

# Package ‘exmedt’

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**Title** Estimating and screening potential mediation pathways of indigenous biomarkers (i.e., mediator) between external environmental exposure and health outcome in a user friendly and efficient way.

**Version** 1.0.0

**Description** Estimating and screening potential mediation pathways of indigenous biomarkers (i.e., mediator) between external environmental exposure and health outcome in a user friendly and efficient way. Especially, when the number and category of exposures and mediators are of high dimension.

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FuncExit	<i>End the module analysis</i>
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### Description

End the module analysis

### Usage

```
FuncExit(PID)
```

### Arguments

PID                      chr. Program ID. It must be the same with the PID generated by InitMedt.

### Author(s)

Bin Wang (corresponding author)

### Examples

```
res <- InitMedt()
res1 <- LoadMedt(PID = res$PID, UseExample = "example#1", DataPath = NULL,
VocaPath = NULL)
res2 <- XMLists(PID = res$PID)
FuncExit(PID = res$PID)
```

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ImptM	<i>Estimate the importance of mediators</i>
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### Description

Estimate the importance of mediators.

### Usage

```
ImptM(PID, OutPath, VarsY, ...)
```

## Arguments

PID	chr. Program ID. It must be the same with the PID generated by InitMedt.
OutPath	chr. Output file directory, e.g. "D:/output". If "default", the current working directory will be set. It should be noted that the slash symbol is "/", not "\".
VarsY	chr. The outcome variable. Either continuous, binary or count type is permitted.
VarsX	chr. Exposure variables included in estimation procedure. When "default" is specified, all exposure variables in the data will be used. The shrinkaged exposure variables are also permitted. It should be noted that there is fixed format for the characters separated with comma and without space, e.g., "X1,X2,X3".
VarsC	chr. Covariates included in estimation procedure. When "default" is specified, all covariates in the data will be used. It should be noted that there is fixed format for the characters separated with comma and without space, e.g., "C1,C2".

## Details

ImptM function estimates the importance of mediators among given exposures. The estimation procedure is mainly realized by the hima function in HIMA package. ImptM also provides another evaluation method by the bama function in bama package. The users can search for these packages for further information.

## Value

A list containing four elements where the raw estimation results as well as the tidy tables for display are stored. The elements of that list include:

1. "MedtImptM\_all": the raw estimation result where the importance of each mediator was evaluated among whole mediators.
2. "MedtImptM\_list": the raw estimation result where the importance of each mediator was evaluated among each mediator group.
3. "MedtImptM\_table1": the tidy table for MedtImptM\_all and MedtImptM\_list, where significant estimations (q value <0.2) are expressed with an asterisk mark (\*).
4. "MedtImptM\_table2": the tidy table for MedtImptM\_all and MedtImptM\_list, where only significant estimations (q value <0.2) are displayed in this table. MedtImptM\_table2 is as same content as MedtImptM\_table1.

## Author(s)

Mengyuan Ren, Bin Wang(corresponding author)

## Examples

```
res <- InitMedt()
res1 <- LoadMedt(PID = res$PID, UseExample = "example#1", DataPath = NULL,
VocaPath = NULL)
res2 <- XMLists(PID = res$PID)
res3 <- ImptM(PID = res$PID, VarsY = "Y1",
VarsX = "default", VarsC = "default")
res4 <- ImptM(PID = res$PID, VarsY = "Y1",
```

```
VarsX = "X1,X2,X3", VarsC = "C1")
```

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InitMedt	<i>Initialize ExpoMediation module</i>
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**Description**

Initialize ExpoMediation module analysis. It can generate an R6 class object integrating all the analysis information.

**Usage**

```
InitMedt()
```

**Details**

InitMedt uses R6 package to generate an R6 class object where parameters to be used for the following mediation module program are initialized and save in that object. All executed function codes in the ExpoMediaton packaged will be recorded in the form of log text in that object. Furthermore, a program ID (i.e., PID) is randomly created for the users to identify their own program.

**Value**

An R6 class object.

**Author(s)**

Mengyuan Ren, Bin Wang(corresponding author)

**Examples**

```
res <- InitMedt()
```

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LoadMedt	<i>Load data file for Mediation module</i>
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**Description**

Load data file for Mediation module

**Usage**

```
LoadMedt(PID = PID, UseExample = "default", ...)
```

**Arguments**

PID	chr. Program ID. It must be the same with the PID generated by InitMedt.
UseExample	chr. Method of uploading data. If "default", user should upload their own data files, or use "example#1" provided by this module.
DataPath	chr. Input data file directory, e.g. "D:/test/eg_Medt_data.xlsx". It should be noted that the slash symbol is "/", not "\".
VocaPath	chr. Input vocabulary file directory, e.g. "D:/test/eg_Medt_data.xlsx". It should be noted that the slash symbol is "/", not "\".

