# Package 'mr.raps'

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**Type** Package

**Title** Two Sample Mendelian Randomization using Robust Adjusted Profile Score

**Version** 0.2

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**Description** Mendelian randomization is a method of identifying and estimating a confounded causal effect using genetic instrumental variables. This packages implements methods for two-sample Mendelian randomization with summary statistics by using Robust Adjusted Profile Score (RAPS). References: Qingyuan Zhao, Jingshu Wang, Jack Bowden, Dylan S. Small. Statistical inference in two-sample summary-data Mendelian randomization using robust adjusted profile score. <arXiv:1801.09652>.

**Imports** stats, graphics, nortest

**License** GPL-3

**RoxygenNote** 6.0.1

**LazyData** true

**NeedsCompilation** no

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## R topics documented:

`mr.raps-package` *Two Sample Mendelian Randomization using Robust Adjusted Profile Score*

## Description

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

`bmi.bmi` *"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(bmi.bmi)
```

## 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 (sam- ple size: 152893)
3. SBP-UKBB: SBP using the United Kingdom BioBank (UKBB) data (sample size: 317754)

### Usage

```
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.

## 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

```
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)

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

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

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)

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)

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

Qingyuan Zhao, Jingshu Wang, Jack Bowden, Dylan S. Small. Statistical inference in two-sample summary-data Mendelian randomization using robust adjusted profile score. https://arxiv.org/abs/1801.09652.

## Examples

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

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

## 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)
```

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