

# Package: nlmr (via r-universe)

September 12, 2024

**Title** Non-linear Mendelian randomisation

**Version** 1.0.3

**Date** 04-01-2023

**Description** Non-linear Mendelian randomization analysis to investigate the shape of exposure-outcome relationships.

**License** GPL-3

**URL** <https://jrs95.github.io/nlmr/>, <https://github.com/jrs95/nlmr>

**BugReports** <https://github.com/jrs95/nlmr/issues>

**Depends** R (>= 3.4.0)

**Imports** ggplot2, matrixStats, metafor

**Encoding** UTF-8

**ByteCompile** true

**LazyData** true

**RoxygenNote** 7.2.3

**Repository** <https://mrcieu.r-universe.dev>

**RemoteUrl** <https://github.com/jrs95/nlmr>

**RemoteRef** HEAD

**RemoteSha** 5a638d056887d7683d350a53a679e0b7f5e1c07f

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fracpoly\_mr

*Fractional polynomial Mendelian randomization***Description**

fracpoly\_mr performs a Mendelian randomization (MR) analysis by fitting fractional polynomial models to localised average causal effects using meta-regression.

**Usage**

```
fracpoly_mr(
  y,
  x,
  g,
  covar = NULL,
  family = "gaussian",
  q = 10,
  xpos = "mean",
  method = "FE",
  d = 1,
  pd = 0.05,
  ci = "model_se",
  nboot = 100,
  fig = FALSE,
  ref = mean(x),
  pref_x = "x",
  pref_x_ref = "x",
  pref_y = "y",
  ci_type = "overall",
  ci_quantiles = 10,
  breaks = NULL
)
```

**Arguments**

y	vector of outcome values
x	vector of exposure values
g	the instrumental variable
covar	data.frame of covariates
family	a description of the error distribution and link function to be used in the model and is a character string naming either the gaussian (i.e. "gaussian" for continuous data) or binomial (i.e. "binomial" for binary data) family function (default: "gaussian")
q	the number of quantiles the exposure distribution is to be split into within which a causal effect will be fitted, known as localised average causal effects (LACE) (default: 10)

xpos	the position used to relate x to the localised average causal effect, this can either be the mean of the x-values within each quantile or a percentile (e.g. 0.5 corresponds to the median value) (default: "mean")
method	meta-regression method parsed to the metafor package, e.g. the fixed-effects model (default: "FE")
d	fractional polynomial degree, the options are: 1, 2, or "both" (default: 1)
pd	p-value cut-off for choosing the best-fitting fractional polynomial of degree 2 over the best-fitting fractional polynomial degree 1, used only if d = "both" (default: 0.05)
ci	the type of 95% confidence interval, there are three options: (i) using the model standard errors ("model_se"), (ii) using bootstrap standard errors ("bootstrap_se"), and (iii) using bootstrap percentile confidence intervals ("bootstrap_per") (default: "model_se")
nboot	the number of bootstrap replications (default: 100)
fig	a logical statement as to whether the user wants the results displayed in a figure (default: FALSE)
ref	the reference point for the figure, this is the value of the function that represents the expected difference in the outcome compared with this reference value when the exposure is set to different values (default: mean(x))
pref_x	the prefix/label for the x-axis (default: "x")
pref_x_ref	the prefix for the reference value displayed on the y-axis (default: "x")
pref_y	the prefix/label for the y-axis (default: "y")
ci_type	the type of confidence interval to be displayed on the graph, where confidence intervals are either presented as bands across the range of x (option: "overall") or as error bars at the mean in each quantile of x (option: "quantile") (default:)
ci_quantiles	the number of quantiles at which confidence intervals are to be displayed (default: 10)
breaks	breaks on the y-axis of the figure

### Value

fracpoly\_mr returns a list of non-linear MR results from the fractional polynomial MR approach:

n	number of individuals
model	the model specifications: number of quantiles (q), position used to relate x to the LACE in each quantiles (xpos), type of confidence interval constructed (ci), number of bootstrap replications performed (nboot)
powers	the powers of the chosen polynomial
coefficients	the regression estimates: regression coefficients (beta), standard errors of regression coefficients (se), lower 95% confidence interval (lci), upper 95% confidence interval (uci), p-value (pval)
lace	the localised average causal effect estimate in each quantile: regression coefficients (beta), standard errors of regression coefficients (se), lower 95% confidence interval (lci), upper 95% confidence interval (uci), p-value (pval)

xcoef	the association between the instrument and the exposure in each quantile: regression coefficients (beta), standard errors of regression coefficients (se)
p_tests	the p-value of the non-linearity tests: p-value of the test between the fractional polynomial degrees (fp_d1_d2), p-value from the fractional polynomial non-linearity test (fp), p-value from the quadratic test (quad), p-value from the Cochran Q test (Q)
p_heterogeneity	the p-value of heterogeneity: p-value of the Cochran Q heterogeneity test (Q), p-value from the trend test (trend).