**Details**

LoadMedt function loads the data file and the vocabulary file into the R6 object that InitMedt created. Noted that there are several data format requirements for the data and vocabulary file. For data file, the first three columns must be named as "SampleID", "SubjectID" and "Group" in sequence. The "Group" variable should be a character variable to categorize data into two groups: "train" and "test" group. Outcome variables should be named as "Y\*". e.g., Y1, Y2, Y3... Similarly, exposure variables should be named as "X\*". e.g., X1, X2, X3..., and mediator variables should be named as "M\*". e.g., M1, M2, M3... For vocabulary file, the first column should be a character variable named "SerialNo" indicating the names of outcome, exposure and mediator variables in the data file. These names should be consistent with the variable names in data file. The second column should be a character variable named "FullName" indicating the full names (labels) of the variables. The third column should be a character variable named "SubgroupName" indicating the groups the exposure or mediator variables belong to.

**Value**

An R6 class object containing the input data and vocabulary file.

**Author(s)**

Mengyuan Ren, Bin Wang(corresponding author)

**Examples**

```
res <- InitMedt()
res1 <- LoadMedt(PID = res$PID, UseExample = "example#1", DataPath = NULL,
  VocaPath = NULL)
```

**Description**

Implement pairwise mediation analyses for each pair of exposure and mediator.

**Usage**

```
Pairwise(PID, OutPath, VarsY, Family, ...)
```

**Arguments**

PID	chr. Program ID. It must be the same with the PID generated by InitMedt.
OutPath	chr. Output file directory, e.g. "D:/output". If "default", the current working directory will be set. It should be noted that the slash symbol is "/", not "\".
VarsY	chr. The outcome variable. Either continuous, binary or count type is permitted.
VarsX	chr. Exposure variables included in pairwise mediation modelling. When "default" is specified, all exposure variables in the data will be used. It should be noted that there is fixed format for the characters separated with comma and without space, e.g., "X1,X2,X3".
VarsM	chr. Mediator variables included in pairwise mediation modelling. When "default" is specified, all mediator variables in the data will be used. It should be noted that there is fixed format for the characters separated with comma and without space, e.g., "M1,M2,M3".
VarsC	chr. Covariates included in pairwise mediation modelling. When "default" is specified, all covariates in the data will be used. It should be noted that there is fixed format for the characters separated with comma and without space, e.g., "C1,C2".
Family	chr. The error distribution and link function to be used in the model. Available options include "linear" and "gaussian" for continuous outcome variables, and "binomial" as well as "poisson" options for binary and count outcome variables.
Iter	num. The number of iteration times. Default is 500. To get a more stable result, a minimum iteration of 1,000 is recommended. To obtain more digits of P value of parameter estimation, a minimum iteration of 5,000 is suggested.

**Details**

Pairwise function implements mediation modelling for each pair of exposure and mediator. Given M exposures and N mediators, an exhaustive rule will be executed and M\*N pair-wised mediation modelling are fitted. The modelling was realized using mediate function in mediation package.

**Value**

A list containing one dataframe that contains the pairwise mediation modelling results.

1. "MedtPairWise\_Stats": pairwise mediation modelling results.

**Author(s)**

Mengyuan Ren, Bin Wang(corresponding author)

## Examples

```
res <- InitMedt()
res1 <- LoadMedt(PID = res$PID, UseExample = "example#1", DataPath = NULL,
VocaPath = NULL)
res2 <- XMlists(PID = res$PID)
res3 <- Pairwise(PID=res$PID, VarsY = "Y1",
VarsX = "default", VarsM = "default", VarsC = "default", Family = "linear",
Iter = 500)
res4 <- Pairwise(PID=res$PID, VarsY = "Y1",
VarsX = "X1,X2,X3", VarsM = "M1,M2,M3", VarsC = "C1", Family = "linear",
Iter = 500)
```

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RedM

---

Mediator dimension reduction

---

## Description

Implement mediator dimension reduction for mediators.

