

Package: RadialMR (via r-universe)

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Title RadialMR

Version 1.2.3

Description A package for implementing radial inverse variance weighted and MR-Egger methods.

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URL <https://github.com/WSpiller/RadialMR>,
<https://wspiller.github.io/RadialMR/>,
<https://mrcieu.r-universe.dev/RadialMR>

Depends R (>= 4.1.0)

Imports ggplot2, magrittr, plotly

Suggests MendelianRandomization, TwoSampleMR (>= 0.5.0)

Remotes MRCIEU/TwoSampleMR

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data_radial	<i>Two Sample Summary GWAS data published in Do et al (2014).</i>
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Description

A dataset containing summary GWAS data for 185 independent SNPs with respect to lipid fractions and coronary heart disease (CHD), previously published in Do et al (2013). Lipid fractions include low-density lipoprotein (LDL-C), high-density lipoprotein (HDL-C), and triglycerides, with association estimates obtained from the Global Lipids Genetics Consortium (GLGC) (Willer et al, 2013). Summary data for CHD was obtained from the CARDIoGRAM study (Schunkert et al, 2011). Association estimates were obtained by regressing each phenotype upon the genetic variant and additional adjusted covariates, with links to further information related to each study presented below.

Usage

data_radial

Format

A data frame with 185 rows and 21 variables. Specifically this includes the following information:

rsid The identification number for each variant
a1 The reference allele for each variant
a2 The other allele for each variant
chr The chromosome number in which each variant is located
pos The genomic position for the genetic variant relative to chromosome number
ldlcbeta The association estimate for the genetic variant obtained by regressing LDL-C upon the genetic variant
hdlcbeta The association estimate obtained by regressing HDL-C upon the genetic variant
tgbeta The association estimate obtained by regressing triglycerides upon the genetic variant
chdbeta The association estimate for CHD obtained by regressing CHD upon the genetic variant
ldlcp2 The p-value corresponding to association estimate ldlcbeta
hdlcp2 The p-value corresponding to association estimate hdlcbeta
tgp2 The p-value corresponding to association estimate tgbeta
chdp2 The p-value corresponding to association estimate chdbeta
ldlcz The z-score corresponding to association estimate ldlcbeta

ldlcse The standard error corresponding to association estimate ldlcbeta
hdlcz The z-score corresponding to association estimate hdlcbeta
hdlcse The standard error corresponding to association estimate hdlcbeta
tgz The z-score corresponding to association estimate tgbeta
tgse The standard error corresponding to association estimate tgbeta
chdz The z-score corresponding to association estimate chdbeta
chdse The standard error corresponding to association estimate chdbeta

Details

data_radial

Author(s)

Wes Spiller; Jack Bowden; Tom Palmer.

Source

- <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3904346/>
- <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3838666/>
- <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3119261/>

Examples

```
head(data_radial)
```

egger_radial

egger_radial

Description

Fits a radial MR-Egger model using first order, second order, or modified second order weights. Outliers are identified using a significance threshold specified by the user. The function returns an object of class "egger", containing regression estimates, a measure of total heterogeneity using Rucker's Q statistic, the individual contribution to overall heterogeneity of each variant, and a data frame for use in constructing the radial plot.

Usage

```
egger_radial(r_input, alpha, weights, summary)
```

Arguments

r_input	A formatted data frame using the <code>format_radial</code> function, or an object of class <code>MRInput</code> generated by <code>MendelianRandomization::mr_input</code> or a <code>data.frame</code> for a single exposure-outcome pair generated by <code>TwoSampleMR::harmonise_data</code> .
alpha	A value specifying the statistical significance threshold for identifying outliers (<code>0.05</code> specifies a p-value threshold of 0.05).
weights	A value specifying the inverse variance weights used to calculate the MR-Egger estimate and Rucker's Q statistic. By default modified second order weights are used, but one can choose to select first order (1), second order (2) or modified second order weights (3).
summary	A logical argument (TRUE or FALSE) indicating whether a summary of results and heterogeneity should be presented (default= TRUE).

Value

An object of class "egger" containing the following components:

`coef` A matrix giving the intercept and slope coefficient, corresponding standard errors, t-statistics, and (two-sided) p-values.

`qstatistic` Rucker's Q statistic for overall heterogeneity.

`df` Degrees of freedom. This is equal to the number of variants -2 when fitting the radial MR-Egger model.

`outliers` A data frame containing variants identified as outliers, with respective Q statistics, chi-squared tests and SNP identification.

`data` A data frame containing SNP IDs, inverse variance weights, the product of the inverse variance weight and ratio estimate for each variant, contribution to overall heterogeneity with corresponding p-value, and a factor indicator showing outlier status.

`confint` A vector giving lower and upper confidence limits for the radial MR-Egger effect estimate.

