

Package: mzipmed (via r-universe)

August 30, 2024

Title Mediation using MZIP Model

Version 1.4.0

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Description We implement functions allowing for mediation analysis to be performed in cases where the mediator is a count variable with excess zeroes. First a function is provided allowing users to perform analysis for zero-inflated count variables using the marginalized zero-inflated Poisson (MZIP) model (Long et al. 2014 <[DOI:10.1002/sim.6293](https://doi.org/10.1002/sim.6293)>). Using the counterfactual approach to mediation and MZIP we can obtain natural direct and indirect effects for the overall population. Using delta method processes variance estimation can be performed instantaneously. Alternatively, bootstrap standard errors can be used. We also provide functions for cases with exposure-mediator interactions with four-way decomposition of total effect.

Encoding UTF-8

LazyData true

Roxygen list(markdown = TRUE)

RoxygenNote 7.1.2

Imports MASS, stats, matrixStats, sandwich

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Depends R (>= 2.10)

Suggests rmarkdown, knitr

VignetteBuilder knitr

Repository <https://ams329.r-universe.dev>

RemoteUrl <https://github.com/ams329/mzipmed>

RemoteRef HEAD

RemoteSha 4cdb39639c710a216fb64afe3cd3962c83a67314

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binoutzimed	<i>Mediation Analysis for Zero-Inflated Count Mediators using MZIP (Binary or Count Outcome)</i>
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Description

This function incorporates the MZIP model into the counterfactual approach to mediation analysis as proposed by Vanderweele when the mediator is a Zero-Inflated count variable for cases with binary or count outcome using a Poisson regression with robust standard errors. Standard Errors for direct and indirect effects are computed using delta method or bootstrapping. Note: This function assumes that the outcome is continuous and all exposure, mediator, outcome, and confounder variables have the same sample size. Binary variables must be dummy coded prior. A Poisson regression with robust standard errors were used to obtain direct and indirect effect estimates on a risk ratio scale because odds ratios are a non-collapsible measure which can cause issues in a mediation framework (see Vanderweele 2016). A logistic-regression can be specified for rare outcomes.

Usage

```
binoutzimed(
  outcome,
  mediator,
  exposure,
  confounder = NULL,
  C = NULL,
  n = 1000,
  X = 1,
  Xstar = 0,
  error = "Delta",
  robust = FALSE,
  zioff = NULL,
  rare = FALSE,
  OFF = NULL
)
```

Arguments

outcome	is the binary or count outcome variable
mediator	is the zero-inflated mediator variable, currently only 1 mediator variable is allowed
exposure	is the primary exposure being considered, only 1 is allowed
confounder	is a vector of confounder variables. If no confounder variables are needed then confounder is set to NULL. If more than 1 confounder is being considered then use the cbind function, e.g. cbind(var1,var2)
C	is a vector for theoretical values of each confounder. By default each each value of C will be the mean value of each confounder.
n	is the number of repetition if bootstrapped errors are used. Default is 1000
X	is the theoretical value for the exposure variable to be set at. The default is to 1
Xstar	is the theoretical value for the exposure variable to be compared to X. The default is 0, so direct, indirect, and proportion mediated values will be for a 1 unit increase in the exposure variable.
error	= 'Delta' for delta method standard errors and = 'Boot' for bootstrap. Default is delta method
robust	indicates if a robust covariance matrix should be used for MZIP in delta method derivations. Default is FALSE.
zloff	(optional) use to specify an offset variable within the MZIP mediator model. Note: Mediator/Offset is used in the outcome model
rare	set to TRUE if the outcome is rare and a logistic-regression should be used instead. Default is FALSE using robust Poisson model
OFF	if an offset is specified a fixed value of the offset variable is required for computation of effects. By default the mean is used.

Value

The function will return a list of 12 elements. GLM is the results of regressing the mediator+exposure+confounder on the outcome using a Poisson model with robust standard errors

MZIP is the results of regressing the exposure and confounders on the mediator using the MZIP model

RRNDE is the risk ratio of the direct effect

RRNIE is the risk ratio of the indirect effect.

