

Package: BESIDEMR (via r-universe)

September 20, 2024

Title BayEsian Set IDentification Mendelian randomization

Version 1.2

Description The R package to perform BayEsian Set IDentification Mendelian randomization (BESIDE-MR).

Depends R (>= 3.5)

License GPL v3

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Repository <https://mrcieu.r-universe.dev>

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AMD_HDL

*Effect of HDL cholesterol on age-related macular degeneration (AMD)***Description**

We performed three-sample MR, where we selected instruments from The Metabolic Syndrome in Men (METSIM) GWAS, then extracted their summary data from MRChallenge2019, where:

1. SNP-HDL:Kettunen et al. Available from: <http://europepmc.org/articles/PMC4814583>
2. SNP-AMD:International AMD Genomics Consortium (IAMGDC) Available from: <http://europepmc.org/articles/PMC4814583>

Usage

```
data(AMD_HDL)
```

Format

A data.frame with 27 rows and 4 variables.

BMA_MRanalysis

*BESIDE-MR fitting function***Description**

Fits BESIDE-MR model. NOTE: β is the estimated causal effect and τ is the heterogeneity variance modelled as precision (i.e. $1/\tau$)

Usage

```
BMA_MRanalysis(
  tau_estimate,
  N_Beta,
  BetaXG,
  BetaYG,
  seBetaXG,
  seBetaYG,
  N_Ins,
  N_Iter,
  Prior,
  tuning_para,
  gen_inits
)
```

Arguments

tau_estimate	Use DL estimate ("DL_approx") or Full Bayesian ("Full_Bayes") approach to analyse data.
N_Beta	one-parameter (=1) or two-parameter (=2) model.
BetaXG	Effect size for X-G association
BetaYG	Effect size for Y-G association
seBetaXG	Standard error for X-G association
seBetaYG	Standard error for Y-G association
N_Ins	Number of genetic instruments
N_Iter	Number of iterations
Prior	A list of hyper parameter for the prior distribution; \$hyper_Beta_mean,\$hyper_Beta_sd ONE PARAMETER MODEL: to specify mean (_mean) and standard deviation (_sd) respectively for the normally distributed β . \$hyper_Prec_shape,\$hyper_Prec_rate ONE PARAMETER MODEL with "Full_Bayes": to specify shape (_shape) and rate (_rate) for the gamma distribution of precision. \$Ins_prob ONE PARAMETER MODEL: assign prior inclusion probability for each instrument. \$hyper_Beta1_mean,\$hyper_Beta1_sd,\$hyper_Beta2_mean,\$hyper_Beta2_sd ONE PARAMETER MODEL: to specify mean and standard deviation for the normally distributed β_1 and β_2 respectively. \$hyper_Prec1_shape,\$hyper_Prec1_rate,\$hyper_Prec2_shape,\$hyper_Prec2_rate TWO PARAMETER MODEL with "Full_Bayes": to specify shape and rate for the gamma distribution of precision. \$Ins1_prob,\$Ins2_prob TWO PARAMETER MODEL: assign prior inclusion probability for each instrument in set 1 or set 2 respectively.
tuning_para	Tuning parameter to ensure sufficient acceptance rate (recommended between 0.25 - 0.45); \$Beta ONE PARAMETER MODEL: for β . \$Prec_LL,\$Prec_UL,\$Prec_gap ONE PARAMETER MODEL with "Full_Bayes": for the upper (_UL), lower (_LL) and gap (_gap) of the precision, this ensures symmetry between the new and the old value. \$Beta1,\$Beta2 TWO PARAMETER MODEL: for β_1 and β_2 respectively. \$Prec1_LL,\$Prec1_UL,\$Prec1_gap,\$Prec2_LL,\$Prec2_UL,\$Prec2_gap TWO PARAMETER MODEL with "Full_Bayes": for the upper, lower and gap of the precision1 and precision2 respectively, this ensures symmetry between the new and the old value.
gen_inits	Initial values to start the iterations; \$Beta ONE PARAMETER MODEL: for β . \$UBPrec,\$LBPrec ONE PARAMETER MODEL with "Full_Bayes": for upper and lower limit of initial value of precision respectively.

`$Ins_L` ONE PARAMETER MODEL: use `randomS.initial.LI()` to generate random initial model space.

`$Beta1, $Beta2` TWO PARAMETER MODEL: for β_1 and β_2 respectively.

`$UBPrec1, $LBPrec1, $UBPrec2, $LBPrec2` TWO PARAMETER MODEL with "Full_Bayes": or upper and lower limit of initial value of precision1 and precision2 respectively.

`$Ins1_L, $Ins2_L` TWO PARAMETER MODEL: use `randomS.initial.LI()` generate random initial model space.