Author(s)

Wes Spiller; Jack Bowden; Tom Palmer.

References

Bowden, J., et al., Improving the visualization, interpretation and analysis of two-sample summary data Mendelian randomization via the Radial plot and Radial regression. *International Journal of Epidemiology*, 2018. 47(4): p. 1264-1278.

Examples

```
# Example using format_radial data
ldl.dat <- data_radial[data_radial[,10]<5e-8,]

ldl.fdat <- format_radial(ldl.dat[,6], ldl.dat[,9],
                        ldl.dat[,15], ldl.dat[,21],
```

```

                                ldl.dat[,1])

egger_radial(ldl.fdat, 0.05, 1, TRUE)

# Example using TwoSampleMR format data
## Not run:
if (require("TwoSampleMR", quietly = TRUE)) {
# Example with one exposure-outcome pair
bmi_exp_dat <- TwoSampleMR::extract_instruments(outcomes = 'ieu-a-2')
chd_out_dat <- TwoSampleMR::extract_outcome_data(
                                snps = bmi_exp_dat$SNP,
                                outcomes = 'ieu-a-7')
tsmrdat <- TwoSampleMR::harmonise_data(exposure_dat = bmi_exp_dat,
                                       outcome_dat = chd_out_dat)
egger_radial(r_input = tsmrdat, alpha = 0.05,
             weights = 1, summary = TRUE)
}

## End(Not run)

# Example using MendelianRandomization format data
if (require("MendelianRandomization", quietly = TRUE)) {
dat <- data_radial[data_radial[,10] < 5e-8,]
mrdat <- MendelianRandomization::mr_input(bx = dat$ldlcbeta,
                                          bxse = dat$ldlcse,
                                          by = dat$chdbeta,
                                          byse = dat$chdse,
                                          snps = dat$rsid)

egger_radial(r_input = mrdat, alpha = 0.05,
             weights = 1, summary = TRUE)
}

```

format_radial

format_radial

Description

A function which restructures summary GWAS data for downstream two-sample Mendelian randomization analyses. Where variant identification numbers are not provided, an index vector is generated corresponding to the ordering of variants provided.

Usage

```
format_radial(BXG, BYG, seBXG, seBYG, RSID)
```

Arguments

BXG A numeric vector of beta-coefficient values for genetic associations with the first variable (exposure).

BYG	A numeric vector of beta-coefficient values for genetic associations with the second variable (outcome).
seBXG	The standard errors corresponding to the beta-coefficients BXG.
seBYG	The standard errors corresponding to the beta-coefficients BYG.
RSID	A vector of names for genetic variants included in the analysis. If variant IDs are not provided (RSID = "NULL"), a vector of ID numbers will be generated.

Value

The function provides a data frame containing the following columns:

SNP	The identification number for each variant
beta.exposure	The association estimate for the genetic variant with respect to the exposure
beta.outcome	The association estimate for the genetic variant with respect to the outcome
se.exposure	The standard error for the variant-exposure association beta.exposure
se.outcome	The standard error for the variant-outcome association beta.outcome

Author(s)

Wes Spiller; Jack Bowden; Tom Palmer.

References

Bowden, J., et al., Improving the visualization, interpretation and analysis of two-sample summary data Mendelian randomization via the Radial plot and Radial regression. *International Journal of Epidemiology*, 2018. 47(4): p. 1264-1278.

Examples

```
ldl.dat <- data_radial[data_radial[,10]<5e-8,]
ldl.fdat <- format_radial(ldl.dat[,6], ldl.dat[,9],
                        ldl.dat[,15], ldl.dat[,21], ldl.dat[,1])
head(ldl.fdat)
class(ldl.fdat)
```

ivw_radial

ivw_radial

Description

Fits a radial inverse variance weighted (IVW) model using a range of weighting specifications. Outliers are determined with respect to their contribution to global heterogeneity, quantified by Cochran's Q-statistic, using a significance threshold specified by the user. The `ivw_radial` function returns an object of class "IVW", containing effect estimates, total estimated heterogeneity using Cochran's Q-statistic, the individual contribution to overall heterogeneity of each variant, and a data frame for used in the downstream plotting functions `plot_radial` and `plotly_radial`.

Usage

```
ivw_radial(r_input, alpha, weights, tol, summary)
```

Arguments

r_input	A formatted data frame using the <code>format_radial</code> function, or an object of class <code>MRInput</code> generated by <code>MendelianRandomization::mr_input</code> or a <code>data.frame</code> for a single exposure-outcome pair generated by <code>TwoSampleMR::harmonise_data</code> .
alpha	A value specifying the statistical significance threshold for identifying outliers (<code>0.05</code> specifies a p-value threshold of 0.05).
weights	A value specifying the inverse variance weights used to calculate IVW estimate and Cochran's Q statistic. By default modified second order weights are used, but one can choose to select first order (1), second order (2) or modified second order weights (3).
tol	A value indicating the tolerance threshold for performing the iterative IVW approach. The value represents the minimum difference between the coefficients of the previous and current iterations required for a further iteration to be performed (default= <code>0.0001</code>).
summary	A logical argument (TRUE or FALSE) indicating whether a summary of results and heterogeneity should be presented (default= TRUE).