### Author(s)

James Staley [jrstaley95@gmail.com](mailto:jrstaley95@gmail.com)

### Examples

```
# IV (g), exposure (x) & outcome (y)
epsx <- rexp(10000)
u <- runif(10000, 0, 1)
g <- rbinom(10000, 2, 0.3)
epsy <- rnorm(10000)
ag <- 0.25
x <- 1 + ag * g + u + epsx
y <- 0.15 * x^2 + 0.8 * u + epsy

# Covariates (covar)
c1 <- rnorm(10000)
c2 <- rnorm(10000)
c3 <- rbinom(10000, 2, 0.33)
covar <- data.frame(c1 = c1, c2 = c2, c3 = as.factor(c3))

# Analyses
fp <- fracpoly_mr(
  y = y, x = x, g = g, covar = covar,
  family = "gaussian", q = 10, d = 1, ci = "model_se",
  fig = TRUE
)
summary(fp)
plm <- piecewise_mr(
  y = y, x = x, g = g, covar = covar,
  family = "gaussian", q = 10, nboot = 100,
  fig = TRUE
)
summary(plm)
```

---

lace *Localised average causal effects*

---

## Description

lace computes the localised average causal effect for each quantile.

## Usage

```
lace(
  y,
  x,
  g,
  covar = NULL,
  q,
  x0q,
  xc_sub = TRUE,
  family = "gaussian",
  xpos = "mean"
)
```

## Arguments

y	vector of outcome values
x	vector of exposure values
g	the instrumental variable
covar	data.frame of covariates
q	the number of quantiles the exposure distribution is to be split into within which a causal effect will be fitted, known as localised average causal effects (LACE) (default: 10)
x0q	quantiles of x0 (the IV-free exposure)
xc_sub	compute the association between the exposure and the instrument in each quantile of x0
family	a description of the error distribution and link function to be used in the model and is a character string naming either the gaussian (i.e. "gaussian" for continuous data) or binomial (i.e. "binomial" for binary data) family function (default: "gaussian")
xpos	the position used to relate x to the localised average causal effect, this can either be the mean of the x-values within each quantile or a percentile (e.g. 0.5 corresponds to the median value) (default: "mean")

**Value**

lace returns a data.frame of the LACE for quantile:

coef	the LACE in each quantile
coef_se	the standard error of the LACE in each quantile
xmean	the mean of the exposure in each quantile
xcoef_sub	the association between the exposure and the instrument in each quantile
xcoef_sub_se	the standard error of the association between the exposure and the instrument in each quantile

**Author(s)**

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---

piecewise\_mr

*Piecewise linear Mendelian randomization*

---

**Description**

piecewise\_mr performs a Mendelian randomization (MR) analysis by fitting a piecewise linear function to localised average causal effects.

**Usage**

```
piecewise_mr(
  y,
  x,
  g,
  covar = NULL,
  family = "gaussian",
  q = 10,
  xpos = "mean",
  nboot = 100,
  fig = TRUE,
  ref = mean(x),
  pref_x = "x",
  pref_x_ref = "x",
  pref_y = "y",
  ci_quantiles = 10,
  breaks = NULL
)
```

**Arguments**

y	vector of outcome values
x	vector of exposure values
g	the instrumental variable
covar	data.frame of covariates
family	a description of the error distribution and link function to be used in the model and is a character string naming either the gaussian (i.e. "gaussian" for continuous data) or binomial (i.e. "binomial" for binary data) family function (default: "gaussian")
q	the number of quantiles the exposure distribution is to be split into within which a causal effect will be fitted, known as localised average causal effects (LACE) (default: 10)
nboot	the number of bootstrap replications (default: 100)
fig	a logical statement as to whether the user wants the results displayed in a figure (default: TRUE)
ref	the reference point for the figure, this is the value of the function that represents the expected difference in the outcome compared with this reference value when the exposure is set to different values (default: mean(x))
pref_x	the prefix/label for the x-axis (default: "x")
pref_x_ref	the prefix for the reference value displayed on the y-axis (default: "x")
pref_y	the prefix/label for the y-axis (default: "y")
ci_quantiles	the number of quantiles at which confidence intervals are to be displayed (default: 10)
breaks	breaks on the y-axis of the figure

