

# Package ‘regmed’

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**Type** Package

**Title** Regularized Mediation Analysis

**Version** 1.1.0

**Date** 2020-06-05

**Description** Mediation analysis for multiple mediators by penalized structural equation models using sparse group lasso. The penalty considers the natural groupings of parameters that determine mediation, as well as encourages sparseness of the model parameters.

**License** GPL (>= 2)

**Depends** R (>= 3.6.0), methods, graphics, glasso

**Imports** knitr, Rcpp, RcppArmadillo

**Suggests** lavaan

**LinkingTo** Rcpp, RcppArmadillo

**NeedsCompilation** yes

**VignetteBuilder** knitr

**URL** <https://cran.r-project.org/package=regmed>

**Author** Jason Sinnwell [aut, cre] (<<https://orcid.org/0000-0003-1964-5522>>),  
Daniel Schaid [aut] (<<https://orcid.org/0000-0003-1457-6433>>),  
Gregory Jenkins [ctb] (<<https://orcid.org/0000-0001-6408-6227>>)

**Maintainer** Jason Sinnwell <[sinnwell.jason@mayo.edu](mailto:sinnwell.jason@mayo.edu)>

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regmed-package	<i>Regularized Mediation Analysis</i>
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## Description

Mediation analysis for multiple mediators by penalized structural equation models using sparse group lasso. The penalty considers the natural groupings of parameters that determine mediation, as well as encourages sparseness of the model parameters.

## Details

The DESCRIPTION file:

```

Package:      regmed
Type:         Package
Title:        Regularized Mediation Analysis
Version:      1.1.0
Date:         2020-06-05
Authors@R:    c( person("Jason", "Sinnwell", email = "sinnwell.jason@mayo.edu", comment=c(ORCID="0000-0003-1964-5522"), Daniel Schaid [aut] (<https://orcid.org/0000-0003-1964-5522>)), Jason Sinnwell [aut, cre] (<https://orcid.org/0000-0003-1964-5522>), Daniel Schaid [aut] (<https://orcid.org/0000-0003-1964-5522>))
Description:  Mediation analysis for multiple mediators by penalized structural equation models using sparse group lasso
License:      GPL (>= 2)
Depends:      R (>= 3.6.0), methods, graphics, glasso
Imports:      knitr, Rcpp, RcppArmadillo
Suggests:     lavaan
LinkingTo:    Rcpp, RcppArmadillo
NeedsCompilation: yes
VignetteBuilder: knitr
URL:          https://cran.r-project.org/package=regmed
Author:       Jason Sinnwell [aut, cre] (<https://orcid.org/0000-0003-1964-5522>), Daniel Schaid [aut] (<https://orcid.org/0000-0003-1964-5522>)
Maintainer:   Jason Sinnwell <sinnwell.jason@mayo.edu>

```

Index of help topics:

```

get.best      Find best fitting regmed model from regmed.grid
              object.
getFit.regmed.grid Retrieve regmed object from regmed.grid object
lavaan.model  Create a lavaan model
plot.regmed   Plot a regmed object
plot.regmed.grid Plots for regmed.grid object.

```

regmed-package	Regularized Mediation Analysis
regmed.fit	Regularized Mediation model for a specified lambda penalty value.
regmed.grid	Regularized mediation models over a vector grid of lambda penalty values.
regmed_example	Example dataset for regmed package
summary.regmed	Summary of regmed object
trim.best	Trim and refit best model chosen from grid

Further information is available in the following vignettes:

regmed\_demo Regularized Mediation Example (source, pdf)

### Author(s)

NA

Maintainer: NA

### References

Schaid, DJ, Sinnwell JP. (2020) Penalized Models for Analysis of Multiple Mediators. To appear in Genetic Epidemiology

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get.best *Find best fitting regmed model from regmed.grid object.*

---

### Description

Find best fitting regmed model from regmed.grid object using minimum BIC to select model.

### Usage

```
get.best(fit.grid)
```

### Arguments

fit.grid a regmed.grid object

### Value

fit best fit regmed object based on minimum BIC  
 grid row out of grid.data of regmed.grid object corresponding to best fit

**Author(s)**

Dan Schaid, Greg Jenkins, Jason Sinnwell

**References**

Schaid, DJ, Sinnwell JP. (2020) Penalized Models for Analysis of Multiple Mediators. To appear in Genetic Epidemiology

**See Also**

[regmed.grid](#)

---

`getFit.regmed.grid`      *Retrieve regmed object from regmed.grid object*

---

**Description**

Retrieve regmed object from regmed.grid object using a selected lambda value. If no lambda value is provided, the best fit (based on minimum BIC) is returned.

