Package ‘mediateSWCRT’

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Title Mediation Analysis in a Stepped Wedge Cluster Randomized Trials

Version 0.3

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Description
Functions for calculating the point and interval estimates of the natural indirect effect (NIE), natural direct effect (NDE), total effect (TE), and mediation proportion (MP) in a stepped wedge cluster randomized trials with a constant treatment effect or an exposure-time dependent treatment effect. We perform the methods considered in Cao and Li (2024) Assessing mediation in cross-sectional stepped wedge cluster randomized trials.

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Depends R (>= 4.3.0)

Imports lme4,stats

Encoding UTF-8

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NeedsCompilation no

R topics documented:

`gen_data_etm` *Generate data in a stepped wedge design with an exposure-time dependent treatment effect*

Description

This function can generate longitudinal data in a stepped wedge design in the presence of an exposure-time dependent treatment effect

Usage

```
gen_data_etm(
  I,
  J,
  n,
  beta,
  gamma,
  theta_e,
  beta_M,
  eta_e,
  sigma_a,
  sigma_ey,
  sigma_tau,
  sigma_em,
  binary.o = 0,
  binary.m = 0
)
```

Arguments

`I`	The number of cluster
`J`	The number of time periods
`n`	The number of individuals per each cluster
`beta`	The underling time trend effect in a outcome model
`gamma`	The underling time trend effect in a mediator model
`theta_e`	The exposure effect (a J-1 vector) on the outcome conditional on mediator and other possible confounders
`beta_M`	The mediator effect on the outcome conditional on other possible confounders
`eta_e`	The exposure effect (a J-1 vector) on the mediator conditional on other possible confounders

`sigma_a` The standard error of random effect in outcome model (assuming it follows normal distribution with mean zero)

`sigma_ey` The standard error of error term in outcome model (assuming it follows normal distribution with mean zero)

`sigma_tau` The standard error of random effect in mediator model (assuming it follows normal distribution with mean zero)

`sigma_em` The standard error of error term in mediator model (assuming it follows normal distribution with mean zero)

`binary.o` (Required) If the outcome is binary, set to 1. If the outcome is continuous, set to 0

`binary.m` (Required) If the mediator is binary, set to 1. If the mediator is continuous, set to 0

Value

A data frame including cluster, period, id, E (time since intervention, i.e., exposure time), A (treatment status indicator), c (the start time of the treatment), alpha (random effects of observations within a cluster), tau (random effects of mediator within a cluster), M (mediator), Y (outcome)

Author(s)

Zhiqiang Cao <zcaoae@connect.ust.hk> and Fan Li <fan.f.li@yale.edu>

References

Kenny A., Voldal E.C., Xia F., Heagerty P.J. and Hughes J.P. Analysis of stepped wedge cluster randomized trials in the presence of a time-varying treatment effect. Statistics in Medicine. 2022;41(22):4311-4339.

Examples

```
I = 9
J = 4
n = 20
beta = cumsum(c(0,0.1,0.1/2,0.1/(2^2)))
gamma = cumsum(c(0,0.3,0.3/2,0.3/(2^2)))
sigma_tau = sigma_a = 0.334
sigma_em = sigma_ey = 1
eta_e = c(0.32,0.4,0.48)
theta_e = c(0.6,0.75,0.9)
# generate continuous outcome and continuous mediator
mydata1 = gen_data_etm(I,J,n,beta,gamma,theta_e,beta_M=0.625,eta_e,sigma_a,sigma_ey,
sigma_tau,sigma_em,binary.o=0,binary.m=0)

# generate continuous outcome and binary mediator
sigma_tau = 0.605   #using this value can produce ICC of mediator model is about 0.1 since
# ICC of binary variable is calculated as sigma_tau^2/(sigma_tau^2+pi^2/3)
mydata2 = gen_data_etm(I,J,n,beta,gamma,theta_e,beta_M=0.625,eta_e,sigma_a,sigma_ey,
sigma_tau,sigma_em,binary.o=0,binary.m=1)

# generate binary outcome and continuous mediator
sigma_a = 0.605
mydata3 = gen_data_etm(I,J,n,beta,gamma,theta_e,beta_M=0.625,eta_e,sigma_a,sigma_ey,
sigma_tau,sigma_em,binary.o=1,binary.m=0)
```

```
# generate binary outcome and binary mediator
sigma_tau = sigma_a = 0.605
mydata4 = gen_data_etm(I,J,n,beta,gamma,theta_e,beta_M=0.625,eta_e,sigma_a,sigma_ey,
sigma_tau,sigma_em,binary.o=1,binary.m=1)

# generate continuous outcome and continuous mediator with different clusters and period
I = 12
J = 5
beta = cumsum(c(0,0.1,0.1/2,0.1/(2^2),0.1/(2^3)))
gamma = cumsum(c(0,0.3,0.3/2,0.3/(2^2),0.3/(2^3)))
eta_e = c(0.32,0.4,0.48,0.56)
theta_e = c(0.6,0.75,0.9,1.05)
sigma_tau = sigma_a = 0.334
sigma_em = sigma_ey = 1
mydata5 = gen_data_etm(I,J,n,beta,gamma,theta_e,beta_M=0.625,eta_e,sigma_a,sigma_ey,
sigma_tau,sigma_em,binary.o=0,binary.m=0)
```

`gen_data_hhm` *Generate data in a stepped wedge design based on Hussey and Hughes model with a constant treatment effect*

Description

This function can generate longitudinal data in a stepped wedge design based on Hussey and Hughes model with a constant treatment effect.

Usage

```
gen_data_hhm(
  I,
  J,
  n,
  beta,
  gamma,
  theta,
  beta_M,
  eta,
  sigma_a,
  sigma_ey,
  sigma_tau,
  sigma_em,
  binary.o = 0,
  binary.m = 0
)
```

Arguments

`I`	The number of cluster
`J`	The number of time periods
`n`	The number of individuals per each cluster
`beta`	The underling time trend effect in a outcome model

gamma	The underling time trend effect in a mediator model
theta	The exposure effect on the outcome conditional on mediator and other possible confounders
beta_M	The mediator effect on the outcome conditional on other possible confounders
eta	The exposure effect on the mediator conditional on other possible confounders
sigma_a	The standard error of random effect in outcome model (assuming it follows normal distribution with mean zero)
sigma_ey	The standard error of error term in outcome model (assuming it follows normal distribution with mean zero)
sigma_tau	The standard error of random effect in mediator model (assuming it follows normal distribution with mean zero)
sigma_em	The standard error of error term in mediator model (assuming it follows normal distribution with mean zero)
binary.o	(Required) If the outcome is binary, set to 1. If the outcome is continuous, set to 0
binary.m	(Required) If the mediator is binary, set to 1. If the mediator is continuous, set to 0

Value

A data frame including cluster, period, id, E (time since intervention, i.e., exposure time), A (treatment status indicator), c (the start time of the treatment), alpha (random effects of observations within a cluster), tau (random effects of mediator within a cluster), M (mediator), Y (outcome)

Author(s)

Zhiqiang Cao <zcaoae@connect.ust.hk> and Fan Li <fan.f.li@yale.edu>

References

Hussey M.A. and Hughes J.P. Design and analysis of stepped wedge cluster randomized trials. Contemporary Clinical Trials. 2007;28(2):182-191.

Kenny A., Voldal E.C., Xia F., Heagerty P.J. and Hughes J.P. Analysis of stepped wedge cluster randomized trials in the presence of a time-varying treatment effect. Statistics in Medicine. 2022;41(22):4311-4339.

Examples

```
I = 9
J = 4
n = 20
beta = cumsum(c(0,0.1,0.1/2,0.1/(2^2)))
gamma = cumsum(c(0,0.3,0.3/2,0.3/(2^2)))
sigma_tau = sigma_a = 0.334
sigma_em = sigma_ey = 1
# generate continuous outcome and continuous mediator
mydata1 = gen_data_hhm(I,J,n,beta,gamma,theta=0.75,beta_M=0.625,eta=0.4,sigma_a,
sigma_ey,sigma_tau,sigma_em,binary.o=0,binary.m=0)

# generate continuous outcome and binary mediator
sigma_tau = 0.605   #using this value can produce ICC of mediator model is about 0.1 since
```

```
# ICC of binary variable is calculated as sigma_tau^2/(sigma_tau^2+pi^2/3)
mydata2 = gen_data_hhm(I,J,n,beta,gamma,theta=0.75,beta_M=0.625,eta=0.4,sigma_a,
sigma_ey,sigma_tau,sigma_em,binary.o=0,binary.m=1)

# generate binary outcome and continuous mediator
sigma_a = 0.605
mydata3 = gen_data_hhm(I,J,n,beta,gamma,theta=0.75,beta_M=0.625,eta=0.4,sigma_a,
sigma_ey,sigma_tau,sigma_em,binary.o=1,binary.m=0)

# generate binary outcome and binary mediator
sigma_tau = sigma_a = 0.605
mydata4 = gen_data_hhm(I,J,n,beta,gamma,theta=0.75,beta_M=0.625,eta=0.4,sigma_a,
sigma_ey,sigma_tau,sigma_em,binary.o=1,binary.m=1)

# generate continuous outcome and continuous mediator with different clusters and period
I = 12
J = 5
beta = cumsum(c(0,0.1,0.1/2,0.1/(2^2),0.1/(2^3)))
gamma = cumsum(c(0,0.3,0.3/2,0.3/(2^2),0.3/(2^3)))
sigma_tau = sigma_a = 0.334
sigma_em = sigma_ey = 1
mydata5 = gen_data_hhm(I,J,n,beta,gamma,theta=0.75,beta_M=0.625,eta=0.4,sigma_a,
sigma_ey,sigma_tau,sigma_em,binary.o=0,binary.m=0)
```

---

gen_data_nem — *Generate data in a stepped wedge design based on nested exchangeable correlation model with a constant treatment effect*

Description

This function can generate longitudinal data in a stepped wedge design based on nested exchangeable correlation model with a constant treatment effect.

Usage

```
gen_data_nem(
  I,
  J,
  n,
  beta,
  gamma,
  theta,
  beta_M,
  eta,
  sigma_a,
  sigma_phi,
  sigma_ey,
  sigma_tau,
  sigma_psi,
  sigma_em,
  binary.o = 0,
  binary.m = 0
)
```

Arguments

I	The number of cluster
J	The number of time periods
n	The number of individuals per each cluster
beta	The underling time trend effect in a outcome model
gamma	The underling time trend effect in a mediator model
theta	The exposure effect on the outcome conditional on mediator and other possible confounders
beta_M	The mediator effect on the outcome conditional on other possible confounders
eta	The exposure effect on the mediator conditional on other possible confounders
sigma_a	The standard error of random effect in outcome model (assuming it follows normal distribution with mean zero)
sigma_phi	The standard error of random effect of cluster-by-time interaction in outcome model (assuming it follows normal distribution with mean zero)
sigma_ey	The standard error of error term in outcome model (assuming it follows normal distribution with mean zero)
sigma_tau	The standard error of random effect in mediator model (assuming it follows normal distribution with mean zero)
sigma_psi	The standard error of random effect of cluster-by-time interaction in mediator model (assuming it follows normal distribution with mean zero)
sigma_em	The standard error of error term in mediator model (assuming it follows normal distribution with mean zero)
binary.o	(Required) If the outcome is binary, set to 1. If the outcome is continuous, set to 0
binary.m	(Required) If the mediator is binary, set to 1. If the mediator is continuous, set to 0

Value

A data frame including cluster, period, id, E (time since intervention, i.e., exposure time), A (treatment status indicator), c (the start time of the treatment), alpha (random effects of outcome within a cluster), phi (random effects of cluster-by-time interaction in outcome model), tau (random effects of mediator within a cluster), psi (random effects of cluster-by-time interaction in mediator model), M (mediator), Y (outcome)

Author(s)

Zhiqiang Cao <zcaoae@connect.ust.hk> and Fan Li <fan.f.li@yale.edu>

References

Li F., Hughes J.P., Hemming K., Taljaard M., Melnick E.R. and Heagerty P.J. Mixed-effects models for the design and analysis of stepped wedge cluster randomized trials: An overview. Statistical Methods in Medical Research. 2021;30(2):612-639.