Value

An object of class "IVW" containing the following components:

coef	The estimated coefficient, its standard error, t-statistic and corresponding (two-sided) p-value.
qstatistic	Cochran's Q statistic for overall heterogeneity.
df	Degrees of freedom. This is equal to the number of variants -1 when fitting the radial IVW model.
outliers	A data frame containing variants identified as outliers, with respective Q statistics, chi-squared tests and SNP identification.
data	A data frame containing SNP IDs, inverse variance weights, the product of the inverse variance weight and ratio estimate for each variant, contribution to overall heterogeneity with corresponding p-value, and a factor indicator showing outlier status.
confint	A vector giving lower and upper confidence limits for the radial IVW effect estimate.
it.coef	The estimated iterative coefficient, its standard error, t-statistic and corresponding (two-sided) p-value.
it.confint	A vector giving lower and upper confidence limits for the iterative radial IVW effect estimate.
fe.coef	The estimated fixed effect exact coefficient, its standard error, t-statistic and corresponding (two-sided) p-value.
fe.confint	A vector giving lower and upper confidence limits for the fixed effect exact radial IVW effect estimate.
re.coef	The estimated random effect exact coefficient, its standard error, t-statistic and corresponding (two-sided) p-value.

re.confint A vector giving lower and upper confidence limits for the random effect exact radial IVW effect estimate.

mf The mean F statistic for the set of genetic variants, indicative of instrument strength.

Author(s)

Wes Spiller; Jack Bowden; Tom Palmer.

References

Bowden, J., et al., Improving the visualization, interpretation and analysis of two-sample summary data Mendelian randomization via the Radial plot and Radial regression. *International Journal of Epidemiology*, 2018. 47(4): p. 1264-1278.

Examples

```
# Example using format_radial data
ldl.dat <- data_radial[data_radial[,10]<5e-8,]
ldl.fdat <- format_radial(ldl.dat[,6], ldl.dat[,9],
                        ldl.dat[,15], ldl.dat[,21], ldl.dat[,1])
ivw_radial(ldl.fdat, 0.05, 1, 0.0001, TRUE)

# Example using TwoSampleMR format data
## Not run:
if (require("TwoSampleMR", quietly = TRUE)) {
# Example with one exposure-outcome pair
bmi_exp_dat <- TwoSampleMR::extract_instruments(outcomes = 'ieu-a-2')
chd_out_dat <- TwoSampleMR::extract_outcome_data(
                snps = bmi_exp_dat$SNP,
                outcomes = 'ieu-a-7')
tsmrdat <- TwoSampleMR::harmonise_data(exposure_dat = bmi_exp_dat,
                                     outcome_dat = chd_out_dat)
ivw_radial(r_input = tsmrdat, alpha = 0.05,
           weights = 1, tol = 0.0001, summary = TRUE)
}

## End(Not run)

# Example using MendelianRandomization format data
if (require("MendelianRandomization", quietly = TRUE)) {
dat <- data_radial[data_radial[,10] < 5e-8,]
mrdat <- MendelianRandomization::mr_input(bx = dat$ldlcbeta,
                                         bxse = dat$ldlcse,
                                         by = dat$chdbeta,
                                         byse = dat$chdse,
                                         snps = dat$rsid)
ivw_radial(r_input = mrdat, alpha = 0.05,
           weights = 1, tol = 0.0001, summary = TRUE)
}
```

mrinput_to_rmr_format *Convert an object of class MRInput from the MendelianRandomization package to the RadialMR rmr_format class*

Description

Creates a data.frame with class rmr_format from an object of class MRInput generated by [MendelianRandomization::mr_i](#)

Usage

```
mrinput_to_rmr_format(dat)
```

Arguments

dat Object from [MendelianRandomization::mr_input](#).

Value

Object of class rmr_format, the RadialMR format

Examples

```
if (require("MendelianRandomization", quietly = TRUE)) {
  dat <- data_radial[data_radial[,10] < 5e-8,]
  dat <- MendelianRandomization::mr_input(bx = dat$ldlcbeta,
                                          bxse = dat$ldlcse,
                                          by = dat$chdbeta,
                                          byse = dat$chdse,
                                          snps = dat$rsid)

  dat <- mrinput_to_rmr_format(dat)
  head(dat)
  class(dat)
}
```

plot_radial *plot_radial*

Description

A function for producing radial IVW and MR-Egger plots either individually or simultaneously. The function allows for a variety of aesthetic and scaling options, utilising the output from the IVW_radial and egger_radial functions.