logRRNDEse is the standard error for the log risk ratio of NDE

RRNDEci is the 95% confidence interval for the direct effect risk ratio

logRRNIEse is the standard error for the indirect effect log risk ratio

RRNIEci is the 95% confidence interval for the indirect effect risk ratio

RRTE is the total effect risk ratio

logRRTEse is the standard error for the total effect log risk ratio

RRTECI is the confidence interval for the total effect risk ratio

PM is the proportion mediated

Examples

```
#Example with delta method
zimed=binoutzimed(outcome=mzipmed_data$binY,mediator=mzipmed_data$ziM,
                  exposure=mzipmed_data$X,confounder=cbind(mzipmed_data$C1,
                  mzipmed_data$C2),error="Delta",robust=FALSE,X=1,Xstar=0,
                  zioff=NULL,OFF=NULL,rare=FALSE)

#Example using bootstrapping, 10 iterations are used for succinctness
zimed2=binoutzimed(outcome=mzipmed_data$binY,mediator=mzipmed_data$ziM,
                  exposure=mzipmed_data$X,confounder=cbind(mzipmed_data$C1,
                  mzipmed_data$C2),error="Boot",n=10,C=c(0,0.5))
```

binoutzimedint

*Mediation Analysis for Zero-Inflated Count Mediators using MZIP
with Exposure-Mediator Interactions (Binary/Count Outcome)*

Description

This function will do the same thing as the binoutzimed function, but includes an exposure-mediator interaction. 4-way decomposition of total effect (Vanderweele) are included in the output.

Usage

```
binoutzimedint(
  outcome,
  mediator,
  exposure,
  confounder = NULL,
  C = NULL,
  n = 1000,
  X = 1,
  Xstar = 0,
  M = NULL,
  error = "Delta",
  robust = FALSE,
  zioff = NULL,
  rare = FALSE,
  OFF = NULL
)
```

Arguments

outcome	is the continuous outcome variable
mediator	is the zero-inflated mediator variable, currently only 1 mediator variable is allowed
exposure	is the primary exposure being considered, only 1 is allowed

confounder	is a vector of confounder variables. If no confounder variables are needed then confounder is set to NULL. If more than 1 confounder is being considered then use the cbind function, e.g. cbind(var1,var2)
C	is a vector for theoretical values of each confounder. If left out the default will be set to the mean of each confounder giving marginal effects
n	is the number of repetitions for bootstrapping. Default is 1000. Setting n when using delta method errors will have no effect on output.
X	is the theoretical value for the exposure variable to be set at. The default is to 1
Xstar	is the theoretical value for the exposure variable to be compared to X. The default is 0, so direct, indirect, and proportion mediated values will be for a 1 unit increase in the exposure variable.
M	is a fixed value for the mediator, M. If M is not specified, M will be set to its mean value
error	= 'Delta' for delta method standard errors and = 'Boot' for bootstrap. Default is delta method
robust	indicates if a robust covariance matrix should be used for MZIP in delta method derivations. Default is FALSE.
zioff	(optional) use to specify an offset variable within the MZIP mediator model. Note: Mediator/Offset is used in the outcome model
rare	set to TRUE if the outcome is rare and a logistic-regression should be used instead. Default is FALSE using robust Poisson model
OFF	if an offset is specified a fixed value of the offset variable is required for derivation of effects. By default the mean is used.

Value

The function will return a list of 34 elements. GLM is the results of regressing the mediator+exposure+confounder on the outcome using a Poisson model with robust standard errors. To assess interaction effect individually look in the glm statement at the 4th parameter estimate

MZIP is the results of regressing the exposure and confounders on the mediator using the MZIP model

RRCDE is the controlled direct effect risk ratio

RRNDE is the natural direct effect risk ratio

RRNIE is the indirect effect risk ratio.

PM is the proportion mediated

logRRCDEse is the standard error for the controlled direct effect log risk ratio

RRCDEci is the 95% confidence interval for the controlled direct effect risk ratio

logRRNDEse is the standard error for the natural direct effect log risk ratio

RRNDEci is the 95% confidence interval for the natural direct effect risk ratio

logRRNIEse is the standard error for the indirect effect log risk ratio

RRNIEci is the 95% confidence interval for the indirect effect risk ratio

Intref is the Interactive Reference effect (not a risk ratio)