Examples

```
I = 9
J = 4
n = 20
beta = cumsum(c(0,0.1,0.1/2,0.1/(2^2)))
gamma = cumsum(c(0,0.3,0.3/2,0.3/(2^2)))
sigma_tau = sigma_a = 0.334
sigma_phi = sigma_psi = 0.6
sigma_em = sigma_ey = 0.8
# generate continuous outcome and continuous mediator
mydata1 = gen_data_nem(I,J,n,beta,gamma,theta=0.75,beta_M=0.625,eta=0.4,sigma_a,
sigma_phi,sigma_ey,sigma_tau,sigma_psi,sigma_em,binary.o=0,binary.m=0)

# generate continuous outcome and binary mediator
mydata2 = gen_data_nem(I,J,n,beta,gamma,theta=0.75,beta_M=0.625,eta=0.4,sigma_a,
sigma_phi,sigma_ey,sigma_tau,sigma_psi,sigma_em,binary.o=0,binary.m=1)

# generate binary outcome and continuous mediator
mydata3 = gen_data_nem(I,J,n,beta,gamma,theta=0.75,beta_M=0.625,eta=0.4,sigma_a,
sigma_phi,sigma_ey,sigma_tau,sigma_psi,sigma_em,binary.o=1,binary.m=0)

# generate binary outcome and binary mediator
mydata4 = gen_data_nem(I,J,n,beta,gamma,theta=0.75,beta_M=0.625,eta=0.4,sigma_a,
sigma_phi,sigma_ey,sigma_tau,sigma_psi,sigma_em,binary.o=1,binary.m=1)

# generate continuous outcome and continuous mediator with different clusters and period
I = 12
J = 5
beta = cumsum(c(0,0.1,0.1/2,0.1/(2^2),0.1/(2^3)))
gamma = cumsum(c(0,0.3,0.3/2,0.3/(2^2),0.3/(2^3)))
mydata5 = gen_data_nem(I,J,n,beta,gamma,theta=0.75,beta_M=0.625,eta=0.4,sigma_a,
sigma_phi,sigma_ey,sigma_tau,sigma_psi,sigma_em,binary.o=0,binary.m=0)
```

`gen_data_nem_etm` *Generate data in a stepped wedge design based on nested exchangeable correlation model with an exposure-time dependent treatment effect*

Description

This function can generate longitudinal data in a stepped wedge design nested exchangeable correlation model in the presence of an exposure-time dependent treatment effect

Usage

```
gen_data_nem_etm(
  I,
  J,
  n,
  beta,
  gamma,
  theta_e,
```

```
  beta_M,
  eta_e,
  sigma_a,
  sigma_phi,
  sigma_ey,
  sigma_tau,
  sigma_psi,
  sigma_em,
  binary.o = 0,
  binary.m = 0
)
```

Arguments

`I`	The number of cluster
`J`	The number of time periods
`n`	The number of individuals per each cluster
`beta`	The underling time trend effect in a outcome model
`gamma`	The underling time trend effect in a mediator model
`theta_e`	The exposure effect (a J-1 vector) on the outcome conditional on mediator and other possible confounders
`beta_M`	The mediator effect on the outcome conditional on other possible confounders
`eta_e`	The exposure effect (a J-1 vector) on the mediator conditional on other possible confounders
`sigma_a`	The standard error of random effect in outcome model (assuming it follows normal distribution with mean zero)
`sigma_phi`	The standard error of random effect of cluster-by-time interaction in outcome model (assuming it follows normal distribution with mean zero)
`sigma_ey`	The standard error of error term in outcome model (assuming it follows normal distribution with mean zero)
`sigma_tau`	The standard error of random effect in mediator model (assuming it follows normal distribution with mean zero)
`sigma_psi`	The standard error of random effect of cluster-by-time interaction in mediator model (assuming it follows normal distribution with mean zero)
`sigma_em`	The standard error of error term in mediator model (assuming it follows normal distribution with mean zero)
`binary.o`	(Required) If the outcome is binary, set to 1. If the outcome is continuous, set to 0
`binary.m`	(Required) If the mediator is binary, set to 1. If the mediator is continuous, set to 0

Value

A data frame including cluster, period, id, E (time since intervention, i.e., exposure time), A (treatment status indicator), c (the start time of the treatment), alpha (random effects of outcome within a cluster), phi (random effects of cluster-by-time interaction in outcome model), tau (random effects of mediator within a cluster), psi (random effects of cluster-by-time interaction in mediator model), M (mediator), Y (outcome)

Author(s)

Zhiqiang Cao <zcaoae@connect.ust.hk> and Fan Li <fan.f.li@yale.edu>

References

Li F., Hughes J.P., Hemming K., Taljaard M., Melnick E.R. and Heagerty P.J. Mixed-effects models for the design and analysis of stepped wedge cluster randomized trials: An overview. Statistical Methods in Medical Research. 2021;30(2):612-639.

Kenny A., Voldal E.C., Xia F., Heagerty P.J. and Hughes J.P. Analysis of stepped wedge cluster randomized trials in the presence of a time-varying treatment effect. Statistics in Medicine. 2022;41(22):4311-4339.

Examples

```
I = 9
J = 4
n = 20
beta = cumsum(c(0,0.1,0.1/2,0.1/(2^2)))
gamma = cumsum(c(0,0.3,0.3/2,0.3/(2^2)))
sigma_tau = sigma_a = 0.334
sigma_phi = sigma_psi = 0.6
sigma_em = sigma_ey = 0.8
eta_e = c(0.32,0.4,0.48)
theta_e = c(0.6,0.75,0.9)
# generate continuous outcome and continuous mediator
mydata1 = gen_data_nem_etm(I,J,n,beta,gamma,theta_e,beta_M=0.625,eta_e,sigma_a,
sigma_phi,sigma_ey,sigma_tau,sigma_psi,sigma_em,binary.o=0,binary.m=0)

# generate continuous outcome and binary mediator
mydata2 = gen_data_nem_etm(I,J,n,beta,gamma,theta_e,beta_M=0.625,eta_e,sigma_a,
sigma_phi,sigma_ey,sigma_tau,sigma_psi,sigma_em,binary.o=0,binary.m=1)

# generate binary outcome and continuous mediator
mydata3 = gen_data_nem_etm(I,J,n,beta,gamma,theta_e,beta_M=0.625,eta_e,sigma_a,
sigma_phi,sigma_ey,sigma_tau,sigma_psi,sigma_em,binary.o=1,binary.m=0)

# generate binary outcome and binary mediator
mydata4 = gen_data_nem_etm(I,J,n,beta,gamma,theta_e,beta_M=0.625,eta_e,sigma_a,
sigma_phi,sigma_ey,sigma_tau,sigma_psi,sigma_em,binary.o=1,binary.m=1)

# generate continuous outcome and continuous mediator with different clusters and period
I = 12
J = 5
beta = cumsum(c(0,0.1,0.1/2,0.1/(2^2),0.1/(2^3)))
gamma = cumsum(c(0,0.3,0.3/2,0.3/(2^2),0.3/(2^3)))
eta_e = c(0.32,0.4,0.48,0.56)
theta_e = c(0.6,0.75,0.9,1.05)
mydata5 = gen_data_nem_etm(I,J,n,beta,gamma,theta_e,beta_M=0.625,eta_e,sigma_a,
sigma_phi,sigma_ey,sigma_tau,sigma_psi,sigma_em,binary.o=0,binary.m=0)
```

`mediate_binaY_binaM_etm` *Mediation analysis function for binary outcome and binary mediator in a stepped wedge design with an exposure-time dependent treatment effect*

Description

After obtaining parameter estimates from generalized linear mixed effect models for both mediator model and outcome model, this function can obtain mediation measures including NIE, NDE, TE and MP with an en exposure-time dependent treatment effect

Usage

```
mediate_binaY_binaM_etm(
  data,
  method = "STA",
  outcome = "Y",
  mediator = "M",
  treatment = "A",
  cluster = "cluster",
  period = "period",
  exposure = "E",
  covariateY = NULL,
  covariateM = NULL,
  a0 = 0,
  a1 = 1
)
```

Arguments

`data`	A dataset, which should include outcome, mediator, treatment, cluster, period variables
`method`	Two approximate methods are provided, one is STA (second-order Taylor approximate), the other is GHQ (Gauss-Hermite Quadrature)
`outcome`	The outcome variable in stepped wedge design
`mediator`	The mediator variable in stepped wedge design
`treatment`	The treatment variable in stepped wedge design. When there is a implementation period, then corresponding treatment status should be set to -1, which is mainly for convenience
`cluster`	The cluster variable in stepped wedge design
`period`	The period variable in stepped wedge design
`exposure`	The exposure time with J levels (e.g., 0,1,2,...,J-1 when there is no implementation period)
`covariateY`	A vector of confounders in the outcome regression (default is NULL)
`covariateM`	A vector of confounders in the mediator regression (default is NULL)
`a0`	The reference treatment level in defining TE and NIE. The default value is 0
`a1`	The treatment level of interest in defining TE and NIE. The default value is 1

Value

A list containing point and interval estimates of NIE, NDE, TE and MP at each exposure time and overall summary mediation measures, as well as Chi-square test result of TE

Author(s)

Zhiqiang Cao <zcaoae@connect.ust.hk> and Fan Li <fan.f.li@yale.edu>

Examples

```
library(lme4)
I = 15
J = 4
n = 20
beta = cumsum(c(0,0.1,0.1/2,0.1/(2^2)))
gamma = cumsum(c(0,0.3,0.3/2,0.3/(2^2)))
eta_e = c(0.6,1.2,2)
theta_e = c(0.6,1,1.8)
sigma_a = 0.605
sigma_tau = 0.605
sigma_em = sigma_ey = 1
set.seed(123456)
mydata1 = gen_data_etm(I,J,n,beta,gamma,theta_e,beta_M=1.2,eta_e,sigma_a,
sigma_ey,sigma_tau,sigma_em,binary.o=1,binary.m=1)
# example 1: mediation analysis without covariates in outcome and mediator models
res1 = mediate_binaY_binaM_etm(data=mydata1, method = "STA")
print(res1)
res1f = mediate_binaY_binaM_etm(data=mydata1, method = "GHQ")
print(res1f)

# example 2: mediation analysis with different covariates in outcome and mediator models
# generate two covariates
covdata = data.frame("X1" = numeric(), "X2" = numeric())
set.seed(100)
for(i in 1:I){
  for(j in 1:J){
     x1_ijk = rnorm(n,mean=0.5)
     x2_ijk = rnorm(n,sd=0.5)
     covdata = rbind(covdata, data.frame(cbind(X1 = x1_ijk, X2 = x2_ijk)))
  }
}

mydata2 = data.frame(mydata1,covdata)
res2 = mediate_binaY_binaM_etm(data=mydata2, method = "STA",
covariateY = c("X1"), covariateM = c("X2"))
print(res2)
res2f = mediate_binaY_binaM_etm(data=mydata2, method = "GHQ",
covariateY = c("X1"), covariateM = c("X2"))
print(res2f)

# example 3: mediation analysis with the same covariates in outcome and mediator models
res3 = mediate_binaY_binaM_etm(data=mydata2, method = "STA",
covariateY = c("X1","X2"), covariateM = c("X1","X2"))
print(res3)
res3f = mediate_binaY_binaM_etm(data=mydata2, method = "GHQ",
covariateY = c("X1","X2"), covariateM = c("X1","X2"))
```

```
print(res3f)

# example 4: mediation analysis with different clusters and periods
I = 16
J = 5
beta = cumsum(c(0,0.1,0.1/2,0.1/(2^2),0.1/(2^3)))
gamma = cumsum(c(0,0.3,0.3/2,0.3/(2^2),0.3/(2^3)))
eta_e = c(0.6,1.2,1.5,1.9)
theta_e = c(0.8,1.6,2,2.3)
set.seed(123456)
mydata3 = gen_data_etm(I,J,n,beta,gamma,theta_e,beta_M=1,eta_e,sigma_a,
sigma_ey,sigma_tau,sigma_em,binary.o=1,binary.m=1)
res4 = mediate_binaY_binaM_etm(data=mydata3,method = "STA")
print(res4)
res4f = mediate_binaY_binaM_etm(data=mydata3,method = "GHQ")
print(res4f)
```

`mediate_binaY_binaM_hhm` *Mediation analysis function for binary outcome and binary mediator in a stepped wedge design based on Hussey and Hughes model with a constant treatment effect*

Description

After obtaining parameter estimates from generalized linear mixed-effect models for both mediator model and outcome model, this function can obtain mediation measures including NIE, NDE, TE and MP assuming a constant treatment effect

Usage

```
mediate_binaY_binaM_hhm(
  data,
  method = "STA",
  outcome = "Y",
  mediator = "M",
  treatment = "A",
  cluster = "cluster",
  period = "period",
  exposure = "E",
  covariateY = NULL,
  covariateM = NULL,
  a0 = 0,
  a1 = 1
)
```

Arguments

`data`	A dataset, which should include outcome, mediator, treatment, cluster, period variables
`method`	Two approximate methods are provided, one is STA (second-order Taylor approximate), the other is GHQ (Gauss-Hermite Quadrature)

`outcome`	The outcome variable in stepped wedge design
`mediator`	The mediator variable in stepped wedge design
`treatment`	The treatment variable in stepped wedge design. When there is a implementation period, then corresponding treatment status should be set to -1, which is mainly for convenience
`cluster`	The cluster variable in stepped wedge design
`period`	The period variable in stepped wedge design
`exposure`	The exposure time with J levels (e.g., 0,1,2,...,J-1 when there is no implementation period). If dataset has no exposure variable, then set it to NULL.
`covariateY`	A vector of confounders in the outcome regression (default is NULL)
`covariateM`	A vector of confounders in the mediator regression (default is NULL)
`a0`	The reference treatment level in defining TE and NIE. The default value is 0
`a1`	The treatment level of interest in defining TE and NIE. The default value is 1

Value

A list containing point and interval estimates of NIE, NDE, TE and MP.