Value

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

`S` A matrix giving the results. ONE PARAMETER MODEL: columns gives sampled values of $\beta, \tau^2, I_1, \dots, I_L$ for all iterations (rows). TWO PARAMETER MODEL: columns gives sampled values of $\beta_1, \beta_2, \tau_1^2, \tau_2^2, I_{11}, \dots, I_{1L}, I_{21}, \dots, I_{2L}$ for all iterations (rows).

`accept_rate` acceptance rate for each of the parameter from `S`.

Author(s)

Chin Yang Shapland; Jack Bowden.

References

Shapland, C.Y., et al., Profile-likelihood Bayesian model averaging for two-sample summary data Mendelian randomization in the presence of horizontal pleiotropy.

Examples

```
# load data
data(AMD_HDL)

# Prior choice for beta, tau and inclusion of instruments
L<-nrow(AMD_HDL)
Ins_prior<-rep(0.5, L)
Prior_DL<-list(hyper_Beta_mean=0, hyper_Beta_sd=1, Ins_prob=Ins_prior)
Prior_gamma<-list(hyper_Beta_mean=0, hyper_Beta_sd=1, hyper_Prec_shape=2, hyper_Prec_rate=0.00005, Ins_prob=Ins_prior)

# Tuning parameter for beta
H_DL<-list(Beta=0.05)
H_gamma<-list(Beta=0.05, Prec_LL=0, Prec_UL=1000000, Prec_gap=150000)

# Generate initial values
gen_inits_DL<-list(Beta=rnorm(1,0,10), Ins_L=randomS.initial.LI(L,Ins_prior))
gen_inits_gamma<-list(Beta=rnorm(1,0,10), UBPrec=1000000, LBPrec=0, Ins_L=randomS.initial.LI(L,Ins_prior))

# One-parameter model
nIter<-50000
#res_DL<-BMA_MRanalysis("DL_approx", 1, AMD_HDL$BetaXG, AMD_HDL$BetaYG, AMD_HDL$seBetaXG, AMD_HDL$seBetaYG, L, nIter)
#res_gamma<-BMA_MRanalysis("Full_Bayes", 1, AMD_HDL$BetaXG, AMD_HDL$BetaYG, AMD_HDL$seBetaXG, AMD_HDL$seBetaYG, L, nIter)
```

BMA_MRanalysis_InsPen *BESIDE-MR fitting function with penalization term*

Description

Sensitivity analysis that fits BESIDE-MR model with penalisation term (η) for number of instruments.

Usage

```
BMA_MRanalysis_InsPen(
  tau_estimate,
  N_Beta,
  BetaXG,
  BetaYG,
  seBetaXG,
  seBetaYG,
  N_Ins,
  N_Iter,
  Prior,
  tuning_para,
  gen_inits,
  Penal_NoInst
)
```

Arguments

tau_estimate	Use DL estimate ("DL_approx") or Full Bayesian ("Full_Bayes") approach to analyse data.
N_Beta	one-parameter (=1) or two-parameter (=2) model.
BetaXG	Effect size for X-G association
BetaYG	Effect size for Y-G association
seBetaXG	Standard error for X-G association
seBetaYG	Standard error for Y-G association
N_Ins	Number of genetic instruments
N_Iter	Number of iterations
Prior	A list of hyper parameter for the prior distribution; \$hyper_Beta_mean,\$hyper_Beta_sd ONE PARAMETER MODEL: to specify mean (<code>_mean</code>) and standard deviation (<code>_sd</code>) respectively for the normally distributed β . \$hyper_Prec_shape,\$hyper_Prec_rate ONE PARAMETER MODEL with "Full_Bayes": to specify shape (<code>_shape</code>) and rate (<code>_rate</code>) for the gamma distribution of precision.