Intrefse is the standard error for Intref

IntrefCI is the CI for Intref

RRPIE is the pure indirect effect risk ratio

logRRPIEse is the standard error of PIE log risk ratio

RRPIECI is the CI for PIE risk ratio
 Intmed is the interactive mediation effect (not a risk ratio)
 Intmedse is the error associated with Intmed
 IntmedCI is the CI for Intmed
 RRTE is the total effect risk ratio
 logRRTEse is the error of the total effect log risk ratio
 RRTECI is the CI for the total effect risk ratio
 Int is the overall additive interaction effect
 Intse is the standard error for the additive interaction
 IntCI is the confidence interval for the interaction effect
 PAINT is the proportion attributable to the interaction effect
 PE is the proportion eliminated
 PACDE is the proportion of the total effect due to neither mediation nor interaction
 PAIntref is the proportion of the total effect due to just interaction
 PAIntmed is the proportion of the total effect attributable to the joint effect of mediation and interaction
 PAPIE is the proportion of the total effect attributable to just mediation
 terr is the total excess relative risk

Examples

```

#Example with exposure-mediator interaction
#This builds upon function without interaction
zimmed=binoutzimedint(outcome=mzipmed_data$binY,mediator=mzipmed_data$ziM,
                      exposure=mzipmed_data$X,confounder=cbind(mzipmed_data$C1,
                      mzipmed_data$C2),error="Delta",robust=FALSE,X=1,Xstar=0,M=NULL,
                      C=NULL,zioff=NULL,OFF=NULL,rare=FALSE)
  
```

lmoutzimed

*Mediation Analysis for Zero-Inflated Count Mediators using MZIP
(Continuous Outcome)*

Description

This function incorporates the MZIP model into the counterfactual approach to mediation analysis as proposed by Vanderweele when the mediator is a Zero-Inflated count variable. Errors for direct and indirect effects are computed using delta method or bootstrap. Note: This function assumes that the outcome is continuous and all exposure, mediator, outcome, and covariates have the same sample size. Binary variables must be dummy coded prior.

Usage

```

lmoutzimed(
  outcome,
  mediator,
  exposure,
  confounder = NULL,
  C = NULL,
  )
  
```

```

n = 1000,
X = 1,
Xstar = 0,
error = "Delta",
robust = FALSE,
zioff = NULL
)

```

Arguments

outcome	is the continuous outcome variable
mediator	is the zero-inflated mediator variable, currently only 1 mediator allowed
exposure	is the primary exposure being considered, only 1 is allowed
confounder	is a vector of confounder variables. If no confounder variables are needed then confounder is set to NULL. If more than 1 confounder is being considered then use the cbind function, e.g. cbind(var1,var2)
C	is a vector for theoretical values of each confounder. By default each each value of C will be the mean value of each confounder.
n	is the number of repetition if bootstrapped errors are used
X	is the theoretical value for the exposure variable to be set at. The default is to 1
Xstar	is the theoretical value for the exposure variable to be compared to X. The default is 0, so direct, indirect, and proportion mediated values will be for a 1 unit increase in the exposure variable.
error	= 'Delta' for delta method standard errors and = 'Boot' for bootstrap. Default is delta method
robust	indicates if a robust covariance matrix should be used for MZIP in delta method derivations. Default is FALSE.
zioff	(optional) use to specify an offset variable within the MZIP mediator model. Note: Mediator/Offset is used in the outcome model

Value

The function will return a list of 12 elements. LM is the results of regressing the mediator+exposure+confounder on the outcome using a linear model
MZIP is the results of regressing the exposure and confounders on the mediator using the MZIP model
NDE is the direct effect
NIE is the indirect effect.
NDEse is the standard error for the direct effect
NDEci is the 95% confidence interval for the direct effect
NIEse is the standard error for the indirect effect
NIEci is the 95% confidence interval for the indirect effect
TE is the total effect
TEse is the standard error for the total effect
TECI is the confidence interval for the total effect
PM is the proportion mediated

Examples

```
#Example with delta method
zimed=lmoutzimed(outcome=mzipmed_data$lmY,mediator=mzipmed_data$ziM,
  exposure=mzipmed_data$X,confounder=cbind(mzipmed_data$C1,
  mzipmed_data$C2),error="Delta",robust=FALSE,X=1,Xstar=0,zioff=NULL)

#Example using bootstrapping, 10 iterations used for succinctness
zimed2=lmoutzimed(outcome=mzipmed_data$lmY,mediator=mzipmed_data$ziM,
  exposure=mzipmed_data$X,confounder=cbind(mzipmed_data$C1,
  mzipmed_data$C2),error="Boot",n=10,C=c(0,0.5))
```

lmoutzimedint	<i>Mediation Analysis for Zero-Inflated Count Mediators using MZIP with Exposure-Mediator Interactions (Continuous Outcome)</i>
---------------	---

Description

This function will do the same thing as the lmoutzimed function, but includes an exposure-mediator interaction. 4-way decomposition of total effect (Vanderweele) are included in the output.