Author(s)

Zhiqiang Cao <zcaoae@connect.ust.hk> and Fan Li <fan.f.li@yale.edu>

Examples

```
library(lme4)
I = 15
J = 4
n = 20
beta = cumsum(c(0,0.1,0.1/2,0.1/(2^2)))
gamma = cumsum(c(0,0.3,0.3/2,0.3/(2^2)))
sigma_a = 0.605
sigma_tau = 0.605
sigma_em = sigma_ey = 1
set.seed(123456)
mydata1 = gen_data_hhm(I,J,n,beta,gamma,theta=1,beta_M=1,eta=1,sigma_a,
sigma_ey,sigma_tau,sigma_em,binary.o=1,binary.m=1)
# example 1: mediation analysis without covariates in outcome and mediator models
res1 = mediate_binaY_binaM_hhm(data=mydata1, method = "STA")
print(res1)
res1f = mediate_binaY_binaM_hhm(data=mydata1, method = "GHQ")
print(res1f)

# example 2: mediation analysis with different covariates in outcome and mediator models
# generate two covariates
covdata = data.frame("X1" = numeric(), "X2" = numeric())
set.seed(100)
for(i in 1:I){
  for(j in 1:J){
     x1_ijk = rnorm(n,mean=0.5)
     x2_ijk = rnorm(n,sd=0.5)
     covdata = rbind(covdata, data.frame(cbind(X1 = x1_ijk, X2 = x2_ijk)))
  }
}
```

```
mydata2 = data.frame(mydata1,covdata)
res2 = mediate_binaY_binaM_hhm(data=mydata2, method = "STA",
covariateY = c("X1"), covariateM = c("X2"))
print(res2)
res2f = mediate_binaY_binaM_hhm(data=mydata2, method = "GHQ",
covariateY = c("X1"), covariateM = c("X2"))
print(res2f)

# example 3: mediation analysis with the same covariates in outcome and mediator models
res3 = mediate_binaY_binaM_hhm(data=mydata2, method = "STA",
covariateY = c("X1","X2"), covariateM = c("X1","X2"))
print(res3)
res3f = mediate_binaY_binaM_hhm(data=mydata2, method = "GHQ",
covariateY = c("X1","X2"), covariateM = c("X1","X2"))
print(res3f)

# example 4: mediation analysis with different clusters and periods
I = 16; J = 5
beta = cumsum(c(0,0.1,0.1/2,0.1/(2^2),0.1/(2^3)))
gamma = cumsum(c(0,0.3,0.3/2,0.3/(2^2),0.3/(2^3)))
set.seed(123456)
mydata3 = gen_data_hhm(I,J,n,beta,gamma,theta=1,beta_M=1,eta=1,sigma_a,
sigma_ey,sigma_tau,sigma_em,binary.o=1,binary.m=1)
res4 = mediate_binaY_binaM_hhm(data=mydata3,method = "STA")
print(res4)
res4f = mediate_binaY_binaM_hhm(data=mydata3,method = "GHQ")
print(res4f)

# example 5: if there are no exposure variable
mydata4 = mydata3[,-4]
res5 = mediate_binaY_binaM_hhm(data=mydata4,method = "STA",exposure=NULL)
print(res5)
```

---

mediate_binaY_binaM_nem

Mediation analysis function for binary outcome and binary mediator in a stepped wedge design based on nested exchangeable correlation model with a constant treatment effect

---

Description

After obtaining parameter estimates from generalized linear mixed-effect models for both mediator model and outcome model, this function can obtain mediation measures including NIE, NDE, TE and MP assuming a constant treatment effect

Usage

```
mediate_binaY_binaM_nem(
  data,
  outcome = "Y",
  mediator = "M",
  treatment = "A",
  cluster = "cluster",
```

```
  period = "period",
  exposure = "E",
  covariateY = NULL,
  covariateM = NULL,
  a0 = 0,
  a1 = 1
)
```

Arguments

data	A dataset, which should include outcome, mediator, treatment, cluster, period variables
outcome	The outcome variable in stepped wedge design
mediator	The mediator variable in stepped wedge design
treatment	The treatment variable in stepped wedge design. When there is a implementation period, then corresponding treatment status should be set to -1, which is mainly for convenience
cluster	The cluster variable in stepped wedge design
period	The period variable in stepped wedge design
exposure	The exposure time with J levels (e.g., 0,1,2,...,J-1 when there is no implementation period). If dataset has no exposure variable, then set it to NULL
covariateY	A vector of confounders in the outcome regression (default is NULL)
covariateM	A vector of confounders in the mediator regression (default is NULL)
a0	The reference treatment level in defining TE and NIE. The default value is 0
a1	The treatment level of interest in defining TE and NIE. The default value is 1

Value

A list containing point and interval estimates of NIE, NDE, TE and MP.

Author(s)

Zhiqiang Cao <zcaoae@connect.ust.hk> and Fan Li <fan.f.li@yale.edu>

Examples

```
library(lme4)
I = 15
J = 4
n = 20
beta = cumsum(c(0,0.1,0.1/2,0.1/(2^2)))
gamma = cumsum(c(0,0.3,0.3/2,0.3/(2^2)))
sigma_tau = sigma_a = 0.334
sigma_phi = sigma_psi = 0.6
sigma_em = sigma_ey = 0.8
set.seed(123456)
mydata1 = gen_data_nem(I,J,n,beta,gamma,theta=1,beta_M=1,eta=1,sigma_a,
sigma_phi,sigma_ey,sigma_tau,sigma_psi,sigma_em,binary.o=1,binary.m=1)
# example 1: mediation analysis without covariates in outcome and mediator models
res1 = mediate_binaY_binaM_nem(data=mydata1)
print(res1)
```

```
# example 2: mediation analysis with different covariates in outcome and mediator models
# generate two covariates
covdata = data.frame("X1" = numeric(), "X2" = numeric())
set.seed(100)
for(i in 1:I){
  for(j in 1:J){
     x1_ijk = rnorm(n,mean=0.5)
     x2_ijk = rnorm(n,sd=0.5)
     covdata = rbind(covdata, data.frame(cbind(X1 = x1_ijk, X2 = x2_ijk)))
  }
}

mydata2 = data.frame(mydata1,covdata)
res2 = mediate_binaY_binaM_nem(data = mydata2, covariateY = c("X1"),
covariateM = c("X2"))
print(res2)

# example 3: mediation analysis with the same covariates in outcome and mediator models
res3 = mediate_binaY_binaM_nem(data = mydata2, covariateY = c("X1","X2"),
covariateM = c("X1","X2"))
print(res3)

# example 4: mediation analysis with different clusters and periods
I = 16; J = 5
beta = cumsum(c(0,0.1,0.1/2,0.1/(2^2),0.1/(2^3)))
gamma = cumsum(c(0,0.3,0.3/2,0.3/(2^2),0.3/(2^3)))
set.seed(123456)
mydata3 = gen_data_nem(I,J,n,beta,gamma,theta=1,beta_M=1,eta=1,sigma_a,
sigma_phi,sigma_ey,sigma_tau,sigma_psi,sigma_em,binary.o=1,binary.m=1)
res4 = mediate_binaY_binaM_nem(data=mydata3)
print(res4)
```

`mediate_binaY_binaM_nem_etm`

Mediation analysis function for binary outcome and binary mediator in a stepped wedge design based on nested exchangeable correlation model with an exposure-time dependent treatment effect

---

Description

After obtaining parameter estimates from generalized linear mixed effect models for both mediator model and outcome model, this function can obtain mediation measures including NIE, NDE, TE and MP with an en exposure-time dependent treatment effect

Usage

```
mediate_binaY_binaM_nem_etm(
  data,
  outcome = "Y",
  mediator = "M",
  treatment = "A",
  cluster = "cluster",
```

```
  period = "period",
  exposure = "E",
  covariateY = NULL,
  covariateM = NULL,
  a0 = 0,
  a1 = 1
)
```

Arguments

data	A dataset, which should include outcome, mediator, treatment, cluster, period variables
outcome	The outcome variable in stepped wedge design
mediator	The mediator variable in stepped wedge design
treatment	The treatment variable in stepped wedge design. When there is a implementation period, then corresponding treatment status should be set to -1, which is mainly for convenience
cluster	The cluster variable in stepped wedge design
period	The period variable in stepped wedge design
exposure	The exposure time with J levels (e.g., 0,1,2,...,J-1 when there is no implementation period)
covariateY	A vector of confounders in the outcome regression (default is NULL)
covariateM	A vector of confounders in the mediator regression (default is NULL)
a0	The reference treatment level in defining TE and NIE. The default value is 0
a1	The treatment level of interest in defining TE and NIE. The default value is 1

Value

A list containing point and interval estimates of NIE, NDE, TE and MP at each exposure time and overall summary mediation measures, as well as Chi-square test result of TE

Author(s)

Zhiqiang Cao <zcaoae@connect.ust.hk> and Fan Li <fan.f.li@yale.edu>

Examples

```
library(lme4)
I = 15
J = 4
n = 20
beta = cumsum(c(0,0.1,0.1/2,0.1/(2^2)))
gamma = cumsum(c(0,0.3,0.3/2,0.3/(2^2)))
eta_e = c(0.6,1.2,2)
theta_e = c(0.6,1,1.8)
sigma_tau = sigma_a = 0.334
sigma_phi = sigma_psi = 0.6
sigma_em = sigma_ey = 0.8
set.seed(123456)
mydata1 = gen_data_nem_etm(I,J,n,beta,gamma,theta_e,beta_M=1.2,eta_e,sigma_a,
sigma_phi,sigma_ey,sigma_tau,sigma_psi,sigma_em,binary.o=1,binary.m=1)
```

```
# example 1: mediation analysis without covariates in outcome and mediator models
res1 = mediate_binaY_binaM_nem_etm(data=mydata1)
print(res1)

# example 2: mediation analysis with different covariates in outcome and mediator models
# generate two covariates
covdata = data.frame("X1" = numeric(), "X2" = numeric())
set.seed(100)
for(i in 1:I){
  for(j in 1:J){
     x1_ijk = rnorm(n,mean=0.5)
     x2_ijk = rnorm(n,sd=0.5)
     covdata = rbind(covdata, data.frame(cbind(X1 = x1_ijk, X2 = x2_ijk)))
  }
}

mydata2 = data.frame(mydata1,covdata)
res2 = mediate_binaY_binaM_nem_etm(data = mydata2, covariateY = c("X1"),
covariateM = c("X2"))
print(res2)

# example 3: mediation analysis with the same covariates in outcome and mediator models
res3 = mediate_binaY_binaM_nem_etm(data = mydata2,
covariateY = c("X1","X2"), covariateM = c("X1","X2"))
print(res3)

# example 4: mediation analysis with different clusters and periods
I = 16
J = 5
beta = cumsum(c(0,0.1,0.1/2,0.1/(2^2),0.1/(2^3)))
gamma = cumsum(c(0,0.3,0.3/2,0.3/(2^2),0.3/(2^3)))
eta_e = c(0.6,1.2,1.5,1.9)
theta_e = c(0.8,1.6,2,2.3)
set.seed(123456)
mydata3 = gen_data_nem_etm(I,J,n,beta,gamma,theta_e,beta_M=1,eta_e,sigma_a,
sigma_phi,sigma_ey,sigma_tau,sigma_psi,sigma_em,binary.o=1,binary.m=1)
res4 = mediate_binaY_binaM_nem_etm(data=mydata3)
print(res4)
```

---

mediate_binaY_contM_etm

Mediation analysis function for binary outcome and continuous mediator in a stepped wedge design with an exposure-time dependent treatment effect

---

Description

After obtaining parameter estimates from linear mixed effect model for mediator model and generalized linear mixed effect model for outcome model, this function can obtain mediation measures including NIE, NDE, TE and MP with an exposure-time dependent treatment effect

Usage

```
mediate_binaY_contM_etm(
  data,
  outcome = "Y",
  mediator = "M",
  treatment = "A",
  cluster = "cluster",
  period = "period",
  exposure = "E",
  covariateY = NULL,
  covariateM = NULL,
  a0 = 0,
  a1 = 1
)
```

Arguments

`data`	A dataset, which should include outcome, mediator, treatment, cluster, period variables
`outcome`	The outcome variable in stepped wedge design
`mediator`	The mediator variable in stepped wedge design
`treatment`	The treatment variable in stepped wedge design. When there is a implementation period, then corresponding treatment status should be set to -1, which is mainly for convenience
`cluster`	The cluster variable in stepped wedge design
`period`	The period variable in stepped wedge design
`exposure`	The exposure time with J levels (e.g., 0,1,2,...,J-1 when there is no implementation period)
`covariateY`	A vector of confounders in the outcome regression (default is NULL)
`covariateM`	A vector of confounders in the mediator regression (default is NULL)
`a0`	The reference treatment level in defining TE and NIE. The default value is 0
`a1`	The treatment level of interest in defining TE and NIE. The default value is 1

