# Package: MRcML (via r-universe)

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οMI	estimate
CMI	i estimate

Estimate with Regular Likelihood

## Description

Estimate theta, b vector, r vector with constrained maximum likelihood.

## Usage

```
cML_estimate(
  b_exp,
  b_out,
  se_exp,
  se_out,
  K,
  initial_theta = 0,
  initial_mu = rep(0, length(b_exp)),
  maxit = 100
)
```

## Arguments

b_exp	Vector of estimated effects for exposure.
b_out	Vector or estimated effects for outcome.
se_exp	Vector of standard errors for exposure.
se_out	Vector of standard errors for outcome.
K	Constraint parameter, number of invalid IVs.
initial_theta	Starting point for theta.
initial_mu	Starting point for mu.
maxit	Maximum number of iteration.

#### Value

A list contains: theta is the estimate causal effect, b\_vec is the estimated vector of b, r\_vec is the estimated vector of r.

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## Description

With multiple perturbed data, get estimated theta, se of estimated theta and negative log-likelihood, using multiple random starting points.

## Usage

```
cML_estimate_DP(
  b_exp,
  b_out,
  se_exp,
  se_out,
  K,
  num_pert = 200,
  random_start = 0,
  maxit = 100
)
```

## Arguments

b_exp	Vector of estimated effects for exposure.
b_out	Vector or estimated effects for outcome.
se_exp	Vector of standard errors for exposure.
se_out	Vector of standard errors for outcome.
K	Constraint parameter, number of invalid IVs.
num_pert	Number of perturbation, default is 200.
random_start	Number of random starting points, default is 0.
maxit	Maximum number of iteration.

#### Value

A list contains: theta\_v is the vector estimated thetas,  $se_v$  is vector of standard errors of estimated thetas,  $l_v$  is vector of negative log-likelihood. Vectors all have length num\_pert.

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cML\_estimate\_random

Estimate with Regular Likelihood Using Multiple Random Start Points

## Description

Get estimated theta, se of estimated theta and negative log-likelihood, using multiple random starting points.

## Usage

```
cML_estimate_random(
  b_exp,
  b_out,
  se_exp,
  se_out,
  K,
  random_start = 0,
  maxit = 100
)
```

### **Arguments**

b_exp	Vector of estimated effects for exposure.
b_out	Vector or estimated effects for outcome.
se_exp	Vector of standard errors for exposure.
se_out	Vector of standard errors for outcome.
K	Constraint parameter, number of invalid IVs.
random_start	Number of random starting points, default is 0.
maxit	Maximum number of iteration.

## Value

A list contains: theta is the estimate causal effect, se is standard error of estimated theta, l is negative log-likelihood, r\_est is estimated r vector.

 $cML\_SdTheta$ 

Standard Error of Estimated Theta

## Description

Get the standard error of estimated theta from constrained maximum likelihood.

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### Usage

```
cML_SdTheta(b_exp, b_out, se_exp, se_out, theta, b_vec, r_vec)
```

## Arguments

b_exp	Vector of estimated effects for exposure.
b_out	Vector or estimated effects for outcome.
se_exp	Vector of standard errors for exposure.
se_out	Vector of standard errors for outcome.
theta	Estimated theta from cML.
b_vec	Estimated vector of b from cML.
r_vec	Estimated vector of r from cML.

## Value

Standard error of theta.

mr\_cML

MRcML method

## Description

This is the main function of MRcML method, without data perturbation.

## Usage

```
mr_cML(
    b_exp,
    b_out,
    se_exp,
    se_out,
    K_vec = 0:(length(b_exp) - 2),
    random_start = 0,
    maxit = 100,
    random_seed = 0,
    n
)
```

## Arguments

b_exp	Vector of estimated effects for exposure.
b_out	Vector or estimated effects for outcome.
se_exp	Vector of standard errors for exposure.
se out	Vector of standard errors for outcome.

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K\_vec Sets of candidate K's, the constraint parameter representing number of invalid

IVs.

random\_start Number of random start points for cML, default is 0.

maxit Maximum number of iterations for each optimization.

random\_seed Random seed, an integer. Default is 0, which does not set random seed; user

could specify a positive integer as random seed to get replicable results.

n Sample size.