Usage

```
lmoutzimedint(
  outcome,
  mediator,
  exposure,
  confounder = NULL,
  C = NULL,
  n = 1000,
  X = 1,
  Xstar = 0,
  M = NULL,
  error = "Delta",
  robust = FALSE,
  zioff = NULL,
  OFF = NULL
)
```

Arguments

outcome	is the continuous outcome variable
mediator	is the zero-inflated mediator variable, currently only 1 mediator variable is allowed
exposure	is the primary exposure being considered, only 1 is allowed
confounder	is a vector of confounder variables. If no confounder variables are needed then confounder is set to NULL. If more than 1 confounder is being considered then use the cbind function, e.g. cbind(var1,var2)

C	is a vector for theoretical values of each confounder. If left out the default will be set to the mean of each confounder giving marginal effects
n	is the number of repetitions for bootstrapping. Default is 1000. Setting n when using delta method errors will have no effect on output.
X	is the theoretical value for the exposure variable to be set at. The default is to 1
Xstar	is the theoretical value for the exposure variable to be compared to X. The default is 0, so direct, indirect, and proportion mediated values will be for a 1 unit increase in the exposure variable.
M	is a fixed value for the mediator, M. If M is not specified, M will be set to its mean value
error	= 'Delta' for delta method standard errors and = 'Boot' for bootstrap. Default is delta method
robust	indicates if a robust covariance matrix should be used for MZIP in delta method derivations. Default is FALSE.
zioff	(optional) used to specify an offset variable within the MZIP mediator model. Note: Mediator/Offset is used in the outcome model
OFF	if an offset is specified a fixed value of the offset is required to compute CDE. By default it is the mean of the offset or 1 if no offset is specified.

Value

The function will return a list of 30 elements. LM is the results of regressing the mediator+exposure+confounder on the outcome using a linear model. To assess interaction effect individually look in the lm statement at the 4th parameter estimate

MZIP is the results of regressing the exposure and confounders on the mediator using the MZIP model

CDE is the controlled direct effect

NDE is the natural direct effect

NIE is the indirect effect.

PM is the proportion mediated

CDEse is the standard error for the controlled direct effect

CDEci is the 95% confidence interval for the controlled direct effect

NDEse is the standard error for the natural direct effect

NDEci is the 95% confidence interval for the natural direct effect

NIEse is the standard error for the indirect effect

NIEci is the 95% confidence interval for the indirect effect

Intref is the Interactive Reference effect

Intrefse is the standard error for Intref

IntrefCI is the CI for Intref

PIE is the pure indirect effect

PIEse is the standard error of PIE

PIECI is the CI for PIE

Intmed is the interactive mediation effect

Intmedse is the error associated with Intmed

IntmedCI is the CI for Intmed

TE is the total effect

TEse is the error of the total effect
 TECI is the CI for the total effect
 Int is the overall additive interaction effect
 Intse is the standard error for the additive interaction
 IntCI is the confidence interval for the interaction effect
 PAINT is the proportion attributable to the interaction effect
 PE is the proportion eliminated

Examples

```
#Example with exposure-mediator interaction
#This builds upon function without interaction
zimed=lmoutzimedint(outcome=mzipmed_data$lmY,mediator=mzipmed_data$ziM,
  exposure=mzipmed_data$X,confounder=cbind(mzipmed_data$C1,
  mzipmed_data$C2),error="Delta",robust=FALSE,X=1,Xstar=0,M=NULL,
  C=NULL,zioff=NULL,OFF=NULL)
```

mzip

Marginalized Zero-Inflated Poisson Regression Model

Description

This function uses the MZIP model to allow you to fit counts variables with excess zeroes while allowing for easy interpretations. This function assumes that the outcome and covariates are all the same sample size without missing data. Covariates must be numerical, so binary predictors such as gender or race need to be dummy coded with zeroes and ones. For more information about this model and interpretations see Long, D Leann et al. "A marginalized zero-inflated Poisson regression model with overall exposure effects." *Statistics in medicine* vol. 33,29 (2014): 5151-65. doi:10.1002/sim.6293. Note: BFGS likelihood optimization was used for this R package. For more information on use of the `offset` argument see vignette.

