Package ‘mr.raps’

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Type Package

Title Two Sample Mendelian Randomization using Robust Adjusted Profile Score

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License GPL-3

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R topics documented:

  mr.raps-package ............................................... 2
  bmi.bmi .......................................................... 2
  bmi.sbp .......................................................... 3
  mr.raps .......................................................... 3

Index 7
Description

Mendelian randomization is a method of identifying and estimating a confounded causal effect using genetic instrumental variables. This package implements methods for two-sample Mendelian randomization with summary statistics by using Robust Adjusted Profile Score (RAPS).

bmiNbmi

"Effect" of Body Mass Index (BMI) on Body Mass Index (BMI)

Description

Summary data obtained by combining three genome-wide association studies:

1. BMI-GIANT: BMI in the Genetic Investigation of ANthropometric Traits (GIANT) consortium (sample size: 339224).
2. BMI-UKBB-1: BMI in a half of the United Kingdom BioBank (UKBB) data (sample size: 234070)
3. SBP-UKBB-2: BMI in the other half of the UKBB data (sample size: 234070)

Usage

data(bmiNbmi)

Format

A data.frame.

Details

The BMI-GIANT dataset is used for SNP selection (column pval.selection). The BMI-UKBB-1 dataset estimates the SNPs' effects on BMI (columns beta.exposure and se.exposure) and the BMI-UKBB-2 dataset provides independent estimates of the same effects (columns beta.outcome and se.outcome).
**bmi.sbp**

**Effect of Body Mass Index (BMI) on Systolic Blood Pressure (SBP)**

**Description**

Summary data obtained by combining three genome-wide association studies:

1. BMI-FEM: BMI in females by the Genetic Investigation of ANthropometric Traits (GIANT) consortium (sample size: 171977).
2. BMI-MAL: BMI in males in the same study by the GIANT consortium (sample size: 152893)
3. SBP-UKBB: SBP using the United Kingdom BioBank (UKBB) data (sample size: 317754)

**Usage**

```r
data(bmi.sbp)
```

**Format**

A data.frame.

**Details**

The BMI-FEM dataset is used for SNP selection (column *pval.selection*). The BMI-MAL dataset estimates the SNPs’ effect on BMI and the SBP-UKBB dataset estimates the SNPs’ on SBP.

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**mr.raps**

**Main function**

**Description**

*mr.raps* is the main function.

- *mr.raps.all*: Quick analysis with all six methods
- *mr.raps.simple*: No overdispersion, l2 loss
- *mr.raps.overdispersed*: Overdispersion, l2 loss
- *mr.raps.simple.robust*: No overdispersion, robust loss
- *mr.raps.overdispersed.robust*: Overdispersed, robust loss
Usage

```r
mr.raps(b_exp, b_out, se_exp, se_out, over.dispersion = FALSE,
loss.function = c("l2", "huber", "tukey"), diagnosis = FALSE,
se.method = c("sandwich", "bootstrap"), k = switch(loss.function[1], l2 =
NULL, huber = 1.345, tukey = 4.685), B = 1000, suppress.warning = FALSE)
```

```r
mr.raps.all(b_exp, b_out, se_exp, se_out)
```

```r
mr.raps.simple(b_exp, b_out, se_exp, se_out, diagnosis = FALSE)
```

```r
mr.raps.overdispersed(b_exp, b_out, se_exp, se_out,
initialization = c("simple", "mode"), suppress.warning = FALSE,
diagnosis = FALSE, niter = 20, tol = .Machine$double.eps^0.5)
```

```r
mr.raps.simple.robust(b_exp, b_out, se_exp, se_out, loss.function = c("huber",
"tukey"), k = switch(loss.function[1], huber = 1.345, tukey = 4.685),
diagnosis = FALSE)
```

```r
mr.raps.overdispersed.robust(b_exp, b_out, se_exp, se_out,
loss.function = c("huber", "tukey"), k = switch(loss.function[1], huber =
1.345, tukey = 4.685), initialization = c("l2", "mode"),
suppress.warning = FALSE, diagnosis = FALSE, niter = 20,
tol = .Machine$double.eps^0.5)
```

Arguments

- `b_exp`: A vector of SNP effects on the exposure variable, usually obtained from a GWAS.
- `b_out`: A vector of SNP effects on the outcome variable, usually obtained from a GWAS.
- `se_exp`: A vector of standard errors of `b_exp`.
- `se_out`: A vector of standard errors of `b_out`.
- `over.dispersion`: Should the model consider overdispersion (systematic pleiotropy)? Default is FALSE.
- `loss.function`: Either the squared error loss (l2) or robust loss functions/scores (huber or tukey).
- `diagnosis`: Should the function returns diagnostic plots and results? Default is FALSE.
- `se.method`: How should the standard error be estimated? Either by sandwich variance formula (default and recommended) or the bootstrap.
- `k`: Threshold parameter in the Huber and Tukey loss functions.
- `B`: Number of bootstrap resamples.
- `suppress.warning`: Should warning messages be suppressed?
- `initialization`: Method to initialize the robust estimator. "Mode" is not supported currently.
- `niter`: Maximum number of interations to solve the estimating equations.
- `tol`: Numerical precision.
Value

A list

- **beta.hat**: Estimated causal effect
- **beta.se**: Standard error of beta.hat
- **beta.p.value**: Two-sided p-value of beta.hat
- **tau2.hat**: Overdispersion parameter if over.dispersion = TRUE
- **tau2.se**: Standard error of tau2.hat
- **std.resid**: Standardized residuals of each SNP, returned if diagnosis = TRUE
- **beta.hat.loo**: Leave-one-out estimates of beta.hat, returned if diagnosis = TRUE
- **beta.hat.bootstrap**: Median of the bootstrap estimates, returned if se.method = "bootstrap"
- **beta.se.bootstrap**: Median absolute deviation of the bootstrap estimates, returned if se.method = "bootstrap"

Functions

- **mr.raps.all**:
- **mr.raps.simple**:
- **mr.raps.overdispersed**:
- **mr.raps.simple.robust**:
- **mr.raps.overdispersed.robust**:

References


Examples

data(bmi.sbp)
attach(bmi.sbp)

```r
## All estimators
mr.raps.all(beta.exposure, beta.outcome, se.exposure, se.outcome)
```

```r
## Diagnostic plots
res <- mr.raps(beta.exposure, beta.outcome, se.exposure, se.outcome, diagnosis = TRUE)
res <- mr.raps(beta.exposure, beta.outcome, se.exposure, se.outcome, TRUE, diagnosis = TRUE)
res <- mr.raps(beta.exposure, beta.outcome, se.exposure, se.outcome, TRUE, "tukey", diagnosis = TRUE)
```

detach(bmi.sbp)

data(bmi.bmi)
attach(bmi.bmi)

## Because both the exposure and the outcome are BMI, the true "causal" effect should be 1.

## All estimators
mr.raps.all(beta.exposure, beta.outcome, se.exposure, se.outcome)

detach(bmi.bmi)
Index

*Topic datasets
  bmi.bmi, 2
  bmi.sbp, 3

bmi.bmi, 2
bmi.sbp, 3

mr.raps, 3
mr.raps-package, 2