Value

A list containing point and interval estimates of NIE, NDE, TE and MP at each exposure time and overall summary mediation measures, as well as Chi-square test result of TE

Author(s)

Zhiqiang Cao <zcaoae@connect.ust.hk> and Fan Li <fan.f.li@yale.edu>

Examples

```
library(lme4)
I = 15
J = 4
n = 20
beta = cumsum(c(0,0.1,0.1/2,0.1/(2^2)))
gamma = cumsum(c(0,0.3,0.3/2,0.3/(2^2)))
```

```
eta_e = c(0.8,1.2,1.6)
theta_e = c(0.60,0.75,0.90)
sigma_a = 0.605
sigma_tau = 0.334
sigma_em = sigma_ey = 1
set.seed(123456)
mydata1 = gen_data_etm(I,J,n,beta,gamma,theta_e,beta_M=0.625,eta_e,sigma_a,
sigma_ey,sigma_tau,sigma_em,binary.o=1,binary.m=0)
# example 1: mediation analysis without covariates in outcome and mediator models
res1 = mediate_binaY_contM_etm(data=mydata1)
print(res1)

# example 2: mediation analysis with different covariates in outcome and mediator models
# generate two covariates
covdata = data.frame("X1" = numeric(), "X2" = numeric())
set.seed(100)
for(i in 1:I){
  for(j in 1:J){
     x1_ijk = rnorm(n,mean=0.5)
     x2_ijk = rnorm(n,sd=0.5)
     covdata = rbind(covdata, data.frame(cbind(X1 = x1_ijk, X2 = x2_ijk)))
  }
}

mydata2 = data.frame(mydata1,covdata)
res2 = mediate_binaY_contM_etm(data=mydata2,covariateY = c("X1"), covariateM = c("X2"))
print(res2)

# example 3: mediation analysis with the same covariates in outcome and mediator models
res3 = mediate_binaY_contM_etm(data=mydata2,covariateY = c("X1","X2"), covariateM = c("X1","X2"))
print(res3)

# example 4: mediation analysis with different clusters and periods
I = 12
J = 5
beta = cumsum(c(0,0.1,0.1/2,0.1/(2^2),0.1/(2^3)))
gamma = cumsum(c(0,0.3,0.3/2,0.3/(2^2),0.3/(2^3)))
eta_e = c(0.4,0.8,1.2,1.6)
theta_e = c(0.60,0.75,0.90,1.05)
set.seed(123456)
mydata3 = gen_data_etm(I,J,n,beta,gamma,theta_e,beta_M=0.625,eta_e,sigma_a,
sigma_ey,sigma_tau,sigma_em,binary.o=1,binary.m=0)
res4 = mediate_binaY_contM_etm(data=mydata3)
print(res4)
```

`mediate_binaY_contM_hhm` *Mediation analysis function for binary outcome and continuous mediator in a stepped wedge design based on Hussey and Hughes model with a constant treatment effect*

Description

After obtaining parameter estimates from linear mixed effect model for mediator model and generalized linear mixed effect model for outcome model, this function can obtain mediation measures including NIE, NDE, TE and MP assuming a constant treatment effect

Usage

```
mediate_binaY_contM_hhm(
  data,
  outcome = "Y",
  mediator = "M",
  treatment = "A",
  cluster = "cluster",
  period = "period",
  exposure = "E",
  covariateY = NULL,
  covariateM = NULL,
  a0 = 0,
  a1 = 1
)
```

Arguments

`data`	A dataset, which should include outcome, mediator, treatment, cluster, period variables
`outcome`	The outcome variable in stepped wedge design
`mediator`	The mediator variable in stepped wedge design
`treatment`	The treatment variable in stepped wedge design. When there is a implementation period, then corresponding treatment status should be set to -1, which is mainly for convenience
`cluster`	The cluster variable in stepped wedge design
`period`	The period variable in stepped wedge design
`exposure`	The exposure time with J levels (e.g., 0,1,2,...,J-1 when there is no implementation period). If dataset has no exposure variable, then set it to NULL
`covariateY`	A vector of confounders in the outcome regression (default is NULL)
`covariateM`	A vector of confounders in the mediator regression (default is NULL)
`a0`	The reference treatment level in defining TE and NIE. The default value is 0
`a1`	The treatment level of interest in defining TE and NIE. The default value is 1

Value

A list containing point and interval estimates of NIE, NDE, TE and MP.

Author(s)

Zhiqiang Cao <zcaoae@connect.ust.hk> and Fan Li <fan.f.li@yale.edu>

Examples

```
library(lme4)
I = 15
J = 4
n = 20
beta = cumsum(c(0,0.1,0.1/2,0.1/(2^2)))
```

```
gamma = cumsum(c(0,0.3,0.3/2,0.3/(2^2)))
sigma_a = 0.605
sigma_tau = 0.334
sigma_em = sigma_ey = 1
set.seed(123456)
mydata1 = gen_data_hhm(I,J,n,beta,gamma,theta=0.75,beta_M=1,eta=0.4,sigma_a,
sigma_ey,sigma_tau,sigma_em,binary.o=1,binary.m=0)
# example 1: mediation analysis without covariates in outcome and mediator models
res1 = mediate_binaY_contM_hhm(data=mydata1)
print(res1)

# example 2: mediation analysis with different covariates in outcome and mediator models
# generate two covariates
covdata = data.frame("X1" = numeric(), "X2" = numeric())
set.seed(100)
for(i in 1:I){
  for(j in 1:J){
     x1_ijk = rnorm(n,mean=0.5)
     x2_ijk = rnorm(n,sd=0.5)
     covdata = rbind(covdata, data.frame(cbind(X1 = x1_ijk, X2 = x2_ijk)))
  }
}

mydata2 = data.frame(mydata1,covdata)
res2 = mediate_binaY_contM_hhm(data=mydata2,covariateY = c("X1"), covariateM = c("X2"))
print(res2)

# example 3: mediation analysis with the same covariates in outcome and mediator models
res3 = mediate_binaY_contM_hhm(data=mydata2,covariateY = c("X1","X2"), covariateM = c("X1","X2"))
print(res3)

# example 4: mediation analysis with different clusters and periods
I = 12
J = 5
beta = cumsum(c(0,0.1,0.1/2,0.1/(2^2),0.1/(2^3)))
gamma = cumsum(c(0,0.3,0.3/2,0.3/(2^2),0.3/(2^3)))
set.seed(123456)
mydata3 = gen_data_hhm(I,J,n,beta,gamma,theta=0.75,beta_M=1,eta=0.4,sigma_a,
sigma_ey,sigma_tau,sigma_em,binary.o=1,binary.m=0)
res4 = mediate_binaY_contM_hhm(data=mydata3)
print(res4)

# example 5: if there are no exposure variable
mydata4 = mydata3[,-4]
res5 = mediate_binaY_contM_hhm(data=mydata4,exposure=NULL)
print(res5)
```

---

mediate_binaY_contM_nem

Mediation analysis function for binary outcome and continuous mediator in a stepped wedge design based on nested exchangeable correlation model with a constant treatment effect

---

Description

After obtaining parameter estimates from linear mixed effect model for mediator model and generalized linear mixed effect model for outcome model, this function can obtain mediation measures including NIE, NDE, TE and MP assuming a constant treatment effect

Usage

```
mediate_binaY_contM_nem(
  data,
  outcome = "Y",
  mediator = "M",
  treatment = "A",
  cluster = "cluster",
  period = "period",
  exposure = "E",
  covariateY = NULL,
  covariateM = NULL,
  a0 = 0,
  a1 = 1
)
```

Arguments

`data`	A dataset, which should include outcome, mediator, treatment, cluster, period variables
`outcome`	The outcome variable in stepped wedge design
`mediator`	The mediator variable in stepped wedge design
`treatment`	The treatment variable in stepped wedge design. When there is a implementation period, then corresponding treatment status should be set to -1, which is mainly for convenience
`cluster`	The cluster variable in stepped wedge design
`period`	The period variable in stepped wedge design
`exposure`	The exposure time with J levels (e.g., 0,1,2,...,J-1 when there is no implementation period). If dataset has no exposure variable, then set it to NULL
`covariateY`	A vector of confounders in the outcome regression (default is NULL)
`covariateM`	A vector of confounders in the mediator regression (default is NULL)
`a0`	The reference treatment level in defining TE and NIE. The default value is 0
`a1`	The treatment level of interest in defining TE and NIE. The default value is 1

Value

A list containing point and interval estimates of NIE, NDE, TE and MP.

Author(s)

Zhiqiang Cao <zcaoae@connect.ust.hk> and Fan Li <fan.f.li@yale.edu>

Examples

```
library(lme4)
I = 15
J = 4
n = 20
beta = cumsum(c(0,0.1,0.1/2,0.1/(2^2)))
gamma = cumsum(c(0,0.3,0.3/2,0.3/(2^2)))
sigma_tau = sigma_a = 0.334
sigma_phi = sigma_psi = 0.6
sigma_em = sigma_ey = 0.8
set.seed(123456)
mydata1 = gen_data_nem(I,J,n,beta,gamma,theta=0.75,beta_M=1,eta=0.4,sigma_a,
sigma_phi,sigma_ey,sigma_tau,sigma_psi,sigma_em,binary.o=1,binary.m=0)
# example 1: mediation analysis without covariates in outcome and mediator models
res1 = mediate_binaY_contM_nem(data=mydata1)
print(res1)

# example 2: mediation analysis with different covariates in outcome and mediator models
# generate two covariates
covdata = data.frame("X1" = numeric(), "X2" = numeric())
set.seed(100)
for(i in 1:I){
  for(j in 1:J){
     x1_ijk = rnorm(n,mean=0.5)
     x2_ijk = rnorm(n,sd=0.5)
     covdata = rbind(covdata, data.frame(cbind(X1 = x1_ijk, X2 = x2_ijk)))
  }
}

mydata2 = data.frame(mydata1,covdata)
res2 = mediate_binaY_contM_nem(data = mydata2,covariateY = c("X1"),
covariateM = c("X2"))
print(res2)

# example 3: mediation analysis with the same covariates in outcome and mediator models
res3 = mediate_binaY_contM_nem(data = mydata2,covariateY = c("X1","X2"),
covariateM = c("X1","X2"))
print(res3)

# example 4: mediation analysis with different clusters and periods
I = 12
J = 5
beta = cumsum(c(0,0.1,0.1/2,0.1/(2^2),0.1/(2^3)))
gamma = cumsum(c(0,0.3,0.3/2,0.3/(2^2),0.3/(2^3)))
set.seed(123456)
mydata3 = gen_data_nem(I,J,n,beta,gamma,theta=0.75,beta_M=1,eta=0.4,sigma_a,
sigma_phi,sigma_ey,sigma_tau,sigma_psi,sigma_em,binary.o=1,binary.m=0)
res4 = mediate_binaY_contM_nem(data=mydata3)
print(res4)
```

mediate_binaY_contM_nem_etm

Mediation analysis function for binary outcome and continuous mediator in a stepped wedge design based on nested exchangeable model with an exposure-time dependent treatment effect

Description

After obtaining parameter estimates from linear mixed effect model for mediator model and generalized linear mixed effect model for outcome model, this function can obtain mediation measures including NIE, NDE, TE and MP with an exposure-time dependent treatment effect

Usage

```
mediate_binaY_contM_nem_etm(
  data,
  outcome = "Y",
  mediator = "M",
  treatment = "A",
  cluster = "cluster",
  period = "period",
  exposure = "E",
  covariateY = NULL,
  covariateM = NULL,
  a0 = 0,
  a1 = 1
)
```

Arguments

`data`	A dataset, which should include outcome, mediator, treatment, cluster, period variables
`outcome`	The outcome variable in stepped wedge design
`mediator`	The mediator variable in stepped wedge design
`treatment`	The treatment variable in stepped wedge design. When there is a implementation period, then corresponding treatment status should be set to -1, which is mainly for convenience
`cluster`	The cluster variable in stepped wedge design
`period`	The period variable in stepped wedge design
`exposure`	The exposure time with J levels (e.g., 0,1,2,...,J-1 when there is no implementation period)
`covariateY`	A vector of confounders in the outcome regression (default is NULL)
`covariateM`	A vector of confounders in the mediator regression (default is NULL)
`a0`	The reference treatment level in defining TE and NIE. The default value is 0
`a1`	The treatment level of interest in defining TE and NIE. The default value is 1

Value

A list containing point and interval estimates of NIE, NDE, TE and MP at each exposure time and overall summary mediation measures, as well as Chi-square test result of TE

Author(s)