	\$Ins_prob ONE PARAMETER MODEL: assign prior inclusion probability for each instrument.
	\$hyper_Beta1_mean,\$hyper_Beta1_sd,\$hyper_Beta2_mean,\$hyper_Beta2_sd ONE PARAMETER MODEL: to specify mean and standard deviation for the normally distributed β_1 and β_2 respectively.
	\$hyper_Prec1_shape, \$hyper_Prec1_rate, \$hyper_Prec2_shape, \$hyper_Prec2_rate TWO PARAMETER MODEL with "Full_Bayes": to specify shape and rate for the gamma distribution of precision.
	\$Ins1_prob, \$Ins2_prob TWO PARAMETER MODEL: assign prior inclusion probability for each instrument in set 1 or set 2 respectively.
tuning_para	Tuning parameter to ensure sufficient acceptance rate (recommended between 0.25 - 0.45); \$Beta ONE PARAMETER MODEL: for β . \$Prec_LL, \$Prec_UL, \$Prec_gap ONE PARAMETER MODEL with "Full_Bayes": for the upper (_UL), lower (_LL) and gap (_gap) of the precision, this ensures symmetry between the new and the old value. \$Beta1, \$Beta2 TWO PARAMETER MODEL: for β_1 and β_2 respectively. \$Prec1_LL, \$Prec1_UL, \$Prec1_gap, \$Prec2_LL, \$Prec2_UL, \$Prec2_gap TWO PARAMETER MODEL with "Full_Bayes": for the upper, lower and gap of the precision1 and precision2 respectively, this ensures symmetry between the new and the old value.
gen_inits	Initial values to start the iterations; \$Beta ONE PARAMETER MODEL: for β . \$SUBPrec, \$LBPrec ONE PARAMETER MODEL with "Full_Bayes": for upper and lower limit of initial value of precision respectively. \$Ins_L ONE PARAMETER MODEL: use randomS.initial.LI() to generate random initial model space. \$Beta1, \$Beta2 TWO PARAMETER MODEL: for β_1 and β_2 respectively. \$SUBPrec1, \$LBPrec1, \$SUBPrec2, \$LBPrec2 TWO PARAMETER MODEL with "Full_Bayes": or upper and lower limit of initial value of precision1 and precision2 respectively. \$Ins1_L, \$Ins2_L TWO PARAMETER MODEL: use randomS.initial.LI() generate random initial model space.
Penal_NoInst	Penalisation term for number of instruments, positive and negative value favours models with many and few instruments respectively. Two values must be specified for the two-parameter model.

Value

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

S A matrix giving the results. ONE PARAMETER MODEL: columns gives sampled values of $\beta, \tau^2, I_1, \dots, I_L$ for all iterations (rows). TWO PARAMETER MODEL: columns gives sampled values of $\beta_1, \beta_2, \tau_1^2, \tau_2^2, I_{11}, \dots, I_{1L}, I_{21}, \dots, I_{2L}$ for all iterations (rows).

accept_rate acceptance rate for each of the parameter from S.

Author(s)

Chin Yang Shapland; Jack Bowden.

References

Shapland, C.Y., et al., Profile-likelihood Bayesian model averaging for two-sample summary data Mendelian randomization in the presence of horizontal pleiotropy.

Examples

```
# load data
data(AMD_HDL)

# Prior choice for beta, tau and inclusion of instruments
L<-nrow(AMD_HDL)
Ins_prior<-rep(0.5, L)
Prior_DL<-list(hyper_Beta_mean=0, hyper_Beta_sd=1, Ins_prob=Ins_prior)
Prior_gamma<-list(hyper_Beta_mean=0, hyper_Beta_sd=1, hyper_Prec_shape=2, hyper_Prec_rate=0.00005, Ins_prob=Ins_prior)

# Tuning parameter for beta
H_DL<-list(Beta=0.05)
H_gamma<-list(Beta=0.05, Prec_LL=0, Prec_UL=1000000, Prec_gap=150000)

# Generate initial values
gen_inits_DL<-list(Beta=rnorm(1,0,10), Ins_L=randomS.initial.LI(L,Ins_prior))
gen_inits_gamma<-list(Beta=rnorm(1,0,10), UBPrec=1000000, LBPrec=0, Ins_L=randomS.initial.LI(L,Ins_prior))

# One-parameter model with penalisation parameter
eta_sense<-5 # penalisation value which favours models with many instruments
nIter<-50000
#res_DL<-BMA_MRanalysis_InsPen("DL_approx",1, AMD_HDL$beta_XL.HDL.C, AMD_HDL$beta_amd, AMD_HDL$sse_XL.HDL.C, AMD_HDL$sse_amd)
#res_gamma<-BMA_MRanalysis_InsPen("Full_Bayes",1, AMD_HDL$beta_XL.HDL.C, AMD_HDL$beta_amd, AMD_HDL$sse_XL.HDL.C, AMD_HDL$sse_amd)
```

randomS.initial.LI *Generate initial model space function*

Description

Generate random initial model space that doesn't produce empty and 1 variable model space.

Usage

```
randomS.initial.LI(L, ins_prior)
```

Arguments

L Number of instruments.
ins_prior prior for inclusion probability for each instrument.

Value

numeric sequence of L length as the indicator variable to initialise in `BMA_MRanalysis()`.

Examples

```
#load data
data(AMD_HDL)

#Prior choice for beta, tau and inclusion of instruments
L<-nrow(AMD_HDL)
Ins_prior<-rep(0.5, L)
randomS.initial.LI(L,Ins_prior)
```

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