Usage

```
mzip(y, pred, print = TRUE, offset = NULL)
```

Arguments

y	is the outcome variable
pred	is a vector of covariates (use <code>cbind</code> for multiple)
print	if =TRUE will give model parameters estimates and overall mean relative risks. Default =TRUE
offset	is an optional variable to be used as an offset, no need to log-transform prior

Value

The function will return a list of results from the MZIP model. In the list G(Gamma) refers to the excess zero/logistic part of the model and A(Alpha) refers to the Poisson/mean part of the model for example. Gest are the gamma coefficients for the logistic part of the MZIP model. Aest are the alpha coefficients for the Poisson part of the MZIP model. _ModelSE are the standard errors for each coefficient in the model. _RobustSE are the robust standard errors for each coefficient in the model. _ModelUpper are the upper confidence limits for each coefficient. _ModelLower are the lower confidence limits. _RobustUpper are the upper confidence limits based on robust standard error. _RobustLower are the lower confidence limits based on robust standard errors. _ModelZ are the Z scores for each coefficient. _RobustZ are the robust Z scores for each coefficient. _ModelZpval are the p-values based on the Z scores for the model. _RobustZpval are the p-values based on the robust z scores. AlphaCov is the covariance matrix for the poisson coefficient estimates Cov is the covariance matrix for the MZIP model RobAlphaCov robust covariance matrix for the Poisson component of MZIP RobCov robust covariance matrix loglik is the log-likelihood of the MZIP model AIC is the Akaike's Information Criterion of the MZIP Model BIC is the Bayesian's Information Criterion of the MZIP Model

Examples

```
test=mzip(y=mzipmed_data$ziY1,pred=cbind(mzipmed_data$X,mzipmed_data$C1,
mzipmed_data$C2),print=FALSE,offset=NULL)

## Not run:
test= mzip(y=mzipmed_data$ziY1,pred=cbind(X=mzipmed_data$X,C1=mzipmed_data$C1,
C2=mzipmed_data$C2),print=TRUE,offset=NULL)

## End(Not run)
```

mzipmed_data

Data to be used in the mzipmed package examples

Description

Data to be used in the mzipmed package examples

Usage

```
mzipmed_data
```

Format

A dataframe with 500 rows and 10 variables.

X Simulated binary exposure \sim Bernoulli(0.5)

C1 Simulated covariate \sim Normal(0,1)

C2 Simulated covariate \sim Beta(2,2)

ziM Zero-inflated count mediator based on X,C1,C2

lmM Continuous mediator based on X,C1,C2 with error term \sim Normal(0,4)

binM Binary mediator based on X,C1,C2

lmY Continuous outcome to be used for ziM

binY Binary outcome to be used for ziM

ziY1 Zero-inflated count outcome to be used for lmM

ziY2 Zero-inflated count outcome to be used for binM

@source Simulated to serve as an example

@examples data(mzipmed_data)

 zioutbinmed

*Mediation Analysis for Zero-Inflated Count Outcomes using MZIP
with binary mediators*

Description

This function incorporates the MZIP model into the counterfactual approach to mediation analysis as proposed by Vanderweele when the outcome is a Zero-Inflated count variable for cases with binary mediators using a logistic regression mediator model. Standard Errors for direct and indirect effects are computed using delta method or bootstrapping. Note: This function assumes that the outcome is continuous and all exposure, mediator, outcome, and confounder variables have the same sample size. Binary variables must be dummy coded prior. See vignette for information on how to use offset command zioff.

Usage

```
zioutbinmed(
  outcome,
  mediator,
  exposure,
  confounder = NULL,
  n = 1000,
  X = 1,
  Xstar = 0,
  C = NULL,
  error = "Delta",
  robust = FALSE,
  zioff = NULL
)
```

Arguments

outcome	is the zero-inflated count outcome variable
mediator	is the binary mediator variable, currently only 1 mediator variable is allowed
exposure	is the primary exposure being considered, only 1 is allowed
confounder	is a vector of confounder variables. If no confounder variables are needed then confounder is set to NULL. If more than 1 confounder is being considered then use the cbind function, e.g. cbind(var1,var2)
n	is the number of repetition if bootstrapped errors are used. Default is 1000
X	is the theoretical value for the exposure variable to be set at. The default is to 1
Xstar	is the theoretical value for the exposure variable to be compared to X. The default is 0, so direct, indirect, and proportion mediated values will be for a 1 unit increase in the exposure variable.
C	is a vector for theoretical values of each confounder. If left out the default will be set to the mean of each confounder giving marginal effects
error	= 'Delta' for delta method standard errors and = 'Boot' for bootstrap. Default is delta method
robust	indicates if a robust covariance matrix should be used for MZIP in delta method derivations. Default is FALSE.
zioff	(optional) use to specify an offset variable within the MZIP outcome model.