## Usage

```
RedM(PID, OutPath, VarsY, Family, ...)
```

## Arguments

PID	chr. Program ID. It must be the same with the PID generated by InitMedt.
OutPath	chr. Output file directory, e.g. "D:/output". If "default", the current working directory will be set. It should be noted that the slash symbol is "/", not "\".
VarsY	chr. The outcome variable. Either continuous, binary or count type is permitted.
VarsX	chr. Exposure variables included in mediation modelling. When "default"(recommended) is specified, all exposure variables in the data will be used. It should be noted that there is fixed format for the characters separated with comma and without space, e.g., "X1,X2,X3".
VarsC	chr. Covariates included in mediation modelling. When "default" is specified, all covariates in the data will be used. It should be noted that there is fixed format for the characters separated with comma and without space, e.g., "C1,C2".
Method	chr. Dimension reduction method. Available options include "mean" and "pdm1"(default). "mean" option is recommended when outcome variable is a binary variable because in some situations error might occur in "pdm1" settings for binary outcome.
Family	chr. The error distribution and link function to be used in the model. Available options include "linear" and "gaussian" for continuous outcome variables, and "binomial" as well as "poisson" options for binary and count outcome variables.
Iter	num. The number of iteration times. Default is 500. To get a more stable result, a minimum iteration of 1,000 is recommended. To obtain more digits of P value of parameter estimation, a minimum iteration of 5,000 is suggested.

## Details

RedM function provides two alternative methods for mediator dimension reduction, including sum method as well as pdm1 method via PDM package. By default, all mediators will be included for dimension reduction. Afterwards, mediation models will be built between given exposures as well as shrinkaged mediator variables.

## Value

A list containing two elements where the mediator dimension reduction modelling results with exposures are stored. That list include:

1. "MedtRedM\_all": a dataframe containing the mediator dimension reduction result where all mediators are considered as one group and that shrinkaged mediator is paired and modelled with each exposure.
2. "MedtRedM\_list": a dataframe containing the mediator dimension reduction result where mediators are shrinkaged in their own subgroups, and these shrinkaged mediators are paired and modelled with each exposure.

## Author(s)

Mengyuan Ren, Bin Wang(corresponding author)

## Examples

```
res <- InitMedt()
res1 <- LoadMedt(PID = res$PID, UseExample = "example#1", DataPath = NULL,
VocaPath = NULL)
res2 <- XMlists(PID = res$PID)
res3 <- RedM(PID=res$PID, VarsY = "Y1", VarsX = "default",
VarsC = "default", Method = "mean", Family = "linear", Iter = 500)
res4 <- RedM(PID=res$PID, VarsY = "Y1", VarsX = "X1,X2,X3",
VarsC = "C1", Method = "mean", Family = "linear", Iter = 500)
```

---

RedX

*Expoures dimension reduction*

---

## Description

Implement dimension reduction for exposures.

## Usage

```
RedX(PID, OutPath, VarsY, Family, ...)
```



## Arguments

PID	chr. Program ID. It must be the same with the PID generated by InitMedt.
OutPath	chr. Output file directory, e.g. "D:/output". If "default", the current working directory will be set. It should be noted that the slash symbol is "/", not "\".
VarsY	chr. The outcome variable. Either continuous, binary or count type is permitted.
VarsC	chr. Covariates included in mediation modelling. When "default" is specified, all covariates in the data will be used. It should be noted that there is fixed format for the characters separated with comma and without space, e.g., "C1,C2".
VarsM	chr. Mediator variables included in pairwise mediation modelling. When "default" is specified, all mediator variables in the data will be used. It should be noted that there is fixed format for the characters separated with comma and without space, e.g., "M1,M2,M3".
Method	chr. Dimension reduction method. Available options include "gcdnet" and "mean"(default). "mean" option is recommended when outcome variable is a binary variable because in some situations low variance of shrinkaged exposure variable might obtain in "gcdnet" settings for binary outcome.
Folds	num. Number of cross validation for gcdnet method. Default is 10.
Family	chr. The error distribution and link function to be used in the model. Available options include "linear" and "gaussian" for continuous outcome variables, and "binomial" as well as "poisson" options for binary and count outcome variables.
Iter	num. The number of iteration times. Default is 500. To get a more stable result, a minimum iteration of 1,000 is recommended. To obtain more digits of P value of parameter estimation, a minimum iteration of 5,000 is suggested.

## Details

RedX function provides two alternative methods for exposure dimension reduction, including sum method as well as adaptive elastic net method via gcdnet package. By default, all exposures will be included for dimension reduction. Afterwards, mediation models will be built between given mediators as well as shrinkaged exposure variables.

