]
### containing all main effects and pairwise interactions of instruments

colnames(G)=paste("g",1:10,sep="")

genius_mulY(Y,A,G,A~(g1+g2+g3+g4+g5+g6+g7+g8+g9+g10)^2);

### continuous exposure
nIV=10; N=2000; beta=0.25;
phi=rep(0.2,nIV); gamma=rep(0.5,nIV); alpha=rep(0.5,nIV);
lambda0=0.5; lambda1=rep(0.5,nIV);
Gn = mvrnorm(N,rep(0,nIV),diag(rep(1,nIV)))
G  = (Gn>0)*1;
U = as.vector(phi%*%t(G))+rnorm(N);
A = as.vector(gamma%*%t(G)) +U + rnorm(N,mean=0,sd=abs(lambda0+as.vector(lambda1%*%t(G))));
Y = exp(beta*A)*(as.vector(alpha%*%t(G)) + U) + rnorm(N);

genius_mulY(Y,A,G);
```

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