Value

The function will return a list of 12 elements. GLM is the logistic model regressing the exposure and covariates on the continuous mediator
MZIP is the results of regressing the exposure, covariates, and mediator on the outcome using the MZIP model
RRNDE is the incidence rate ratio of the direct effect
RRNIE is the incidence rate ratio of the indirect effect.
logRRNDEse is the standard error for the log rate ratio of NDE
RRNDEci is the 95% confidence interval for the direct effect rate ratio
logRRNIEse is the standard error for the indirect effect log rate ratio
RRNIEci is the 95% confidence interval for the indirect effect rate ratio
RRTE is the total effect rate ratio
logRRTEse is the standard error for the total effect log rate ratio
RRTECI is the confidence interval for the total effect rate ratio
PM is the proportion mediated

Examples

```
#Example using delta method
ziout=zioutbinmed(outcome=mzipmed_data$ziY2,mediator=mzipmed_data$binM,
                  exposure=mzipmed_data$X,confounder=cbind(mzipmed_data$C1,
                  mzipmed_data$C2),error="Delta",robust=FALSE,X=1,Xstar=0,zioff=NULL)

## Not run:
#Example using bootstrapping with 10 iterations
ziout2=zioutbinmed(outcome=mzipmed_data$ziY2,mediator=mzipmed_data$binM,
```

```
exposure=mzipmed_data$X,confounder=cbind(mzipmed_data$C1,
mzipmed_data$C2),error="Boot",n=10,C=c(0,0.5),zioff=NULL)
```

```
## End(Not run)
```

```
zioutbinmedint
```

Mediation Analysis for Zero-Inflated Count Outcomes using MZIP with Exposure-Mediator Interactions (Binary Outcome)

Description

This function will do the same thing as the zioutbinmed function, but includes an exposure-mediator interaction. 4-way decomposition of total effect (Vanderweele) are included in the output.

Usage

```
zioutbinmedint(
  outcome,
  mediator,
  exposure,
  confounder = NULL,
  n = 1000,
  M = NULL,
  X = 1,
  Xstar = 0,
  C = NULL,
  error = "Delta",
  robust = FALSE,
  zioff = NULL
)
```

Arguments

outcome	is the zero-inflated count outcome variable
mediator	is the binary mediator variable, currently only 1 mediator variable is allowed
exposure	is the primary exposure being considered, only 1 is allowed
confounder	is a vector of confounder variables. If no confounder variables are needed then confounder is set to NULL. If more than 1 confounder is being considered then use the cbind function, e.g. cbind(var1,var2)
n	is the number of repetitions for bootstrapping. Default is 1000. Setting n when using delta method errors will have no effect on output.
M	is a fixed value for the mediator, M. If M is not specified, M will be set to its mean value
X	is the theoretical value for the exposure variable to be set at. The default is to 1

Xstar	is the theoretical value for the exposure variable to be compared to X. The default is 0, so direct, indirect, and proportion mediated values will be for a 1 unit increase in the exposure variable.
C	is a vector for theoretical values of each confounder. If left out the default will be set to the mean of each confounder giving marginal effects
error	= 'Delta' for delta method standard errors and = 'Boot' for bootstrap. Default is delta method
robust	indicates if a robust covariance matrix should be used for MZIP in delta method derivations. Default is FALSE.
zloff	(optional) use to specify an offset variable within the MZIP outcome model.

Value

The function will return a list of 34 elements. MZIP is the results of regressing the mediator+exposure+confounder on the outcome using MZIP. To assess interaction effect individually look in the glm statement at the 4th parameter estimate

GLM is the results of regressing the exposure and confounders on the mediator using logistic regression

RRCDE is the controlled direct effect incidence rate ratio

RRNDE is the natural direct effect incidence rate ratio

RRNIE is the indirect effect incidence rate ratio.