**Usage**

```
getFit.regmed.grid(obj, lambda)
```

**Arguments**

<code>obj</code>	regmed.grid object
<code>lambda</code>	lambda value used to select regmed object from regmed.grid object (lambda must be a value used in obj). If left NULL, returned value will be based on minimum BIC.

**Value**

regmed object

---

lavaan.model	<i>Create a lavaan model</i>
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---

**Description**

Create a lavaan model for input to `lavan::sem()`

**Usage**

```
lavaan.model(y.name, x.name, med.name, medcov)
```

**Arguments**

<code>y.name</code>	character string of name of y variable
<code>x.name</code>	character string of name of x variable
<code>med.name</code>	vector of character strings of names for mediators
<code>medcov</code>	matrix of mediation covariances (square dimension to correspond with <code>med.name</code> ). This matrix is fixed in the sem model, and typically from a <code>regmed</code> object

**Value**

a character string that describes the mediation model

**Author(s)**

Dan Schaid, Greg Jenkins, Jason Sinnwell

**Examples**

```
## NOT RUN:  
## See vignette: regmed_demo
```

---

plot.regmed	<i>Plot a regmed object</i>
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**Description**

Plot `regmed` object with arrows from exposure (x) to mediators, and from mediators to outcome (y). Mediators are plotted from top to bottom according to the size of their effect ( $\text{size} = \alpha * \beta$ )

**Usage**

```
## S3 method for class 'regmed'  
plot(x, cex=.9, lwd=1.5, lty=1, ...)
```

**Arguments**

x	regmed object, returned from <code>regmed.fit()</code>
cex	character size for labels in the diagram
lwd	line width for arrows in the diagram
lty	line type for arrows in the diagram
...	optional arguments for plot method

**Details**

Arrows are colored red when corresponding alpha/beta is positive, and blue when corresponding alpha/beta is negative. Same for delta, direct effect.

**Value**

nothing is returned

**Author(s)**

Daniel Schaid

**See Also**

[regmed.fit](#) arrows

**Examples**

```
data(regmed_example)

y <- regmed_example$y
x <- regmed_example$x
med <- regmed_example[, -c(1,2)]
fit.grid <- regmed.grid(x, med, y, lambda.vec = c(seq(from=1, to=0, by = -.1)), frac.lasso=.8)

fit.trim <- trim.best(fit.grid)
which.med <- colnames(med)
med.selected <- med[, which.med]

fit.regmed <- regmed.fit(x, med.selected, y, lambda = 0.2, frac.lasso=.8)
plot(fit.regmed)
```

---

plot.regmed.grid      *Plots for regmed.grid object.*

---

### Description

Creates 2 plots: (1) BIC vs. lambda, and (2) Coefficients Alpha and Beta of mediator vs. lambda.

### Usage

```
## S3 method for class 'regmed.grid'  
plot(x, as.log=FALSE, ...)
```

### Arguments

x	regmed.grid object, returned by the regmed.grid() function
as.log	Logical; if TRUE, plot lambda on the log scale
...	optional arguments for plot method

### Value

nothing is returned

### Author(s)

Dan Schaid, Greg Jenkins, Jason Sinnwell

### See Also

[regmed.grid](#),

### Examples

```
data(regmed_example)  
y <- regmed_example$y  
x <- regmed_example$x  
med <- regmed_example[, -c(1,2)]  
fit.grid <- regmed.grid(x, med, y, lambda.vec= c(seq(from=1, to=0, by = -.1)), frac.lasso=.8)  
plot(fit.grid)
```

regmed.fit

*Regularized Mediation model for a specified lambda penalty value.***Description**

Fit regularized mediation model for a specified lambda penalty value. Structural equation models for analysis of multiple mediators are extended by creating a sparse group lasso penalized model such that the penalty considers the natural groupings of the pair of parameters that determine mediation, as well as encourages sparseness of the model parameters. The model is  $x[\alpha] \rightarrow \text{mediator} \rightarrow [\beta] \text{outcome}$ , where alpha and beta are the parameters for the indirect effect of x on y, through the mediator. The model also allows a direct effect of x on y:  $x[\delta] \rightarrow y$ .