Usage

```
plot_radial(r_object, radial_scale, show_outliers, scale_match)
```

Arguments

r_object	An object of class "IVW" or "egger". For visualising both estimates simultaneously, both objects should be included as a vector c(A,B), where A and B denote the "IVW" and "egger" objects respectively.
radial_scale	Indicates whether to produce a plot including a full radial scale (TRUE), or a scatterplot showing only the effect estimates (FALSE).
show_outliers	Indicates whether to display only the set of variants identified as outliers (TRUE) or the complete set of variants (FALSE). Note that when (show_outliers=TRUE), non-outlying variants further from the origin than the furthest outlier will cause an error message that one or more points have been omitted. These are non-outlying variants beyond the scale. If no outliers are present, a plot will be produced using the full set of variants, with an accompanying message indicating the absence of outliers.
scale_match	Indicates whether x and y axes should have the same range (TRUE), or different ranges (FALSE) This improves the interpretation of the radial scale, and is set to FALSE when the radial scale is omitted from the plot.

Value

A ggplot object containing a radial plot of either the IVW, MR-Egger, or both estimates simultaneously.

Author(s)

Wes Spiller; Jack Bowden; Tom Palmer.

References

Bowden, J., et al., Improving the visualization, interpretation and analysis of two-sample summary data Mendelian randomization via the Radial plot and Radial regression. *International Journal of Epidemiology*, 2018. 47(4): p. 1264-1278.

Examples

```
ldl.dat <- data_radial[data_radial[,10]<5e-8,]
ldl.fdat <- format_radial(ldl.dat[,6], ldl.dat[,9],
                        ldl.dat[,15], ldl.dat[,21], ldl.dat[,1])
ivw.object <- ivw_radial(ldl.fdat, 0.05, 1, 0.0001, TRUE)
plot_radial(ivw.object)
egger.object <- egger_radial(ldl.fdat, 0.05, 1, TRUE)
plot_radial(egger.object)
```

plotly_radial	<i>plotly_radial</i>
---------------	----------------------

Description

A function for producing interactive radial IVW and MR-Egger plots individually. The function utilises the output from the `IVW_radial` and `egger_radial` functions.

Usage

```
plotly_radial(r_object, TEST)
```

Arguments

<code>r_object</code>	An object of class "IVW" or "egger".
<code>TEST</code>	Logical; indicating whether testing the function

Value

A plotly object containing a radial plot of either the IVW or MR-Egger estimates. Hovering the mouse over individual datapoints will highlight the corresponding SNP identification number for that observation.

Author(s)

Wes Spiller; Jack Bowden; Tom Palmer.

References

Bowden, J., et al., Improving the visualization, interpretation and analysis of two-sample summary data Mendelian randomization via the Radial plot and Radial regression. *International Journal of Epidemiology*, 2018. 47(4): p. 1264-1278.

Examples

```
ldl.dat <- data_radial[data_radial[,10]<5e-8,]  
ldl.fdat <- format_radial(ldl.dat[,6], ldl.dat[,9],  
                        ldl.dat[,15], ldl.dat[,21], ldl.dat[,1])  
ivw.object <- ivw_radial(ldl.fdat, 0.05, 1, 0.0001, TRUE)  
plotly_radial(ivw.object)
```

tsmr_to_rmr_format	<i>Convert a data.frame containing a single exposure - outcome pair generated by <code>TwoSampleMR::harmonise_data()</code> to the RadialMR <code>rmr_format</code> class</i>
--------------------	---

Description

Creates an object of RadialMR format, i.e. of class `rmr_format`, for a single exposure - outcome pair.

Usage

```
tsmr_to_rmr_format(dat)
```

Arguments

`dat` Output for a single exposure-outcome pair from [TwoSampleMR::harmonise_data](#).

Details

Only the rows where the column `mr_keep` are TRUE are kept.

Value

Object of class `rmr_format`, the RadialMR format

Examples

```
## Not run:
if (require("TwoSampleMR", quietly = TRUE)) {
  # Example with one exposure-outcome pair
  bmi_exp_dat <- TwoSampleMR::extract_instruments(outcomes = 'ieu-a-2')
  chd_out_dat <- TwoSampleMR::extract_outcome_data(
    snps = bmi_exp_dat$SNP,
    outcomes = 'ieu-a-7'
  )
  dat <- TwoSampleMR::harmonise_data(exposure_dat = bmi_exp_dat,
                                    outcome_dat = chd_out_dat)

  dat <- tsmr_to_rmr_format(dat)
  class(dat)
  head(dat)
}

## End(Not run)
```

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