PM is the proportion mediated

logRRCDEse is the standard error for the controlled direct effect log rate ratio

RRCDEci is the 95% confidence interval for the controlled direct effect rate ratio

logRRNDEse is the standard error for the natural direct effect log rate ratio

RRNDEci is the 95% confidence interval for the natural direct effect rate ratio

logRRNIEse is the standard error for the indirect effect log rate ratio

RRNIEci is the 95% confidence interval for the indirect effect rate ratio

Intref is the Interactive Reference effect (not a ratio)

Intrefse is the standard error for Intref

IntrefCI is the CI for Intref

RRPIE is the pure indirect effect incidence rate ratio

logRRPIEse is the standard error of PIE log rate ratio

RRPIECI is the CI for PIE rate ratio

Intmed is the interactive mediation effect (not a ratio)

Intmedse is the error associated with Intmed

IntmedCI is the CI for Intmed

RRTE is the total effect incidence rate ratio

logRRTEse is the error of the total effect log rate ratio

RRTECI is the CI for the total effect rate ratio

Int is the overall additive interaction effect

Intse is the standard error for the additive interaction

IntCI is the confidence interval for the interaction effect

PAINT is the proportion attributable to the interaction effect

PE is the proportion eliminated

PACDE is the proportion of the total effect due to neither mediation nor interaction

PAIntref is the proportion of the total effect due to just interaction

PAIntmed is the proportion of the total effect attributable to the joint effect of mediation and interaction

PAPIE is the proportion of the total effect attributable to just mediation

terr is the total excess relative risk

Examples

```
zimout=zioutbinmedint(outcome=mzipmed_data$ziY2,mediator=mzipmed_data$binM,
                      exposure=mzipmed_data$X,confounder=cbind(mzipmed_data$C1,
mzipmed_data$C2),error="Delta",robust=FALSE,X=1,Xstar=0,M=NULL,C=NULL,
                      zioff=NULL)
```

 zioutlmed

Mediation Analysis for Zero-Inflated Count Outcomes using MZIP

Description

This function incorporates the MZIP model into the counterfactual approach to mediation analysis as proposed by Vanderweele when the outcome is a Zero-Inflated count variable for cases with continuous mediators. Standard Errors for direct and indirect effects are computed using delta method or bootstrapping. Note: This function assumes that the outcome is continuous and all exposure, mediator, outcome, and confounder variables have the same sample size. Binary variables must be dummy coded prior. See vignette for information on use of the offset.

Usage

```
zioutlmed(
  outcome,
  mediator,
  exposure,
  confounder = NULL,
  X = 1,
  Xstar = 0,
  error = "Delta",
  n = 1000,
  robust = FALSE,
  zioff = NULL
)
```

Arguments

outcome	is the zero-inflated count outcome variable
mediator	is the continuous mediator variable, currently only 1 mediator variable is allowed
exposure	is the primary exposure being considered, only 1 is allowed

confounder	is a vector of confounder variables. If no confounder variables are needed then confounder is set to NULL. If more than 1 confounder is being considered then use the cbind function, e.g. cbind(var1,var2)
X	is the theoretical value for the exposure variable to be set at. The default is to 1
Xstar	is the theoretical value for the exposure variable to be compared to X. The default is 0, so direct, indirect, and proportion mediated values will be for a 1 unit increase in the exposure variable.
error	= 'Delta' for delta method standard errors and = 'Boot' for bootstrap. Default is delta method
n	is the number of repetition if bootstrapped errors are used. Default is 1000
robust	indicates if a robust covariance matrix should be used for MZIP in delta method derivations. Default is FALSE.
zloff	(optional) use to specify an offset variable within the MZIP outcome model.

Value

The function will return a list of 12 elements. LM is the linear model regressing the exposure and covariates on the continuous mediator

MZIP is the results of regressing the exposure, covariates, and mediator on the outcome using the MZIP model

RRNDE is the incidence rate ratio of the direct effect

RRNIE is the incidence rate ratio of the indirect effect.

logRRNDEse is the standard error for the log rate ratio of NDE

RRNDEci is the 95% confidence interval for the direct effect rate ratio

logRRNIEse is the standard error for the indirect effect log rate ratio

RRNIEci is the 95% confidence interval for the indirect effect rate ratio

RRTE is the total effect rate ratio

logRRTEse is the standard error for the total effect log rate ratio

RRTECI is the confidence interval for the total effect rate ratio

PM is the proportion mediated

Examples

```
#Example using delta method
ziout=zioutlmed(outcome=mzipmed_data$ziY1,mediator=mzipmed_data$lM,
                exposure=mzipmed_data$X,confounder=cbind(mzipmed_data$C1,
                mzipmed_data$C2),error="Delta",robust=FALSE,X=1,Xstar=0,
                zloff=NULL)

#Example using bootstrapping, 10 iterations used for succinctness
ziout2=zioutlmed(outcome=mzipmed_data$ziY1,mediator=mzipmed_data$lM,
                 exposure=mzipmed_data$X, confounder=cbind(mzipmed_data$C1,
                 mzipmed_data$C2),error="Boot",n=10,zloff=NULL)
```

zioutlmedint *Mediation Analysis for Zero-Inflated Count Outcomes using MZIP
with Exposure-Mediator Interactions*

Description

This function will do the same thing as the zioutlmed function, but includes an exposure-mediator interaction. 4-way decomposition of total effect (Vanderweele) are included in the output.

