Package 'mr.raps'

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Type Package

Title Two Sample Mendelian Randomization using Robust Adjusted Profile Score

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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

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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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