Package: mr.divw (via r-universe)

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Title debiased inverse-variance weighted estimator for univariable and multivariable Mendelian randomization

Version 0.1.0

Description Perform causal effect estimation for summary-data Mendelian randomization using IVW, dIVW and MV-SRIVW estimators.

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RemoteRef suggestions

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Contents

`bmi.cad` *Effect of Body Mass Index (BMI) on Coronary Artery Disease (CAD)*

Description

It contains independent datasets from three genome-wide association studies (GWASs):

1. Exposure dataset: A GWAS for BMI in round 2 of the UK BioBank (sample size: 336,107), `http://www.nealelab.is/uk-biobank`.
2. Outcome dataset: A GWAS A GWAS for CAD from the CARDIoGRAMplusC4D consortium (sample size: ~185,000), with genotype imputation using the 1000 Genome Project, (PubMed 26343387).
3. Selection dataset: A GWAS for BMI in the Japanese population (sample size: 173,430), (PubMed 28892062).

Usage

```
data(bmi.cad)
```

Format

A `data.frame` with 1119 rows and 42 variables.

Source

`https://github.com/qingyuanzhao/mr.raps`

`data_gen_individual` *Summary Statistics from Simulated Individual-level data*

Description

Summary Statistics from Simulated Individual-level data

Usage

```
data_gen_individual(
  case = c("case4", "case5", "case6", "case7"),
  true_var = FALSE
)
```

Arguments

`case`	Simulation scenario used in Section 5.3 in Ye et al., (2020).
`true_var`	Do se.exposure, se.outcome, se.selection equal the true standard deviations or the estimated standard errors. Default is FALSE.

Value

A data frame

References

Ting Ye, Jun Shao, Hyunseung Kang (2020). Debiased Inverse-Variance Weighted Estimator in Two-Sample Summary-Data Mendelian Randomization.https://arxiv.org/abs/1911.09802.

`data_gen_summary` *Summary Statistics Simulated from the BMI-CAD Dataset*

Description

Summary Statistics Simulated from the BMI-CAD Dataset

Usage

```
data_gen_summary(case = c("case1", "case2", "case3", "case3_pleiotropy"))
```

Arguments

`case`	Simulation scenario used in Section 5.1 in Ye et al., (2020).

Value

A data frame

References

Ting Ye, Jun Shao, Hyunseung Kang (2020). Debiased Inverse-Variance Weighted Estimator in Two-Sample Summary-Data Mendelian Randomization.https://arxiv.org/abs/1911.09802.

`hdl_subfractions` *Effects of HDL subfractions on Coronary Artery Disease (CAD)*

Description

It contains SNP-exposure and SNP-outcome association summary statistics from the following genome-wide association studies (GWASs):

1. Exposure dataset: A GWAS for traditional lipids http://csg.sph.umich.edu/willer/public/lipids2013/ (PubMed 24097068); A GWAS for subfractions http://www.computationalmedicine.fi/data\#NMR_GWAS (PubMed 27005778).
2. Outcome dataset: A GWAS for CAD from the CARDIoGRAMplusC4D consortium http://www.cardiogramplusc4d.org/data-downloads/ (PubMed 28714975).
3. Selection dataset: A GWAS for traditional lipids https://www.ebi.ac.uk/gwas/studies/GCST007141 (PubMed 29507422); A GWAS for subfractions http://csg.sph.umich.edu/boehnke/public/metsim-2017-lipoproteins/ (PubMed 29084231).

Usage

```
data(hdl_subfractions)
```

Format

A list with 3 elements with the first element being a data.frame with 24 columns (see below for column descriptions), the second element being an empty data.frame, the third element being an estimated correlation matrix.

SNP SNP rsid

effect_allele effect allele

other_allele other allele

gamma_exp1,...,gamma_exp9 Estimated associations of each SNP with respectively traditional lipids HDL, LDL, TG, and HDL subfractions S-HDL-P, S-HDL-TG, M-HDL-P, M-HDL-C, L-HDL-P, and L-HDL-C.

se_exp1,...,se_exp9 Standard error estiamtes for gamma_exp1,...,gamma_exp9

gamma_out1 Estimated SNP-outcome association

se_out1 Standard error estimate for gamma_out1

selection_pvals p-values for SNP-exposure associations in the selection dataset

Source

`https://github.com/tye27/mr.divw`

`mr.divw` *Main function for dIVW*

Description

Main function for dIVW

Usage

```
mr.divw(
  beta.exposure,
  beta.outcome,
  se.exposure,
  se.outcome,
  alpha = 0.05,
  pval.selection = NULL,
  lambda = 0,
  over.dispersion = FALSE,
  diagnostics = FALSE,
  overlap = FALSE,
  gen_cor = 0
)
```