Zhiqiang Cao <zcaoae@connect.ust.hk> and Fan Li <fan.f.li@yale.edu>

Examples

```
library(lme4)
I = 15
J = 4
n = 20
beta = cumsum(c(0,0.1,0.1/2,0.1/(2^2)))
gamma = cumsum(c(0,0.3,0.3/2,0.3/(2^2)))
eta_e = c(0.8,1.2,1.6)
theta_e = c(0.60,0.75,0.90)
sigma_tau = sigma_a = 0.334
sigma_phi = sigma_psi = 0.6
sigma_em = sigma_ey = 0.8
set.seed(123456)
mydata1 = gen_data_nem_etm(I,J,n,beta,gamma,theta_e,beta_M=0.625,eta_e,sigma_a,
sigma_phi,sigma_ey,sigma_tau,sigma_psi,sigma_em,binary.o=1,binary.m=0)
# example 1: mediation analysis without covariates in outcome and mediator models
res1 = mediate_binaY_contM_nem_etm(data=mydata1)
print(res1)

# example 2: mediation analysis with different covariates in outcome and mediator models
# generate two covariates
covdata = data.frame("X1" = numeric(), "X2" = numeric())
set.seed(100)
for(i in 1:I){
  for(j in 1:J){
     x1_ijk = rnorm(n,mean=0.5)
     x2_ijk = rnorm(n,sd=0.5)
     covdata = rbind(covdata, data.frame(cbind(X1 = x1_ijk, X2 = x2_ijk)))
  }
}

mydata2 = data.frame(mydata1,covdata)
res2 = mediate_binaY_contM_nem_etm(data = mydata2,covariateY = c("X1"),
covariateM = c("X2"))
print(res2)

# example 3: mediation analysis with the same covariates in outcome and mediator models
res3 = mediate_binaY_contM_nem_etm(data = mydata2,covariateY = c("X1","X2"),
covariateM = c("X1","X2"))
print(res3)

# example 4: mediation analysis with different clusters and periods
I = 12
J = 5
beta = cumsum(c(0,0.1,0.1/2,0.1/(2^2),0.1/(2^3)))
gamma = cumsum(c(0,0.3,0.3/2,0.3/(2^2),0.3/(2^3)))
eta_e = c(0.4,0.8,1.2,1.6)
theta_e = c(0.60,0.75,0.90,1.05)
set.seed(123456)
mydata3 = gen_data_nem_etm(I,J,n,beta,gamma,theta_e,beta_M=0.625,eta_e,sigma_a,
sigma_phi,sigma_ey,sigma_tau,sigma_psi,sigma_em,binary.o=1,binary.m=0)
res4 = mediate_binaY_contM_nem_etm(data=mydata3)
```

```
print(res4)
```

`mediate_contY_binaM_etm` *Mediation analysis function for continuous outcome and binary mediator in a stepped wedge with an exposure-time dependent treatment effect*

Description

After obtaining parameter estimates from linear mixed effect model for outcome model and generalized linear mixed effect model for mediator model, this function can obtain mediation measures including NIE, NDE, TE and MP with an exposure-time dependent treatment effect

Usage

```
mediate_contY_binaM_etm(
  data,
  method = "STA",
  outcome = "Y",
  mediator = "M",
  treatment = "A",
  cluster = "cluster",
  period = "period",
  exposure = "E",
  covariateY = NULL,
  covariateM = NULL,
  a0 = 0,
  a1 = 1
)
```

Arguments

`data`	A dataset, which should include outcome, mediator, treatment, cluster, period variables
`method`	Two approximate methods are provided, one is STA (second-order Taylor approximate), the other is GHQ (Gauss-Hermite Quadrature)
`outcome`	The outcome variable in stepped wedge design
`mediator`	The mediator variable in stepped wedge design
`treatment`	The treatment variable in stepped wedge design. When there is a implementation period, then corresponding treatment status should be set to -1, which is mainly for convenience
`cluster`	The cluster variable in stepped wedge design
`period`	The period variable in stepped wedge design
`exposure`	The exposure time with J levels (e.g., 0,1,2,...,J-1 when there is no implementation period)
`covariateY`	A vector of confounders in the outcome regression (default is NULL)
`covariateM`	A vector of confounders in the mediator regression (default is NULL)
`a0`	The reference treatment level in defining TE and NIE. The default value is 0
`a1`	The treatment level of interest in defining TE and NIE. The default value is 1

Value

A list containing point and interval estimates of NIE, NDE, TE and MP at each exposure time and overall summary mediation measures, as well as Chi-square test result of TE

Author(s)

Zhiqiang Cao <zcaoae@connect.ust.hk> and Fan Li <fan.f.li@yale.edu>

Examples

```
library(lme4)
I = 15
J = 4
n = 20
beta = cumsum(c(0,0.1,0.1/2,0.1/(2^2)))
gamma = cumsum(c(0,0.3,0.3/2,0.3/(2^2)))
eta_e = c(0.5,1.3,2.1)
theta_e = c(0.6,1,1.4)
sigma_a = 0.334
sigma_tau = 0.605
sigma_em = sigma_ey = 1
set.seed(123456)
mydata1 = gen_data_etm(I,J,n,beta,gamma,theta_e,beta_M=1.2,eta_e,sigma_a,
sigma_ey,sigma_tau,sigma_em,binary.o=0,binary.m=1)
# example 1: mediation analysis without covariates in outcome and mediator models
res1 = mediate_contY_binaM_etm(data=mydata1, method = "STA")
print(res1)
res1f = mediate_contY_binaM_etm(data=mydata1, method = "GHQ")
print(res1f)

# example 2: mediation analysis with different covariates in outcome and mediator models
# generate two covariates
covdata = data.frame("X1" = numeric(), "X2" = numeric())
set.seed(100)
for(i in 1:I){
  for(j in 1:J){
     x1_ijk = rnorm(n,mean=0.5)
     x2_ijk = rnorm(n,sd=0.5)
     covdata = rbind(covdata, data.frame(cbind(X1 = x1_ijk, X2 = x2_ijk)))
  }
}

mydata2 = data.frame(mydata1,covdata)
res2 = mediate_contY_binaM_etm(data=mydata2, method = "STA",
covariateY = c("X1"), covariateM = c("X2"))
print(res2)
res2f = mediate_contY_binaM_etm(data=mydata2, method = "GHQ",
covariateY = c("X1"), covariateM = c("X2"))
print(res2f)

# example 3: mediation analysis with the same covariates in outcome and mediator models
res3 = mediate_contY_binaM_etm(data=mydata2, method = "STA",
covariateY = c("X1","X2"), covariateM = c("X1","X2"))
print(res3)
res3f = mediate_contY_binaM_etm(data=mydata2, method = "GHQ",
covariateY = c("X1","X2"), covariateM = c("X1","X2"))
```

```
print(res3f)

# example 4: mediation analysis with different clusters and periods
I = 12
J = 5
beta = cumsum(c(0,0.1,0.1/2,0.1/(2^2),0.1/(2^3)))
gamma = cumsum(c(0,0.3,0.3/2,0.3/(2^2),0.3/(2^3)))
eta_e = c(0.5,1.2,1.9,2.6)
theta_e = c(0.3,0.6,0.9,1.2)
set.seed(123456)
mydata3 = gen_data_etm(I,J,n,beta,gamma,theta_e,beta_M=1.2,eta_e,sigma_a,
sigma_ey,sigma_tau,sigma_em,binary.o=0,binary.m=1)
res4 = mediate_contY_binaM_etm(data=mydata3,method = "STA")
print(res4)
res4f = mediate_contY_binaM_etm(data=mydata3,method = "GHQ")
print(res4f)
```

`mediate_contY_binaM_hhm`

Mediation analysis function for continuous outcome and binary mediator in a stepped wedge design based on Hussey and Hughes model with a constant treatment effect

---

Description

After obtaining parameter estimates from linear mixed effect model for outcome model and generalized linear mixed effect model for mediator model, this function can obtain mediation measures including NIE, NDE, TE and MP assuming a constant treatment effect

Usage

```
mediate_contY_binaM_hhm(
  data,
  method = "STA",
  outcome = "Y",
  mediator = "M",
  treatment = "A",
  cluster = "cluster",
  period = "period",
  exposure = "E",
  covariateY = NULL,
  covariateM = NULL,
  a0 = 0,
  a1 = 1
)
```

Arguments

`data`	A dataset, which should include outcome, mediator, treatment, cluster, period variables
`method`	Two approximate methods are provided, one is STA (second-order Taylor approximate), the other is GHQ (Gauss-Hermite Quadrature)

outcome	The outcome variable in stepped wedge design
mediator	The mediator variable in stepped wedge design
treatment	The treatment variable in stepped wedge design. When there is a implementation period, then corresponding treatment status should be set to -1, which is mainly for convenience
cluster	The cluster variable in stepped wedge design
period	The period variable in stepped wedge design
exposure	The exposure time with J levels (e.g., 0,1,2,...,J-1 when there is no implementation period). If dataset has no exposure, then set it to NULL
covariateY	A vector of confounders in the outcome regression (default is NULL)
covariateM	A vector of confounders in the mediator regression (default is NULL)
a0	The reference treatment level in defining TE and NIE. The default value is 0
a1	The treatment level of interest in defining TE and NIE. The default value is 1

Value

A list containing point and interval estimates of NIE, NDE, TE and MP.

Author(s)

Zhiqiang Cao <zcaoae@connect.ust.hk> and Fan Li <fan.f.li@yale.edu>

Examples

```
library(lme4)
I = 15
J = 4
n = 20
beta = cumsum(c(0,0.1,0.1/2,0.1/(2^2)))
gamma = cumsum(c(0,0.3,0.3/2,0.3/(2^2)))
sigma_a = 0.334
sigma_tau = 0.605
sigma_em = sigma_ey = 1
set.seed(123456)
mydata1 = gen_data_hhm(I,J,n,beta,gamma,theta=0.75,beta_M=1.2,eta=0.6,
sigma_a,sigma_ey,sigma_tau,sigma_em,binary.o=0,binary.m=1)
# example 1: mediation analysis without covariates in outcome and mediator models
res1 = mediate_contY_binaM_hhm(data=mydata1, method = "STA")
print(res1)
res1f = mediate_contY_binaM_hhm(data=mydata1, method = "GHQ")
print(res1f)

# example 2: mediation analysis with different covariates in outcome and mediator models
# generate two covariates
covdata = data.frame("X1" = numeric(), "X2" = numeric())
set.seed(100)
for(i in 1:I){
  for(j in 1:J){
     x1_ijk = rnorm(n,mean=0.5)
     x2_ijk = rnorm(n,sd=0.5)
     covdata = rbind(covdata, data.frame(cbind(X1 = x1_ijk, X2 = x2_ijk)))
  }
}
```

```
mydata2 = data.frame(mydata1,covdata)
res2 = mediate_contY_binaM_hhm(data=mydata2, method = "STA",
covariateY = c("X1"), covariateM = c("X2"))
print(res2)
res2f = mediate_contY_binaM_hhm(data=mydata2, method = "GHQ",
covariateY = c("X1"), covariateM = c("X2"))
print(res2f)

# example 3: mediation analysis with the same covariates in outcome and mediator models
res3 = mediate_contY_binaM_hhm(data=mydata2, method = "STA",
covariateY = c("X1","X2"), covariateM = c("X1","X2"))
print(res3)
res3f = mediate_contY_binaM_hhm(data=mydata2, method = "GHQ",
covariateY = c("X1","X2"), covariateM = c("X1","X2"))
print(res3f)

# example 4: mediation analysis with different clusters and periods
I = 12
J = 5
beta = cumsum(c(0,0.1,0.1/2,0.1/(2^2),0.1/(2^3)))
gamma = cumsum(c(0,0.3,0.3/2,0.3/(2^2),0.3/(2^3)))
set.seed(123456)
mydata3 = gen_data_hhm(I,J,n,beta,gamma,theta=0.75,beta_M=1,eta=0.8,
sigma_a,sigma_ey,sigma_tau,sigma_em,binary.o=0,binary.m=1)
res4 = mediate_contY_binaM_hhm(data=mydata3,method = "STA")
print(res4)
res4f = mediate_contY_binaM_hhm(data=mydata3,method = "GHQ")
print(res4f)

# example 5: if there are no exposure variable
mydata4 = mydata3[,-4]
res5 = mediate_contY_binaM_hhm(data=mydata4,method = "STA",exposure=NULL)
print(res5)
```

`mediate_contY_binaM_nem` *Mediation analysis function for continuous outcome and binary mediator in a stepped wedge design based on nested exchangeable correlation model with a constant treatment effect*

Description

After obtaining parameter estimates from linear mixed effect model for outcome model and generalized linear mixed effect model for mediator model, this function can obtain mediation measures including NIE, NDE, TE and MP assuming a constant treatment effect

Usage

```
mediate_contY_binaM_nem(
  data,
  outcome = "Y",
  mediator = "M",
  treatment = "A",
```

```
  cluster = "cluster",
  period = "period",
  exposure = "E",
  covariateY = NULL,
  covariateM = NULL,
  a0 = 0,
  a1 = 1
)
```

Arguments

data	A dataset, which should include outcome, mediator, treatment, cluster, period variables
outcome	The outcome variable in stepped wedge design
mediator	The mediator variable in stepped wedge design
treatment	The treatment variable in stepped wedge design. When there is a implementation period, then corresponding treatment status should be set to -1, which is mainly for convenience
cluster	The cluster variable in stepped wedge design
period	The period variable in stepped wedge design
exposure	The exposure time with J levels (e.g., 0,1,2,...,J-1 when there is no implementation period). If dataset has no exposure, then set it to NULL
covariateY	A vector of confounders in the outcome regression (default is NULL)
covariateM	A vector of confounders in the mediator regression (default is NULL)
a0	The reference treatment level in defining TE and NIE. The default value is 0
a1	The treatment level of interest in defining TE and NIE. The default value is 1

Value

A list containing point and interval estimates of NIE, NDE, TE and MP.