**Usage**

```
regmed.fit(x, mediator, y, lambda, frac.lasso, x.std=TRUE, med.std=TRUE,
max.outer=5000, max.inner=100, step.multiplier = 0.5, wt.delta = .5, print.iter=FALSE)
```

**Arguments**

x	vector representing "exposure" variable (sometimes called instrumental variable)
mediator	matrix of mediators, rows are observations, columns are different mediators
y	vector representing outcome
lambda	lambda penalty parameter
frac.lasso	fraction of penalty (lambda) that is allocated to L1 penalty (lasso). The remaining fraction, (1-frac.lasso) is allocated to group-lasso penalty, where the group is the pair of parameters alpha and beta that determine mediation ( $x [\alpha] \rightarrow \text{mediator} \rightarrow [\beta] y$ ).
x.std	logical (TRUE/FALSE) whether to standardize x by dividing by standard deviation of x. Note that x will be centered on its mean.
med.std	logical (TRUE/FALSE) whether to standardize mediators by dividing each mediator by its standard deviation. Note that mediators will be centered on their means.
max.outer	maximum number of outer loop iterations. The outer loop cycles over several inner loops.
max.inner	maximum number of iterations for each inner loop. There is an inner loop for each pair of alpha-beta parameters for each mediator, an inner loop for direct effect (delta), and inner loops for residual variances for x and for y.
step.multiplier	a value between 0 and 1 for backtracking, to shrink step size. Value of 0.5 is typical default.
wt.delta	a weight $\geq 0$ for how much weight should be given to shrinking delta parameter, by penalty $\lambda * wt.\delta$ .
print.iter	print iteration history during fitting routine

**Value**

regmed object, with S3 methods available: plot, print, summary

**Author(s)**

Dan Schaid, Greg Jenkins, Jason Sinnwell

**References**

Schaid, DJ, Sinnwell JP. (2020) Penalized Models for Analysis of Multiple Mediators. To appear in Genetic Epidemiology

**See Also**

[plot.regmed](#) [summary.regmed](#)

**Examples**

```
data(regmed_example)

y <- regmed_example$y
x <- regmed_example$x
med <- regmed_example[, -c(1,2)]
fit.grid <- regmed.grid(x, med, y, lambda.vec= c(seq(from=1, to=0, by = -.1)), frac.lasso=.8)
fit.trim <- trim.best(fit.grid)
which.med <- colnames(med)
med.selected <- med[, which.med]

fit.regmed <- regmed.fit(x, med.selected, y, lambda = 0.2, frac.lasso=.8)
summary(fit.regmed)
```

---

regmed.grid

*Regularized mediation models over a vector grid of lambda penalty values.*

---

**Description**

Fit regularized mediation models over a vector grid of lambda penalty values. Structural equation models for analysis of multiple mediators are extended by creating a sparse group lasso penalized model such that the penalty considers the natural groupings of the pair of parameters that determine mediation, as well as encourages sparseness of the model parameters. The model is  $x[\alpha] \rightarrow \text{mediator} \rightarrow [\beta]\text{outcome}$ , where alpha and beta are the parameters for the indirect effect of x on y, through the mediator. The model also allows a direct effect of x on y:  $x[\delta] \rightarrow y$ .

**Usage**

```
regmed.grid(x, mediator, y, lambda.vec, frac.lasso=0.8, max.outer=5000,
max.inner=100, x.std=TRUE, med.std=TRUE, step.multiplier = 0.5,
wt.delta = .5, print.iter=FALSE)
```

**Arguments**

x	vector representing "exposure" variable (sometimes called instrumental variable)
mediator	matrix of mediators, rows are observations, columns are different mediators
y	vector representing outcome
lambda.vec	vector of lambda penalty parameters
frac.lasso	fraction of penalty (lambda) that is allocated to L1 penalty (lasso). The remaining fraction, (1-frac.lasso) is allocated to group-lasso penalty, where the group is the pair of parameters alpha and beta that determine mediation ( $x \rightarrow [\alpha] \rightarrow \text{mediator} \rightarrow [\beta] \rightarrow y$ ).
max.outer	maximum number of outer loop iterations. The outer loop cycles over several inner loops.
max.inner	maximum number of iterations for each inner loop. There is an inner loop for each pair of alpha-beta parameters for each mediator, an inner loop for direct effect (delta), and inner loops for residual variances for x and for y.
x.std	logical (TRUE/FALSE) whether to standardize x by dividing by standard deviation of x. Note that x will be centered on its mean.
med.std	logical (TRUE/FALSE) whether to standardize mediators by dividing each mediator by its standard deviation. Note that mediators will be centered on their means.
step.multiplier	a value between 0 and 1 for backtracking, to shrink step size. Value of 0.5 is typical default.
wt.delta	a weight $\geq 0$ for how much weight should be given to shrinking delta parameter, by penalty $\lambda * \text{wt.delta}$ .
print.iter	print iteration history during fitting routine

**Details**

Although outcome y is not required to be scaled by its standard deviation, it can be beneficial to scale y. This helps with setting range of lambda penalty parameters, because when all x, y, and mediators are scaled, it is reasonable to consider lambda values within the range of 0 to 1. See reference for details of algorithm.