Arguments

`beta.exposure`	A vector of SNP effects on the exposure vairable, usually obtained from a GWAS
`beta.outcome`	A vector of SNP effects on the outcome vairable, usually obtained from a GWAS
`se.exposure`	A vecor of standard errors of `beta.exposure`
`se.outcome`	A vector of standard errors of `beta.outcome`
`alpha`	Confidence interval has level 1-alpha
`pval.selection`	A vector of p-values calculated based on the selection dataset that is used for IV selection. It is not required when lambda=0
`lambda`	The specified z-score threhold. Default is 0 (without thresholding)
`over.dispersion`	Should the model consider balanced horizontal pleiotropy. Default is FALSE
`diagnostics`	Should the function returns the q-q plot for assumption diagnosis. Default is FALSE
`overlap`	Should the model consider overlapping exposure and outcome datasets. Default is FALSE
`gen_cor`	If overlap = TRUE, provide an estimate of the correlation between the effect of the genetic variants on the exposure and the outcome. Default value is 0, meaning that the exposure and outcome datasets are non-overlapping.

Value

A list

beta.hat Estimated causal effect

beta.se Standard error of `beta.hat`

condition A measure that needs to be large for reliable asymptotic approximation based on the dIVW estimator. It is recommended to be greater than 20

tau.square Overdispersion parameter if `over.dispersion=TRUE`

n.IV Number of IVs used in the dIVW estimator

IV IVs that are used in the dIVW estimator

References

Ting Ye, Jun Shao, Hyunseung Kang (2020). Debiased Inverse-Variance Weighted Estimator in Two-Sample Summary-Data Mendelian Randomization.https://arxiv.org/abs/1911.09802.

Examples

```
data(bmi.cad)
with(bmi.cad,
  mr.divw(beta.exposure, beta.outcome, se.exposure, se.outcome, diagnostics=TRUE)
)
```

`mr.eo` *MR-EO Algorithm to Adaptively Find the Optimal Z-score Threhold.*

Description

MR-EO Algorithm to Adaptively Find the Optimal Z-score Threhold.

Usage

```
mr.eo(
  lambda.start,
  beta.exposure,
  beta.outcome,
  se.exposure,
  se.outcome,
  pval.selection,
  over.dispersion = FALSE,
  max_opt_iter = 5
)
```

Arguments

`lambda.start`	Initial value for lambda (the z-score threshold).
`beta.exposure`	A vector of SNP effects on the exposure vairable, usually obtained from a GWAS
`beta.outcome`	A vector of SNP effects on the outcome vairable, usually obtained from a GWAS
`se.exposure`	A vecor of standard errors of `beta.exposure`
`se.outcome`	A vector of standard errors of `beta.outcome`
`pval.selection`	A vector of p-values calculated based on the selection dataset that is used for IV selection
`over.dispersion`	Should the model consider balanced horizontal pleiotropy. Default is FALSE
`max_opt_iter`	Maximum number of iterations. Default is 5

Details

`mr.eo` is an adaptive algorithm that finds the optimal z-socre threshold that leads to the dIVW estimator with the smallest variance.

Value

A list

lambda.opt Optimal z-socre threshold

n.iter Number of iterations to find `lambda.opt`

References

Ting Ye, Jun Shao, Hyunseung Kang (2020). Debiased Inverse-Variance Weighted Estimator in Two-Sample Summary-Data Mendelian Randomization.https://arxiv.org/abs/1911.09802.

Examples

```
df <- data_gen_summary("case1")
lambda.opt <- with(df,
  mr.eo(0, beta.exposure, beta.outcome, se.exposure, se.outcome,
    pval.selection)$lambda.opt
)
with(df,
  mr.divw(beta.exposure, beta.outcome, se.exposure, se.outcome,
    pval.selection = pval.selection, lambda = lambda.opt)
)

data(bmi.cad)
lambda.opt <- with(bmi.cad,
  mr.eo(0, beta.exposure, beta.outcome, se.exposure, se.outcome,
    pval.selection)$lambda.opt
)
with(bmi.cad,
  mr.divw(beta.exposure, beta.outcome, se.exposure, se.outcome,
    pval.selection = pval.selection, lambda = lambda.opt)
)
```

`mvmr.ivw` *Perform inverse-variance weighted (IVW) estimator for two-sample summary-data multivariable Mendelian randomization*

Description

Perform inverse-variance weighted (IVW) estimator for two-sample summary-data multivariable Mendelian randomization

Usage

```
mvmr.ivw(beta.exposure, se.exposure, beta.outcome, se.outcome, gen_cor = NULL)
```

Arguments

`beta.exposure`	A data.frame or matrix. Each row contains the estimated marginal effect of a SNP on K exposures, usually obtained from a GWAS
`se.exposure`	A data.frame or matrix of estimated standard errors of beta.exposure
`beta.outcome`	A vector of the estimated marginal effect of a SNP on outcome, usually obtained from a GWAS
`se.outcome`	A vector of estimated standard errors of beta.outcome

`gen_cor`	A K-by-K matrix for the estimated shared correlation matrix between the effect of the genetic variants on each exposure, where K is the number of exposure. The correlations can either be estimated, be assumed to be zero, or fixed at zero using non-overlapping samples of each exposure GWAS. Default input is NULL, meaning that an identity matrix is used as the correlation matrix.