Author(s)

Zhiqiang Cao <zcaoae@connect.ust.hk> and Fan Li <fan.f.li@yale.edu>

Examples

```
library(lme4)
I = 15
J = 4
n = 20
beta = cumsum(c(0,0.1,0.1/2,0.1/(2^2)))
gamma = cumsum(c(0,0.3,0.3/2,0.3/(2^2)))
sigma_tau = sigma_a = 0.334
sigma_phi = sigma_psi = 0.6
sigma_em = sigma_ey = 0.8
set.seed(123456)
mydata1 = gen_data_nem(I,J,n,beta,gamma,theta=0.75,beta_M=1.2,eta=0.6,sigma_a,
sigma_phi,sigma_ey,sigma_tau,sigma_psi,sigma_em,binary.o=0,binary.m=1)
# example 1: mediation analysis without covariates in outcome and mediator models
res1 = mediate_contY_binaM_nem(data=mydata1)
```

```
print(res1)

# example 2: mediation analysis with different covariates in outcome and mediator models
# generate two covariates
covdata = data.frame("X1" = numeric(), "X2" = numeric())
set.seed(100)
for(i in 1:I){
  for(j in 1:J){
     x1_ijk = rnorm(n,mean=0.5)
     x2_ijk = rnorm(n,sd=0.5)
     covdata = rbind(covdata, data.frame(cbind(X1 = x1_ijk, X2 = x2_ijk)))
  }
}

mydata2 = data.frame(mydata1,covdata)
res2 = mediate_contY_binaM_nem(data = mydata2, covariateY = c("X1"),
covariateM = c("X2"))
print(res2)

# example 3: mediation analysis with the same covariates in outcome and mediator models
res3 = mediate_contY_binaM_nem(data = mydata2,
covariateY = c("X1","X2"), covariateM = c("X1","X2"))
print(res3)

# example 4: mediation analysis with different clusters and periods
I = 12
J = 5
beta = cumsum(c(0,0.1,0.1/2,0.1/(2^2),0.1/(2^3)))
gamma = cumsum(c(0,0.3,0.3/2,0.3/(2^2),0.3/(2^3)))
set.seed(123456)
mydata3 = gen_data_nem(I,J,n,beta,gamma,theta=0.75,beta_M=1,eta=0.8,sigma_a,
sigma_phi,sigma_ey,sigma_tau,sigma_psi,sigma_em,binary.o=0,binary.m=1)
res4 = mediate_contY_binaM_nem(data=mydata3)
print(res4)
```

`mediate_contY_binaM_nem_etm`
Mediation analysis function for continuous outcome and binary mediator in a stepped wedge based on nested exchangeable correlation model with an exposure-time dependent treatment effect

---

Description

After obtaining parameter estimates from linear mixed effect model for outcome model and generalized linear mixed effect model for mediator model, this function can obtain mediation measures including NIE, NDE, TE and MP with an exposure-time dependent treatment effect

Usage

```
mediate_contY_binaM_nem_etm(
  data,
  outcome = "Y",
  mediator = "M",
```

```
  treatment = "A",
  cluster = "cluster",
  period = "period",
  exposure = "E",
  covariateY = NULL,
  covariateM = NULL,
  a0 = 0,
  a1 = 1
)
```

Arguments

data	A dataset, which should include outcome, mediator, treatment, cluster, period variables
outcome	The outcome variable in stepped wedge design
mediator	The mediator variable in stepped wedge design
treatment	The treatment variable in stepped wedge design. When there is a implementation period, then corresponding treatment status should be set to -1, which is mainly for convenience
cluster	The cluster variable in stepped wedge design
period	The period variable in stepped wedge design
exposure	The exposure time with J levels (e.g., 0,1,2,...,J-1 when there is no implementation period)
covariateY	A vector of confounders in the outcome regression (default is NULL)
covariateM	A vector of confounders in the mediator regression (default is NULL)
a0	The reference treatment level in defining TE and NIE. The default value is 0
a1	The treatment level of interest in defining TE and NIE. The default value is 1

Value

A list containing point and interval estimates of NIE, NDE, TE and MP at each exposure time and overall summary mediation measures, as well as Chi-square test result of TE

Author(s)

Zhiqiang Cao <zcaoae@connect.ust.hk> and Fan Li <fan.f.li@yale.edu>

Examples

```
library(lme4)
I = 15
J = 4
n = 20
beta = cumsum(c(0,0.1,0.1/2,0.1/(2^2)))
gamma = cumsum(c(0,0.3,0.3/2,0.3/(2^2)))
eta_e = c(0.5,1.3,2.1)
theta_e = c(0.6,1,1.4)
sigma_tau = sigma_a = 0.334
sigma_phi = sigma_psi = 0.6
sigma_em = sigma_ey = 0.8
set.seed(123456)
```

```
mydata1 = gen_data_nem_etm(I,J,n,beta,gamma,theta_e,beta_M=1.2,eta_e,sigma_a,
sigma_phi,sigma_ey,sigma_tau,sigma_psi,sigma_em,binary.o=0,binary.m=1)
# example 1: mediation analysis without covariates in outcome and mediator models
res1 = mediate_contY_binaM_nem_etm(data=mydata1)
print(res1)

# example 2: mediation analysis with different covariates in outcome and mediator models
# generate two covariates
covdata = data.frame("X1" = numeric(), "X2" = numeric())
set.seed(100)
for(i in 1:I){
  for(j in 1:J){
     x1_ijk = rnorm(n,mean=0.5)
     x2_ijk = rnorm(n,sd=0.5)
     covdata = rbind(covdata, data.frame(cbind(X1 = x1_ijk, X2 = x2_ijk)))
  }
}

mydata2 = data.frame(mydata1,covdata)
res2 = mediate_contY_binaM_nem_etm(data = mydata2, covariateY = c("X1"),
covariateM = c("X2"))
print(res2)

# example 3: mediation analysis with the same covariates in outcome and mediator models
res3 = mediate_contY_binaM_nem_etm(data = mydata2,
covariateY = c("X1","X2"), covariateM = c("X1","X2"))
print(res3)

# example 4: mediation analysis with different clusters and periods
I = 12
J = 5
beta = cumsum(c(0,0.1,0.1/2,0.1/(2^2),0.1/(2^3)))
gamma = cumsum(c(0,0.3,0.3/2,0.3/(2^2),0.3/(2^3)))
eta_e = c(0.5,1.2,1.9,2.6)
theta_e = c(0.3,0.6,0.9,1.2)
set.seed(123456)
mydata3 = gen_data_nem_etm(I,J,n,beta,gamma,theta_e,beta_M=1.2,eta_e,sigma_a,
sigma_phi,sigma_ey,sigma_tau,sigma_psi,sigma_em,binary.o=0,binary.m=1)
res4 = mediate_contY_binaM_nem_etm(data=mydata3)
print(res4)
```

`mediate_contY_contM_etm`

Mediation analysis function for continuous outcome and continuous mediator in a stepped wedge design with an exposure-time dependent treatment effect

---

Description

After obtaining parameter estimates from linear mixed-effects models for both outcome and mediator models, this function can obtain mediation measures including NIE, NDE, TE and MP with an exposure-time dependent treatment effect

Usage

```
mediate_contY_contM_etm(
  data,
  outcome = "Y",
  mediator = "M",
  treatment = "A",
  cluster = "cluster",
  period = "period",
  exposure = "E",
  covariateY = NULL,
  covariateM = NULL,
  a0 = 0,
  a1 = 1
)
```

Arguments

`data`	A dataset, which should include outcome, mediator, treatment, cluster, period variables
`outcome`	The outcome variable in stepped wedge design
`mediator`	The mediator variable in stepped wedge design
`treatment`	The treatment variable in stepped wedge design. When there is a implementation period, then corresponding treatment status should be set to -1, which is mainly for convenience
`cluster`	The cluster variable in stepped wedge design
`period`	The period variable in stepped wedge design
`exposure`	The exposure time with J levels (e.g., 0,1,2,...,J-1 when there is no implementation period)
`covariateY`	A vector of confounders in the outcome regression (default is NULL)
`covariateM`	A vector of confounders in the mediator regression (default is NULL)
`a0`	The reference treatment level in defining TE and NIE. The default value is 0
`a1`	The treatment level of interest in defining TE and NIE. The default value is 1

Value

A list containing point and interval estimates of NIE, NDE, TE and MP at each exposure time and overall summary mediation measures, as well as Chi-square test result of TE

Author(s)

Zhiqiang Cao <zcaoae@connect.ust.hk> and Fan Li <fan.f.li@yale.edu>

Examples

```
library(lme4)
I = 15
J = 4
n = 20
beta = cumsum(c(0,0.1,0.1/2,0.1/(2^2)))
gamma = cumsum(c(0,0.3,0.3/2,0.3/(2^2)))
```

```
eta_e = c(0.5,0.8,1.1)
theta_e = c(0.5,1.0,1.5)
sigma_tau = sigma_a = 0.334
sigma_em = sigma_ey = 1
set.seed(123456)
mydata1 = gen_data_etm(I,J,n,beta,gamma,theta_e,beta_M=0.8,eta_e,sigma_a,
sigma_ey,sigma_tau,sigma_em,binary.o=0,binary.m=0)
# example 1: mediation analysis without covariates in outcome and mediator models
res1 = mediate_contY_contM_etm(data = mydata1)
print(res1)

# example 2: mediation analysis with different covariates in outcome and mediator models
# generate two covariates
covdata = data.frame("X1" = numeric(), "X2" = numeric())
set.seed(100)
for(i in 1:I){
  for(j in 1:J){
     x1_ijk = rnorm(n,mean=0.5)
     x2_ijk = rnorm(n,sd=0.5)
     covdata = rbind(covdata, data.frame(cbind(X1 = x1_ijk, X2 = x2_ijk)))
  }
}
mydata2 = data.frame(mydata1,covdata)
res2 = mediate_contY_contM_etm(data = mydata2, covariateY = c("X1"),
covariateM = c("X2"))
print(res2)

# example 3: mediation analysis with the same covariates in outcome and mediator models
res3 = mediate_contY_contM_etm(data = mydata2, covariateY = c("X1","X2"),
covariateM = c("X1","X2"))
print(res3)

# example 4: mediation analysis with different clusters and periods
I = 12
J = 5
beta = cumsum(c(0,0.1,0.1/2,0.1/(2^2),0.1/(2^3)))
gamma = cumsum(c(0,0.3,0.3/2,0.3/(2^2),0.3/(2^3)))
eta_e = c(0.4,0.6,0.8,1.0)
theta_e = c(0.6,0.75,0.9,1.05)
set.seed(123456)
mydata3 = gen_data_etm(I,J,n,beta,gamma,theta_e,beta_M=0.8,eta_e,sigma_a,sigma_ey,
sigma_tau,sigma_em,binary.o=0,binary.m=0)
res4 = mediate_contY_contM_etm(data=mydata3)
print(res4)
```

---

mediate_contY_contM_hhm

Mediation analysis function for continuous outcome and continuous mediator in a stepped wedge design based on Hussey and Hughes model with a constant treatment effect

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Description

After obtaining parameter estimates from linear mixed-effects models for both outcome and mediator models, this function can obtain mediation measures including NIE, NDE, TE and MP assuming a constant treatment effect

Usage

```
mediate_contY_contM_hhm(
  data,
  outcome = "Y",
  mediator = "M",
  treatment = "A",
  cluster = "cluster",
  period = "period",
  exposure = "E",
  covariateY = NULL,
  covariateM = NULL,
  a0 = 0,
  a1 = 1
)
```

Arguments

`data`	A dataset, which should include outcome, mediator, treatment, cluster, period variables
`outcome`	The outcome variable in stepped wedge design (continuous)
`mediator`	The mediator variable in stepped wedge design (continuous)
`treatment`	The treatment variable in stepped wedge design. When there is a implementation period, then corresponding treatment status should be set to -1, which is mainly for convenience
`cluster`	The cluster variable in stepped wedge design
`period`	The period variable in stepped wedge design
`exposure`	The exposure time with J levels (e.g., 0,1,2,...,J-1 when there is no implementation period). If dataset has no exposure variable, then set it to NULL
`covariateY`	A vector of confounders in the outcome regression (default is NULL)
`covariateM`	A vector of confounders in the mediator regression (default is NULL)
`a0`	The reference treatment level in defining TE and NIE. The default value is 0
`a1`	The treatment level of interest in defining TE and NIE. The default value is 1

Value

A list containing point and interval estimates of NIE, NDE, TE and MP.