**Value**

piecewise\_mr returns a list of non-linear MR results from the piecewise linear function MR approach:

n	number of individuals
model	the model specifications: number of quantiles (q), number of bootstrap replications performed (nboot)
coefficients	the regression estimates: regression coefficients (beta), standard errors of regression coefficients (se), lower 95% confidence interval (lci), upper 95% confidence interval (uci), p-value (pval)
lace	the localised average causal effect estimate in each quantile: regression coefficients (beta), standard errors of regression coefficients (se), lower 95% confidence interval (lci), upper 95% confidence interval (uci), p-value (pval)
xcoef	the association between the instrument and the exposure in each quantile: regression coefficients (beta), standard errors of regression coefficients (se)
p_tests	the p-value of the non-linearity tests: p-value from the quadratic test (quad), p-value from the Cochran Q test (Q)

p\_heterogeneity

the p-value of heterogeneity: p-value of the Cochran Q heterogeneity test (Q),  
p-value from the trend test (trend).

### Author(s)

James Staley [jrstaley95@gmail.com](mailto:jrstaley95@gmail.com)

### Examples

```
# IV (g), exposure (x) & outcome (y)
epsx <- rexp(10000)
u <- runif(10000, 0, 1)
g <- rbinom(10000, 2, 0.3)
epsy <- rnorm(10000)
ag <- 0.25
x <- 1 + ag * g + u + epsx
y <- 0.15 * x^2 + 0.8 * u + epsy

# Covariates (covar)
c1 <- rnorm(10000)
c2 <- rnorm(10000)
c3 <- rbinom(10000, 2, 0.33)
covar <- data.frame(c1 = c1, c2 = c2, c3 = as.factor(c3))

# Analyses
fp <- fracpoly_mr(
  y = y, x = x, g = g, covar = covar,
  family = "gaussian", q = 10, d = 1, ci = "model_se",
  fig = TRUE
)
summary(fp)
plm <- piecewise_mr(
  y = y, x = x, g = g, covar = covar,
  family = "gaussian", q = 10, nboot = 100,
  fig = TRUE
)
summary(plm)
```

---

`print.fracpoly_mr`      *Print fracpoly\_mr*

---

### Description

print method for class "fracpoly\_mr".

### Usage

```
## S3 method for class 'fracpoly_mr'
print(x, ...)
```



**Arguments**

x                    an object of class "fracpoly\_mr"

**Author(s)**

James Staley [jrstaley95@gmail.com](mailto:jrstaley95@gmail.com)

---

*print.piecewise\_mr*      *Print piecewise\_mr*

---

**Description**

print method for class "piecewise\_mr".

**Usage**

```
## S3 method for class 'piecewise_mr'  
print(x, ...)
```

**Arguments**

x                    an object of class "piecewise\_mr"

**Author(s)**

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---

*print.summary.fracpoly\_mr*  
                          *Print summary of fracpoly\_mr*

---

**Description**

print.summary method for class "fracpoly\_mr".

**Usage**

```
## S3 method for class 'summary.fracpoly_mr'  
print(x, ...)
```

**Arguments**

x                    an object of class "fracpoly\_mr"

**Author(s)**

James Staley [jrstaley95@gmail.com](mailto:jrstaley95@gmail.com)

---

```
print.summary.piecewise_mr
    Print summary of piecewise_mr
```

---

**Description**

print.summary method for class "piecewise\_mr".

**Usage**

```
## S3 method for class 'summary.piecewise_mr'
print(x, ...)
```

**Arguments**

x                    an object of class "piecewise\_mr".

**Author(s)**

James Staley [jrstaley95@gmail.com](mailto:jrstaley95@gmail.com)

---

```
summary.fracpoly_mr    Summary of fracpoly_mr
```

---

**Description**

summary method for class "fracpoly\_mr".

**Usage**

```
## S3 method for class 'fracpoly_mr'
summary(x, ...)
```

**Arguments**

x                    an object of class "fracpoly\_mr"

**Author(s)**

James Staley [jrstaley95@gmail.com](mailto:jrstaley95@gmail.com)

---

summary.piecewise\_mr *Summary of piecewise\_mr*

---

### **Description**

summary method for class "piecewise\_mr".

### **Usage**

```
## S3 method for class 'piecewise_mr'  
summary(x, ...)
```

### **Arguments**

x                    an object of class "piecewise\_mr"

### **Author(s)**

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