## Value

A list containing three elements where the exposure dimension reduction variables as well as their mediation modelling results with mediators are stored. That list include:

1. "MedtRedX\_ERSall": a dataframe containing the exposure dimension reduction result where all exposures are considered as one group (ERS\_All).
2. "MedtRedX\_ERSlist": a dataframe containing the exposure dimension reduction results where exposures are shrinkaged in their own subgroups.
3. "MedtRedX\_Stats": a dataframe containing the mediation modelling results where the shrinkaged exposure variables were paired with each mediator provided.

## Author(s)

Mengyuan Ren, Bin Wang(corresponding author)

## Examples

```
res <- InitMedt()
res1 <- LoadMedt(PID = res$PID, UseExample = "example#1", DataPath = NULL,
VocaPath = NULL)
res2 <- XMlists(PID = res$PID)
res3 <- RedX(PID=res$PID, VarsY = "Y1",
VarsC = "default", VarsM = "default", Method = "mean", Folds = 10,
Family = "linear", Iter = 500)
res4 <- RedX(PID=res$PID, VarsY = "Y1",
VarsC = "C1", VarsM = "M1,M2,M3", Method = "mean", Folds = 10,
Family = "linear",Iter = 500)
```

---

RedXM

---

*Exposure and mediator dimension reduction*


---

## Description

Implement exposure and mediator dimension reduction. It should be noted that the exposure dimension reduction result has been built by RedX function prior to using it.

## Usage

```
RedXM(PID, OutPath, VarsY, Family, ...)
```

## Arguments

PID	chr. Program ID. It must be the same with the PID generated by InitMedt.
OutPath	chr. Output file directory, e.g. "D:/output". If "default", the current working directory will be set. It should be noted that the slash symbol is "/", not "\".
VarsY	chr. The outcome variable. Either continuous, binary or count type is permitted.
VarsC	chr. Covariates included in mediation modelling. When "default" is specified, all covariates in the data will be used. It should be noted that there is fixed format for the characters separated with comma and without space, e.g., "C1,C2".
Method	chr. Dimension reduction method. Available options include "mean" and "pdm1"(default). "mean" option is recommended when outcome variable is a binary variable because in some situations error might occur in "pdm1" settings for binary outcome.
Family	chr. The error distribution and link function to be used in the model. Available options include "linear" and "gaussian" for continuous outcome variables, and "binomial" as well as "poisson" options for binary and count outcome variables.
Iter	num. The number of iteration times. Default is 500. To get a more stable result, a minimum iteration of 1,000 is recommended. To obtain more digits of P value of parameter estimation, a minimum iteration of 5,000 is suggested.

## Details

RedXM function provides two alternative methods for mediator dimension reduction, including sum method as well as pdm1 method via PDM package. By default, all mediators will be included for dimension reduction. Afterwards, mediation models will be built between shrinkaged exposure variables as well as shrinkaged mediator variables. Prior to using RedXM, make sure that RedX function has been executed to obtain shrinkaged exposure variables.

## Value

A list containing two elements where the mediator dimension reduction modelling results with shrinkaged exposures are stored. That list include:

1. "MedtRedXM\_all": a dataframe containing the mediator dimension reduction result where all mediators are considered as one group and that shrinkaged mediator is paired and modelled with shrinkaged exposures.
2. "MedtRedXM\_list": a dataframe containing the mediator dimension reduction result where mediators are shrinkaged in their own subgroups, and these shrinkaged mediators are paired and modelled with shrinkaged exposures.

## Author(s)

Mengyuan Ren, Bin Wang(corresponding author)

## Examples

```
res <- InitMedt()
res1 <- LoadMedt(PID = res$PID, UseExample = "example#1", DataPath = NULL,
VocaPath = NULL)
res2 <- XMlists(PID = res$PID)
res3 <- RedX(PID=res$PID, VarsY = "Y1",
VarsC = "default", VarsM = "default", Method = "mean", Folds = 10,
Family = "linear", Iter = 500)
res4 <- RedXM(PID=res$PID, VarsY = "Y1",
VarsC = "default", Method = "mean", Family = "linear", Iter = 500)
res5 <- RedXM(PID=res$PID, VarsY = "Y1",
VarsC = "C1", Method = "mean", Family = "linear", Iter = 500)
```

---

VizMedtPair

Visualize pairwise mediation modelling result

---

## Description

Visualize the pairwise mediation result. It should be noted that the pairwise mediation modelling result has been built by Pairwise function prior to using it.

## Usage

```
VizMedtPair(PID, OutPath, ...)
```

## Arguments

PID	chr. Program ID. It must be the same with the PID generated by InitMedt.
OutPath	chr. Output file directory, e.g. "D:/output". If "default", the current working directory will be set. It should be noted that the slash symbol is "/", not "\".
Brightness	chr. Visualization brightness. Available options include "light" and "dark".
Palette	chr. Visualization palette. Available options include "default1", "default2" and "Journal". The "Journal" option provides several journal preference styles including cell, nature, science, lancet, nejm, and jama.