Author(s)

Zhiqiang Cao <zcaoae@connect.ust.hk> and Fan Li <fan.f.li@yale.edu>

Examples

```
library(lme4)
I = 15
J = 4
n = 20
beta = cumsum(c(0,0.1,0.1/2,0.1/(2^2)))
gamma = cumsum(c(0,0.3,0.3/2,0.3/(2^2)))
sigma_tau = sigma_a = 0.334
sigma_em = sigma_ey = 1
set.seed(123456)
mydata1 = gen_data_hhm(I,J,n,beta,gamma,theta=0.75,beta_M=0.625,eta=0.4,
sigma_a,sigma_ey,sigma_tau,sigma_em,binary.o=0,binary.m=0)
# example 1: mediation analysis without covariates in outcome and mediator models
res1 = mediate_contY_contM_hhm(data=mydata1)
print(res1)

# example 2: mediation analysis with different covariates in outcome and mediator models
# generate two covariates
covdata = data.frame("X1" = numeric(), "X2" = numeric())
set.seed(100)
for(i in 1:I){
  for(j in 1:J){
     x1_ijk = rnorm(n,mean=0.5)
     x2_ijk = rnorm(n,sd=0.5)
     covdata = rbind(covdata, data.frame(cbind(X1 = x1_ijk, X2 = x2_ijk)))
  }
}
mydata2 = data.frame(mydata1,covdata)
res2 = mediate_contY_contM_hhm(data = mydata2, covariateY = c("X1"),
covariateM = c("X2"))
print(res2)

# example 3: mediation analysis with the same covariates in outcome and mediator models
res3 = mediate_contY_contM_hhm(data = mydata2, covariateY = c("X1","X2"),
covariateM = c("X1","X2"))
print(res3)

# example 4: mediation analysis with different clusters and periods
I = 12
J = 5
beta = cumsum(c(0,0.1,0.1/2,0.1/(2^2),0.1/(2^3)))
gamma = cumsum(c(0,0.3,0.3/2,0.3/(2^2),0.3/(2^3)))
set.seed(123456)
mydata3 = gen_data_hhm(I,J,n,beta,gamma,theta=0.75,beta_M=0.625,eta=0.4,
sigma_a,sigma_ey,sigma_tau,sigma_em,binary.o=0,binary.m=0)
res4 = mediate_contY_contM_hhm(data=mydata3)
print(res4)

# example 5: if there are no exposure variable
mydata4 = mydata3[,-4]
res5 = mediate_contY_contM_hhm(data=mydata4,exposure=NULL)
print(res5)
```

mediate_contY_contM_nem

Mediation analysis function for continuous outcome and continuous mediator in a stepped wedge design based on nested exchangeable correlation model with a constant treatment effect

Description

After obtaining parameter estimates from linear mixed-effects models for both outcome and mediator models, this function can obtain mediation measures including NIE, NDE, TE and MP assuming a constant treatment effect

Usage

```
mediate_contY_contM_nem(
  data,
  outcome = "Y",
  mediator = "M",
  treatment = "A",
  cluster = "cluster",
  period = "period",
  exposure = "E",
  covariateY = NULL,
  covariateM = NULL,
  a0 = 0,
  a1 = 1
)
```

Arguments

`data`	A dataset, which should include outcome, mediator, treatment, cluster, period variables
`outcome`	The outcome variable in stepped wedge design (continuous)
`mediator`	The mediator variable in stepped wedge design (continuous)
`treatment`	The treatment variable in stepped wedge design. When there is a implementation period, then corresponding treatment status should be set to -1, which is mainly for convenience
`cluster`	The cluster variable in stepped wedge design
`period`	The period variable in stepped wedge design
`exposure`	The exposure time with J levels (e.g., 0,1,2,...,J-1 when there is no implementation period). If dataset has no exposure variable, then set it to NULL
`covariateY`	A vector of confounders in the outcome regression (default is NULL)
`covariateM`	A vector of confounders in the mediator regression (default is NULL)
`a0`	The reference treatment level in defining TE and NIE. The default value is 0
`a1`	The treatment level of interest in defining TE and NIE. The default value is 1

Value

A list containing point and interval estimates of NIE, NDE, TE and MP.

Author(s)

Zhiqiang Cao <zcaoae@connect.ust.hk> and Fan Li <fan.f.li@yale.edu>

Examples

```
library(lme4)
I = 15
J = 4
n = 20
beta = cumsum(c(0,0.1,0.1/2,0.1/(2^2)))
gamma = cumsum(c(0,0.3,0.3/2,0.3/(2^2)))
sigma_tau = sigma_a = 0.334
sigma_phi = sigma_psi = 0.6
sigma_em = sigma_ey = 0.8
set.seed(123456)
mydata1 = gen_data_nem(I,J,n,beta,gamma,theta=0.75,beta_M=0.625,eta=0.4,sigma_a,
sigma_phi,sigma_ey,sigma_tau,sigma_psi,sigma_em,binary.o=0,binary.m=0)
# example 1: mediation analysis without covariates in outcome and mediator models
res1 = mediate_contY_contM_nem(data=mydata1)
print(res1)

# example 2: mediation analysis with different covariates in outcome and mediator models
# generate two covariates
covdata = data.frame("X1" = numeric(), "X2" = numeric())
set.seed(100)
for(i in 1:I){
  for(j in 1:J){
     x1_ijk = rnorm(n,mean=0.5)
     x2_ijk = rnorm(n,sd=0.5)
     covdata = rbind(covdata, data.frame(cbind(X1 = x1_ijk, X2 = x2_ijk)))
  }
}
mydata2 = data.frame(mydata1,covdata)
res2 = mediate_contY_contM_nem(data = mydata2,covariateY = c("X1"),
covariateM = c("X2"))
print(res2)

# example 3: mediation analysis with the same covariates in outcome and mediator models
res3 = mediate_contY_contM_nem(data = mydata2,covariateY = c("X1","X2"),
covariateM = c("X1","X2"))
print(res3)

# example 4: mediation analysis with different clusters and periods
I = 12
J = 5
beta = cumsum(c(0,0.1,0.1/2,0.1/(2^2),0.1/(2^3)))
gamma = cumsum(c(0,0.3,0.3/2,0.3/(2^2),0.3/(2^3)))
set.seed(123456)
mydata3 = gen_data_nem(I,J,n,beta,gamma,theta=0.75,beta_M=0.625,eta=0.4,sigma_a,
sigma_phi,sigma_ey,sigma_tau,sigma_psi,sigma_em,binary.o=0,binary.m=0)
res4 = mediate_contY_contM_nem(data=mydata3)
print(res4)
```

`mediate_contY_contM_nem_etm`

Mediation analysis function for continuous outcome and continuous mediator in a stepped wedge design based on nested exchangeable correlation model with an exposure-time dependent treatment effect

---

Description

After obtaining parameter estimates from linear mixed-effects models for both outcome and mediator models, this function can obtain mediation measures including NIE, NDE, TE and MP with an exposure-time dependent treatment effect in a nested exchangeable correlation model

Usage

```
mediate_contY_contM_nem_etm(
  data,
  outcome = "Y",
  mediator = "M",
  treatment = "A",
  cluster = "cluster",
  period = "period",
  exposure = "E",
  covariateY = NULL,
  covariateM = NULL,
  a0 = 0,
  a1 = 1
)
```

Arguments

`data`	A dataset, which should include outcome, mediator, treatment, cluster, period variables
`outcome`	The outcome variable in stepped wedge design
`mediator`	The mediator variable in stepped wedge design
`treatment`	The treatment variable in stepped wedge design. When there is a implementation period, then corresponding treatment status should be set to -1, which is mainly for convenience
`cluster`	The cluster variable in stepped wedge design
`period`	The period variable in stepped wedge design
`exposure`	The exposure time with J levels (e.g., 0,1,2,...,J-1 when there is no implementation period)
`covariateY`	A vector of confounders in the outcome regression (default is NULL)
`covariateM`	A vector of confounders in the mediator regression (default is NULL)
`a0`	The reference treatment level in defining TE and NIE. The default value is 0
`a1`	The treatment level of interest in defining TE and NIE. The default value is 1

Value

A list containing point and interval estimates of NIE, NDE, TE and MP at each exposure time and overall summary mediation measures, as well as Chi-square test result of TE

Author(s)

Zhiqiang Cao <zcaoae@connect.ust.hk> and Fan Li <fan.f.li@yale.edu>

Examples

```
library(lme4)
I = 15
J = 4
n = 20
beta = cumsum(c(0,0.1,0.1/2,0.1/(2^2)))
gamma = cumsum(c(0,0.3,0.3/2,0.3/(2^2)))
eta_e = c(0.5,0.8,1.1)
theta_e = c(0.5,1.0,1.5)
sigma_tau = sigma_a = 0.334
sigma_phi = sigma_psi = 0.6
sigma_em = sigma_ey = 0.8
set.seed(123456)
mydata1 = gen_data_nem_etm(I,J,n,beta,gamma,theta_e,beta_M=0.8,eta_e,sigma_a,
sigma_phi,sigma_ey,sigma_tau,sigma_psi,sigma_em,binary.o=0,binary.m=0)
# example 1: mediation analysis without covariates in outcome and mediator models
res1 = mediate_contY_contM_nem_etm(data=mydata1)
print(res1)

# example 2: mediation analysis with different covariates in outcome and mediator models
# generate two covariates
covdata = data.frame("X1" = numeric(), "X2" = numeric())
set.seed(100)
for(i in 1:I){
  for(j in 1:J){
     x1_ijk = rnorm(n,mean=0.5)
     x2_ijk = rnorm(n,sd=0.5)
     covdata = rbind(covdata, data.frame(cbind(X1 = x1_ijk, X2 = x2_ijk)))
  }
}
mydata2 = data.frame(mydata1,covdata)
res2 = mediate_contY_contM_nem_etm(data = mydata2, covariateY = c("X1"),
covariateM = c("X2"))
print(res2)

# example 3: mediation analysis with the same covariates in outcome and mediator models
res3 = mediate_contY_contM_nem_etm(data = mydata2, covariateY = c("X1","X2"),
covariateM = c("X1","X2"))
print(res3)

# example 4: mediation analysis with different clusters and periods
I = 12
J = 5
beta = cumsum(c(0,0.1,0.1/2,0.1/(2^2),0.1/(2^3)))
gamma = cumsum(c(0,0.3,0.3/2,0.3/(2^2),0.3/(2^3)))
eta_e = c(0.4,0.6,0.8,1.0)
theta_e = c(0.6,0.75,0.9,1.05)
```

```
set.seed(123456)
mydata3 = gen_data_nem_etm(I,J,n,beta,gamma,theta_e,beta_M=0.8,eta_e,sigma_a,
sigma_phi,sigma_ey,sigma_tau,sigma_psi,sigma_em,binary.o=0,binary.m=0)
res4 = mediate_contY_contM_nem_etm(data=mydata3)
print(res4)
```

---

mediate_swcrt *Mediation analysis in a stepped wedge cluster randomized trials based on Hussey and Hughes model*

Description

Function for calculating the point and interval estimates for the NIE, NDE, TE and MP in a stepped wedge cluster randomized trials with constant treatment effect or exposure-time dependent treatment effect

Usage

```
mediate_swcrt(
  data,
  method = "STA",
  outcome = "Y",
  mediator = "M",
  treatment = "A",
  cluster = "cluster",
  period = "period",
  exposure = "E",
  covariate.outcome = NULL,
  covariate.mediator = NULL,
  a0 = 0,
  a1 = 1,
  binary.o = 0,
  binary.m = 0,
  time.dependent = FALSE
)
```

Arguments

data	(Required) The name of the dataset
method	Two approximate methods are provided, one is STA (second-order Taylor approximate), the other is GHQ (Gauss-Hermite Quadrature) when both the outcome and mediator are continuous, the method choice is irrelevant; when the outcome is binary and mediator is continuous, we default to the STA method
outcome	(Required) Name of the outcome variable, which should be either a continuous or binary datatype
mediator	(Required) Name of the mediator variable, which should be either a continuous or binary datatype
treatment	(Required) Name of the treatment variable, which should be either a continuous or binary datatype. When there is a implementation period, then corresponding treatment status should be set to -1, which is mainly for convenience

cluster (Required) Name of the cluster variable, which should be a factor

period (Required) Name of the period variable, which should be a factor

exposure Name of the exposure time variable, which should be a factor. For time-dependent model, this argument is required. For constant treatment effect model, if dataset has no exposure variable, then set it to NULL

covariate.outcome
A vector of names showing the confounding variables used in the outcome model. The default value is NULL, which represents no confounding variables. We only accepted continuous and binary confounding variables, if one confounding variable is categorical, please set it to a series of binary variables in advance

covariate.mediator
A vector of names showing the confounding variables used in the mediator model. The default value is NULL, which represents no confounding variables. We only accepted continuous and binary confounding variables, if one confounding variable is categorical, please set it to a series of binary variables in advance

a0 The reference treatment level in defining TE and NIE. The default value is 0

a1 The treatment level of interest in defining TE and NIE. The default value is 1

binary.o (Required) If the outcome is binary, set to 1. If the outcome is continuous, set to 0

binary.m (Required) If the mediator is binary, set to 1. If the mediator is continuous, set to 0

time.dependent (Required) If the treatment effect is time-dependent, set to TRUE. If the treatment effect is constant, set to FALSE

Value

A list containing point and interval estimates of NIE, NDE, TE and MP under constant treatment effect structure; or a list containing point and interval estimates of NIE, NDE, TE and MP at each exposure time and overall summary mediation measures, as well as Chi-square test result of TE under exposure-time treatment effect structure

Author(s)

Zhiqiang Cao <zcaoae@connect.ust.hk> and Fan Li <fan.f.li@yale.edu>

References

Cao Z. and Fan Li. Assessing mediation in cross-sectional stepped wedge cluster randomized trials. under review. 2024;0(0):1-24.