Usage

```
zioutlmedint(
  outcome,
  mediator,
  exposure,
  confounder = NULL,
  n = 1000,
  M = NULL,
  X = 1,
  Xstar = 0,
  C = NULL,
  error = "Delta",
  robust = FALSE,
  zioff = NULL
)
```

Arguments

outcome	is the zero-inflated count outcome variable
mediator	is the continuous mediator variable, currently only 1 mediator variable is allowed
exposure	is the primary exposure being considered, only 1 is allowed
confounder	is a vector of confounder variables. If no confounder variables are needed then confounder is set to NULL. If more than 1 confounder is being considered then use the cbind function, e.g. cbind(var1,var2)
n	is the number of repetitions for bootstrapping. Default is 1000. Setting n when using delta method errors will have no effect on output.
M	is a fixed value for the mediator, M. If M is not specified, M will be set to its mean value
X	is the theoretical value for the exposure variable to be set at. The default is to 1
Xstar	is the theoretical value for the exposure variable to be compared to X. The default is 0, so direct, indirect, and proportion mediated values will be for a 1 unit increase in the exposure variable.
C	is a vector for theoretical values of each confounder. If left out the default will be set to the mean of each confounder giving marginal effects

error	= 'Delta' for delta method standard errors and = 'Boot' for bootstrap. Default is delta method
robust	indicates if a robust covariance matrix should be used for MZIP in delta method derivations. Default is FALSE.
zioff	(optional) use to specify an offset variable within the MZIP outcome model.

Value

The function will return a list of 34 elements. MZIP is the results of regressing the mediator+exposure+confounder on the outcome using MZIP. To assess interaction effect individually look in the glm statement at the 4th parameter estimate

LM is the results of regressing the exposure and confounders on the mediator using linear regression

RRCDE is the controlled direct effect incidence rate ratio

RRNDE is the natural direct effect incidence rate ratio

RRNIE is the indirect effect incidence rate ratio.

PM is the proportion mediated

logRRCDEse is the standard error for the controlled direct effect log rate ratio

RRCDEci is the 95% confidence interval for the controlled direct effect rate ratio

logRRNDEse is the standard error for the natural direct effect log rate ratio

RRNDEci is the 95% confidence interval for the natural direct effect rate ratio

logRRNIEse is the standard error for the indirect log rate ratio

RRNIEci is the 95% confidence interval for the indirect effect rate ratio

Intref is the Interactive Reference effect (not a ratio)

Intrefse is the standard error for Intref

IntrefCI is the CI for Intref

RRPIE is the pure indirect effect incidence rate ratio

logRRPIEse is the standard error of PIE log rate ratio

RRPIECI is the CI for PIE rate ratio

Intmed is the interactive mediation effect (not a ratio)

Intmedse is the error associated with Intmed

IntmedCI is the CI for Intmed

RRTE is the total effect incidence rate ratio

logRRTEse is the error of the total effect log rate ratio

RRTECI is the CI for the total effect rate ratio

Int is the overall additive interaction effect

Intse is the standard error for the additive interaction

IntCI is the confidence interval for the interaction effect

PAINT is the proportion attributable to the interaction effect

PE is the proportion eliminated

PACDE is the proportion of the total effect due to neither mediation nor interaction

PAIntref is the proportion of the total effect due to just interaction

PAIntmed is the proportion of the total effect attributable to the joint effect of mediation and interaction

PAPIE is the proportion of the total effect attributable to just mediation

terr is the total excess relative risk

Examples

```
zimout=zioutlmedint(outcome=mzipmed_data$ziY1,mediator=mzipmed_data$lmM,
```

```
exposure=mzipmed_data$X,confounder=cbind(mzipmed_data$C1,  
mzipmed_data$C2),error="Delta",robust=FALSE,X=1,Xstar=0,M=NULL,C=NULL,  
zloff=NULL)
```

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