## Details

VizMedtPair draws a visualized display for pairwise modelling results. Prior to using VizMedtPair, make sure that the users have built mediation models by Pairwise function.

## Value

A list containing two elements where the visualized pairwise modelling plot as well as the organized plotting data are stored. The elements of that list include:

1. "plotdata": a dataframe containing the organized plotting data extracted from #' pairwise mediation modelling result.
2. "plot": a visualized plot for pairwise mediation result.

## Author(s)

Mengyuan Ren, Bin Wang(corresponding author)

## Examples

```
res <- InitMedt()
res1 <- LoadMedt(PID = res$PID, UseExample = "example#1", DataPath = NULL,
VocaPath = NULL)
res2 <- XMLists(PID = res$PID)
res3 <- PairWise(PID=res$PID, VarsY = "Y1",
VarsX = "default", VarsM = "default", VarsC = "default", Family = "linear",
Iter = 500)
res4 <- VizMedtPair(PID=res$PID, Brightness = "Bright",
Palette = "default1")
```

VizRedXM

*Visualize RedXM mediation modelling result***Description**

Visualize the RedXM mediation result. It should be noted that the RedXM mediation modelling result has been built by RedXM function prior to using it.

**Usage**

```
VizRedXM(PID, OutPath, ...)
```

**Arguments**

PID	chr. Program ID. It must be the same with the PID generated by InitMedt.
OutPath	chr. Output file directory, e.g. "D:/output". If "default", the current working directory will be set. It should be noted that the slash symbol is "/", not "\".
Brightness	chr. Visualization brightness. Available options include "Light" and "Dark".
Palette	chr. Visualization palette. Available options include "default1", "default2" and "Journal". The "Journal" option provides several journal preference styles including cell, nature, science, lancet, nejm, and jama.

**Details**

VizRedXM draws a visualized display for RedXM results. Prior to using VizMedtPair, make sure that the users have built mediation models by RedXM function.

**Value**

A list containing two elements where the visualized exposure and mediator dimension reduction plot as well as the organized plotting data are stored. The elements of that list include:

1. "MedtRedXM\_plotadta": a dataframe containing the organized plotting data extracted from exposure and mediator dimension reduction result.
2. "MedtRedXM\_plot": a visualized plot for exposure and mediator dimension reduction result.

**Author(s)**

Mengyuan Ren, Bin Wang(corresponding author)

**Examples**

```
res <- InitMedt()
res1 <- LoadMedt(PID = res$PID, UseExample = "example#1", DataPath = NULL,
VocaPath = NULL)
res2 <- XMlists(PID = res$PID)
res3 <- RedX(PID=res$PID, VarsY = "Y1",
```

```
VarsC = "default", VarsM = "default", Method = "mean", Folds = 10,
Family = "linear", Iter = 500)
res4 <- RedXM(PID=res$PID, VarsY = "Y1",
VarsC = "default", Method = "mean", Family = "linear", Iter = 500)
res5 <- VizRedXM(PID=res$PID, Brightness = "bright",
Palette = "nature")
```

---

XMLists

---

*Divide exposures and mediators into different groups*


---

**Description**

Divide exposures and mediators into different groups according to the information specified in vocabulary file.

**Usage**

```
XMLists(PID, OutPath)
```

**Arguments**

PID	chr. Program ID. It must be the same with the PID generated by InitMedt.
OutPath	chr. Output file directory, e.g. "D:/output". If "default", the current working directory will be set. It should be noted that the slash symbol is "/", not "\".

**Details**

XMLists divides all exposures and mediators into different groups. Therefore, the group information (i.e., the "Subgroup" variable) in vocabulary file is essential for XMLists function. Before using XMList, the users must provide the information in advance and upload it by LoadMedt function.

**Value**

A list containing two lists where exposure and mediator variables were respectively categorized into subgroups in the form of dataframe. The elements of that list include:

1. "ExpoList": a list containing several dataframes that represent various exposure subgroups.
2. "MediList": a list containing several dataframes that represent various mediator subgroups.

**Author(s)**

Mengyuan Ren, Bin Wang (corresponding author)

**Examples**

```
res <- InitMedt()
res1 <- LoadMedt(PID = res$PID, UseExample = "example#1", DataPath = NULL,
VocaPath = NULL)
res2 <- XMLists(PID = res$PID)
```

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