Examples

```
library(lme4)
I = 15
J = 4
n = 20
beta = cumsum(c(0,0.1,0.1/2,0.1/(2^2)))
gamma = cumsum(c(0,0.3,0.3/2,0.3/(2^2)))
sigma_tau = sigma_a = 0.334
sigma_em = sigma_ey = 1
```

```
set.seed(123456)
mydata1 = gen_data_hhm(I,J,n,beta,gamma,theta=0.75,beta_M=0.625,eta=0.4,sigma_a,
sigma_ey,sigma_tau,sigma_em,binary.o=0,binary.m=0)
covdata = data.frame("X1" = numeric(), "X2" = numeric())
set.seed(100)
for(i in 1:I){
  for(j in 1:J){
     x1_ijk = rnorm(n)
     x2_ijk = rnorm(n,sd=0.1)
     covdata = rbind(covdata, data.frame(cbind(X1 = x1_ijk, X2 = x2_ijk)))
  }
}
mydata1 = data.frame(mydata1,covdata)
# example 1: constant treatment effect, mediation analysis of continuous outcome
# and continuous mediator without covariates, with different covariates in outcome
# and mediator models, as well as with the same covariates in both models
res1 = mediate_swcrt(data=mydata1)
print(res1)
res1f = mediate_swcrt(data=mydata1,covariate.outcome = c("X1"),
covariate.mediator = c("X2"))
print(res1f)
res1ff = mediate_swcrt(data=mydata1,covariate.outcome = c("X1","X2"),
covariate.mediator = c("X1","X2"))
print(res1ff)

# example 2: constant treatment effect, mediation analysis of binary outcome
# and continuous mediator without covariates
I = 15
J = 4
n = 20
beta = cumsum(c(0,0.1,0.1/2,0.1/(2^2)))
gamma = cumsum(c(0,0.3,0.3/2,0.3/(2^2)))
sigma_a = 0.605
sigma_tau = 0.334
sigma_em = sigma_ey = 1
set.seed(123456)
mydata2 = gen_data_hhm(I,J,n,beta,gamma,theta=0.75,beta_M=1,eta=0.4,sigma_a,
sigma_ey,sigma_tau,sigma_em,binary.o=1,binary.m=0)
res2 = mediate_swcrt(data=mydata2,binary.o = 1)
print(res2)

# example 3: exposure-time dependent treatment effect, mediation analysis of
# continuous outcome and continuous mediator without covariates
I = 15
J = 4
n = 20
beta = cumsum(c(0,0.1,0.1/2,0.1/(2^2)))
gamma = cumsum(c(0,0.3,0.3/2,0.3/(2^2)))
sigma_tau = sigma_a = 0.334
sigma_em = sigma_ey = 1
eta_e = c(0.5,0.8,1.1)
theta_e = c(0.5,1.0,1.5)
set.seed(123456)
mydata3 = gen_data_etm(I,J,n,beta,gamma,theta_e,beta_M=0.8,eta_e,sigma_a,
sigma_ey,sigma_tau,sigma_em,binary.o=0,binary.m=0)
res3 = mediate_swcrt(data=mydata3,time.dependent = TRUE)
print(res3)
```

```
# example 4: exposure-time dependent treatment effect, mediation analysis of
# continuous outcome and binary mediator with the same covariates in both models
I = 15
J = 4
n = 20
beta = cumsum(c(0,0.1,0.1/2,0.1/(2^2)))
gamma = cumsum(c(0,0.3,0.3/2,0.3/(2^2)))
eta_e = c(0.5,1.3,2.1)
theta_e = c(0.6,1,1.4)
sigma_a = 0.334
sigma_tau = 0.605
sigma_em = sigma_ey = 1
set.seed(123456)
mydata4 = gen_data_etm(I,J,n,beta,gamma,theta_e,beta_M=1.2,eta_e,sigma_a,
sigma_ey,sigma_tau,sigma_em,binary.o=0,binary.m=1)
set.seed(100)
for(i in 1:I){
  for(j in 1:J){
     x1_ijk = rnorm(n)
     x2_ijk = rnorm(n,sd=0.5)
     covdata = rbind(covdata, data.frame(cbind(X1 = x1_ijk, X2 = x2_ijk)))
  }
}
mydata4 = data.frame(mydata4,covdata)
# using default STA method
res4 = mediate_swcrt(data=mydata4,covariate.outcome = c("X1","X2"),
covariate.mediator = c("X1","X2"),binary.m = 1, time.dependent = TRUE)
print(res4)
# using GHQ method
res4f = mediate_swcrt(data=mydata4,method = "GHQ",covariate.outcome = c("X1","X2"),
covariate.mediator = c("X1","X2"),binary.m = 1, time.dependent = TRUE)
print(res4f)
```

`mediate_swcrt_nem` *Mediation analysis in a stepped wedge cluster randomized trials based on nested exchangeable correlation model*

Description

Function for calculating the point and interval estimates for the NIE, NDE, TE and MP in a stepped wedge cluster randomized trials based on nested exchangeable correlation model with constant treatment effect or exposure-time dependent treatment effect

Usage

```
mediate_swcrt_nem(
  data,
  outcome = "Y",
  mediator = "M",
  treatment = "A",
  cluster = "cluster",
```

```
  period = "period",
  exposure = "E",
  covariate.outcome = NULL,
  covariate.mediator = NULL,
  a0 = 0,
  a1 = 1,
  binary.o = 0,
  binary.m = 0,
  time.dependent = FALSE
)
```

Arguments

`data` (Required) The name of the dataset

`outcome` (Required) Name of the outcome variable, which should be either a continuous or binary datatype

`mediator` (Required) Name of the mediator variable, which should be either a continuous or binary datatype

`treatment` (Required) Name of the treatment variable, which should be either a continuous or binary datatype. When there is a implementation period, then corresponding treatment status should be set to -1, which is mainly for convenience

`cluster` (Required) Name of the cluster variable, which should be a factor

`period` (Required) Name of the period variable, which should be a factor

`exposure` Name of the exposure time variable, which should be a factor. For time-dependent model, this argument is required. For constant treatment effect model, if dataset has no exposure variable, then set it to NULL

`covariate.outcome`
A vector of names showing the confounding variables used in the outcome model. The default value is NULL, which represents no confounding variables. We only accepted continuous and binary confounding variables, if one confounding variable is categorical, please set it to a series of binary variables in advance

`covariate.mediator`
A vector of names showing the confounding variables used in the mediator model. The default value is NULL, which represents no confounding variables. We only accepted continuous and binary confounding variables, if one confounding variable is categorical, please set it to a series of binary variables in advance

`a0` The reference treatment level in defining TE and NIE. The default value is 0

`a1` The treatment level of interest in defining TE and NIE. The default value is 1

`binary.o` (Required) If the outcome is binary, set to 1. If the outcome is continuous, set to 0

`binary.m` (Required) If the mediator is binary, set to 1. If the mediator is continuous, set to 0

`time.dependent` (Required) If the treatment effect is time-dependent, set to TRUE. If the treatment effect is constant, set to FALSE

Value

A list containing point and interval estimates of NIE, NDE, TE and MP under constant treatment effect structure; or a list containing point and interval estimates of NIE, NDE, TE and MP at each exposure time and overall summary mediation measures, as well as Chi-square test result of TE under exposure-time treatment effect structure

Author(s)

Zhiqiang Cao <zcaoae@connect.ust.hk> and Fan Li <fan.f.li@yale.edu>

References

Cao Z. and Fan Li. Assessing mediation in cross-sectional stepped wedge cluster randomized trials. under review. 2024;0(0):1-24.

Examples

```
library(lme4)
I = 15
J = 4
n = 20
beta = cumsum(c(0,0.1,0.1/2,0.1/(2^2)))
gamma = cumsum(c(0,0.3,0.3/2,0.3/(2^2)))
sigma_tau = sigma_a = 0.334
sigma_phi = sigma_psi = 0.6
sigma_em = sigma_ey = 0.8
set.seed(123456)
mydata1 = gen_data_nem(I,J,n,beta,gamma,theta=0.75,beta_M=0.625,eta=0.4,sigma_a,
sigma_phi,sigma_ey,sigma_tau,sigma_psi,sigma_em,binary.o=0,binary.m=0)
covdata = data.frame("X1" = numeric(), "X2" = numeric())
set.seed(100)
for(i in 1:I){
  for(j in 1:J){
     x1_ijk = rnorm(n)
     x2_ijk = rnorm(n,sd=0.1)
     covdata = rbind(covdata, data.frame(cbind(X1 = x1_ijk, X2 = x2_ijk)))
  }
}
mydata1 = data.frame(mydata1,covdata)
# example 1: constant treatment effect, mediation analysis of continuous outcome
# and continuous mediator without covariates, with different covariates in outcome
# and mediator models, as well as with the same covariates in both models
res1 = mediate_swcrt_nem(data = mydata1)
print(res1)
res1f = mediate_swcrt_nem(data = mydata1,covariate.outcome = c("X1"),
covariate.mediator = c("X2"))
print(res1f)
res1ff = mediate_swcrt_nem(data = mydata1,covariate.outcome = c("X1","X2"),
covariate.mediator = c("X1","X2"))
print(res1ff)

# example 2: constant treatment effect, mediation analysis of binary outcome
# and continuous mediator without covariates
mydata2 = gen_data_nem(I,J,n,beta,gamma,theta=0.75,beta_M=1,eta=0.4,sigma_a,
sigma_phi,sigma_ey,sigma_tau,sigma_psi,sigma_em,binary.o=1,binary.m=0)
res2 = mediate_swcrt_nem(data=mydata2,binary.o = 1)
```

```
print(res2)

# example 3: exposure-time dependent treatment effect, mediation analysis of
# continuous outcome and continuous mediator without covariates
eta_e = c(0.5,0.8,1.1)
theta_e = c(0.5,1.0,1.5)
set.seed(123456)
mydata3 = gen_data_nem_etm(I,J,n,beta,gamma,theta_e,beta_M=0.8,eta_e,sigma_a,
sigma_phi,sigma_ey,sigma_tau,sigma_psi,sigma_em,binary.o=0,binary.m=0)
res3 = mediate_swcrt_nem(data=mydata3,time.dependent = TRUE)
print(res3)

# example 4: exposure-time dependent treatment effect, mediation analysis of
# continuous outcome and binary mediator with the same covariates in both models
eta_e = c(0.5,1.3,2.1)
theta_e = c(0.6,1,1.4)
set.seed(123456)
mydata4 = gen_data_nem_etm(I,J,n,beta,gamma,theta_e,beta_M=1.2,eta_e,sigma_a,
sigma_phi,sigma_ey,sigma_tau,sigma_psi,sigma_em,binary.o=0,binary.m=1)
set.seed(100)
for(i in 1:I){
  for(j in 1:J){
     x1_ijk = rnorm(n)
     x2_ijk = rnorm(n,sd=0.5)
     covdata = rbind(covdata, data.frame(cbind(X1 = x1_ijk, X2 = x2_ijk)))
  }
}
mydata4 = data.frame(mydata4,covdata)
res4 = mediate_swcrt_nem(data = mydata4,covariate.outcome = c("X1","X2"),
covariate.mediator = c("X1","X2"),binary.m = 1, time.dependent = TRUE)
print(res4)
```

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