Value

A list with elements

`beta.hat`	Estimated direct effects of each exposure on the outcome
`beta.se`	Estimated standard errors of beta.hat
`iv_strength_parameter`	The minimum eigenvalue of the sample IV strength matrix, which quantifies the IV strength in the sample

Examples

```
data("hdl_subfractions")
# Estimate the effect of S-HDL-P on CAS risk, adjusting for HDL, LDL, and TG
# Columns: SNP effects on HDL, LDL, TG, and S-HDL-P respectively
beta.exposure <- hdl_subfractions$data[,
  c("gamma_exp1","gamma_exp2","gamma_exp3","gamma_exp4")]
se.exposure <- hdl_subfractions$data[,c("se_exp1","se_exp2","se_exp3","se_exp4")]
beta.outcome <- hdl_subfractions$data$gamma_out1
se.outcome <- hdl_subfractions$data$se_out1
P <- hdl_subfractions$cor.mat[c(1:4),c(1:4)]
mvmr.ivw(beta.exposure = beta.exposure,
se.exposure = se.exposure,
beta.outcome = beta.outcome,
se.outcome = se.outcome,
gen_cor = P)
```

`mvmr.srivw` *Perform spectral regularized inverse-variance weighted (SRIVW) estimator for summary-data multivariable Mendelian randomization*

Description

Perform spectral regularized inverse-variance weighted (SRIVW) estimator for summary-data multivariable Mendelian randomization

Usage

```
mvmr.srivw(
  beta.exposure,
  se.exposure,
  beta.outcome,
```

```
  se.outcome,
  phi_cand = 0,
  over.dispersion = TRUE,
  overlap = FALSE,
  gen_cor = NULL
)
```

Arguments

`beta.exposure`	A data.frame or matrix. Each row contains the estimated marginal effect of a SNP on K exposures, usually obtained from a GWAS
`se.exposure`	A data.frame or matrix of estimated standard errors of beta.exposure
`beta.outcome`	A vector of the estimated marginal effect of a SNP on outcome, usually obtained from a GWAS
`se.outcome`	A vector of estimated standard errors of beta.outcome
`phi_cand`	A vector of tuning parameters for SRIVW estimator. Default is 0. To use the recommended set for the tuning parameter, simply set phi_cand = NULL.
`over.dispersion`	Should the model consider balanced horizontal pleiotropy? Default is TRUE.
`overlap`	Should the model consider overlapping exposure and outcome datasets? Default is FALSE.
`gen_cor`	If overlap = FALSE, provide a K-by-K matrix for the estimated shared correlation matrix between the effect of the genetic variants on each exposure, where K is the number of exposure. If overlap = TRUE, provide a (K+1)-by-(K+1) matrix for the estimated shared correlation matrix between the effect of the genetic variants on each exposure and the outcome, where the last index position corresponds to the outcome. The correlations can either be estimated, be assumed to be zero, or fixed at zero. Default input is NULL, meaning that an identity matrix is used as the correlation matrix.

Value

A list with elements

`beta.hat`	Estimated direct effects of each exposure on the outcome
`beta.se`	Estimated standard errors of beta.hat
`iv_strength_parameter`	The minimum eigenvalue of the sample IV strength matrix, which quantifies the IV strength in the sample
`phi_selected`	The selected tuning parameter for the SRIVW estimator
`tau.square`	Overdispersion parameter if `over.dispersion=TRUE`

Examples

```
data("hdl_subfractions")
# Estimate the effect of S-HDL-P on CAS risk, adjusting for HDL, LDL, and TG
# Columns: SNP effects on HDL, LDL, TG, and S-HDL-P respectively
```

```
beta.exposure <- hdl_subfractions$data[,
  c("gamma_exp1","gamma_exp2","gamma_exp3","gamma_exp4")]
se.exposure <- hdl_subfractions$data[,c("se_exp1","se_exp2","se_exp3","se_exp4")]
beta.outcome <- hdl_subfractions$data$gamma_out1
se.outcome <- hdl_subfractions$data$se_out1
# last index must correspond to the outcome
P <- hdl_subfractions$cor.mat[c(1:4,10),c(1:4,10)]
mvmr.srivw(beta.exposure = beta.exposure,
se.exposure = se.exposure,
beta.outcome = beta.outcome,
se.outcome = se.outcome,
gen_cor = P,
phi_cand = NULL,
over.dispersion = FALSE,
overlap = TRUE)
```

`table_publish` *Published Table 4*

Description

Published Table 4

Usage

```
table_publish()
```

Value

A table

Examples

```
table_publish()
```

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