**Value**

regmed.grid object

**Author(s)**

Dan Schaid, Greg Jenkins, Jason Sinnwell

**References**

Schaid, DJ, Sinnwell JP. (2020) Penalized Models for Analysis of Multiple Mediators. To appear in Genetic Epidemiology

**See Also**

[plot.regmed.grid](#) [regmed.fit](#)

**Examples**

```
data(regmed_example)

y <- regmed_example$y
x <- regmed_example$x
med <- regmed_example[, -c(1,2)]
fit.grid <- regmed.grid(x, med, y, lambda.vec= c(seq(from=1, to=0, by = -.1)), frac.lasso=.8)
fit.grid
```

---

regmed\_example

*Example dataset for regmed package*

---

**Description**

Example methylation Dataset from public data source with 85 observations, and narrowed down to 6 variables for the example.

**Usage**

```
data("regmed_example")
```

**Format**

A data frame with 85 observations on the following 6 variables.

x a numeric vector for exposure

y a numeric vector for stress response

med.cg01644731 a numeric vector for methylation as a mediator

med.cg06890779 a numeric vector for methylation as a mediator

med.cg00000029 a numeric vector for methylation as a mediator

med.cg00000108 a numeric vector, for methylation as a mediator

**Source**

E-GEOD-77445 - Genome-wide DNA methylation levels.

---

summary.regmed

*Summary of regmed object*


---

### Description

Summarizes alpha and beta coefficients of mediation effect, and delta for direct effect, in a regularized mediation model (regmed object).

### Usage

```
## S3 method for class 'regmed'
summary(object, ...)
```

### Arguments

object            regmed object  
 ...              optional arguments for summary method

### Details

Prints summary of model fit. Alpha and beta represent the indirect mediation effects:  $x[\text{alpha}] \rightarrow \text{mediator} \rightarrow [\text{beta}]\text{outcome}$ . Delta represents the direct effect:  $x[\text{delta}] \rightarrow y$ .  $\text{Var}(x)$  and  $\text{Var}(y)$  represent the residual variances. The sum of  $\text{alpha} \cdot \text{beta}$  represents the total mediation effect.

### Value

invisible, data.frame for alpha/beta pairs in fitted object

### Author(s)

Dan Schaid, Greg Jenkins, Jason Sinnwell

---

trim.best

*Trim and refit best model chosen from grid*


---

### Description

Get the best fitting model (based on minimum BIC) from grid of models, trim off mediators with small effects ( $\text{alpha} \cdot \text{beta} < \text{mediator.epsilon}$ ), then refit with specified lambda penalty, keeping all other parameters fixed at values specified when grid object was created.

### Usage

```
trim.best(obj, lambda = 0.0, mediator.epsilon = 1e-04)
```

**Arguments**

obj                    regmed.grid object created by regmed.grid  
lambda                lambda penalty parameter  
mediator.epsilon  
                      tolerance to remove mediator if  $\lambda\beta < \text{mediator.epsilon}$

**Value**

An object of regmed class

**Author(s)**

Dan Schaid, Greg Jenkins, Jason Sinnwell

**See Also**

[regmed.grid](#)

**Examples**

```
data(regmed_example)

y <- regmed_example$y
x <- regmed_example$x
med <- regmed_example[, -c(1,2)]
fit.grid <- regmed.grid(x, med, y, lambda.vec= c(seq(from=1, to=0, by = -.1)), frac.lasso=.8)
fit.trim <- trim.best(fit.grid)
data(regmed_example)

y <- regmed_example$y
x <- regmed_example$x
med <- regmed_example[, -c(1,2)]
fit.grid <- regmed.grid(x, med, y, lambda.vec= c(seq(from=1, to=0, by = -.1)), frac.lasso=.8)
fit.trim <- trim.best(fit.grid)
summary(fit.trim)
```

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