### Value

A list contains full results of cML methods. MA\_BIC\_theta, MA\_BIC\_se, MA\_BIC\_p: Estimate of theta, its standard error and p-value from cML-MA-BIC. Similarly for BIC\_theta, BIC\_se, BIC\_p from cML-BIC; for MA\_AIC\_theta, MA\_AIC\_se, MA\_AIC\_p from cML-MA-AIC; for AIC\_DP\_theta, AIC\_DP\_se, AIC\_DP\_p from cML-AIC. BIC\_invalid is the set of invalid IVs selected by cML-BIC, AIC\_invalid is the set of invalid IVs selected by cML-BIC, aIC\_invalid is the set of invalid IVs selected by cML-AIC. BIC\_vec is the BIC vector.

mr\_cML\_DP

MRcML method with Data Perturbation

#### **Description**

This is the main function of MRcML method with data perturbation.

#### Usage

```
mr_cML_DP(
  b_exp,
  b_out,
  se_exp,
  se_out,
  K_vec = 0:(length(b_exp) - 2),
  random_start = 0,
  random_start_pert = 0,
  maxit = 100,
  num_pert = 200,
  random_seed = 0,
  n
)
```

### **Arguments**

b\_expb\_outb\_coutb\_coutVector or estimated effects for outcome.se\_expVector of standard errors for exposure.

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se\_out Vector of standard errors for outcome.

K\_vec Sets of candidate K's, the constraint parameter representing number of invalid

IVs.

random\_start Number of random start points for cML, default is 0.

random\_start\_pert

Number of random start points for cML with data perturbation, default is 0.

maxit Maximum number of iterations for each optimization.

num\_pert Number of perturbation, default is 200.

random\_seed Random seed, an integer. Default is 0, which does not set random seed; user

could specify a positive integer as random seed to get replicable results.

n Sample size.

#### Value

A list contains full results of cML methods. MA\_BIC\_theta, MA\_BIC\_se, MA\_BIC\_p: Estimate of theta, its standard error and p-value from cML-MA-BIC. Similarly for BIC\_theta, BIC\_se, BIC\_p from cML-BIC; for MA\_BIC\_DP\_theta, MA\_BIC\_DP\_se, MA\_BIC\_DP\_p from cML-MA-BIC-DP; for BIC\_DP\_theta, BIC\_DP\_se, BIC\_DP\_p from cML-BIC-DP. BIC\_invalid is the set of invalid IVs selected by cML-BIC.

mr\_cML\_DP\_Overlap

MRcML method for overlapping samples with Data Perturbation

### **Description**

This is the main function of MRcML method for overlapping samples with data perturbation.

#### Usage

```
mr_cML_DP_Overlap(
  b_exp,
  b_out,
  se_exp,
  se_out,
  K_vec = 0:(length(b_exp) - 2),
  random_start = 0,
  random_start_pert = 0,
  maxit = 100,
  num_pert = 100,
  random_seed = 0,
  n,
  rho = 0
)
```

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#### **Arguments**

b_exp	Vector of estimated effects for exposure.	
b_out	Vector or estimated effects for outcome.	
se_exp	Vector of standard errors for exposure.	
se_out	Vector of standard errors for outcome.	
K_vec	Sets of candidate K's, the constraint parameter representing number of invalid IVs.	
random_start	Number of random start points for cML, default is 0.	
random_start_pert		
	Number of random start points for cML with data perturbation, default is 0.	
maxit	Maximum number of iterations for each optimization.	
num_pert	Number of perturbation, default is 200.	
random_seed	Random seed, an integer. Default is 0, which does not set random seed; user could specify a positive integer as random seed to get replicable results.	

n Sample size.

rho Correlation between GWAS summary statistics due to overlapping samples.

#### Value

A list contains full results of cML methods. MA\_BIC\_theta, MA\_BIC\_se, MA\_BIC\_p: Estimate of theta, its standard error and p-value from cML-MA-BIC. Similarly for BIC\_theta, BIC\_se, BIC\_p from cML-BIC; for MA\_BIC\_DP\_theta, MA\_BIC\_DP\_se, MA\_BIC\_DP\_p from cML-MA-BIC-DP; for BIC\_DP\_theta, BIC\_DP\_se, BIC\_DP\_p from cML-BIC-DP. BIC\_invalid is the set of invalid IVs selected by cML-BIC.

mr\_cML\_Overlap

MRcML method for overlapping samples

#### **Description**

This is the main function of MRcML method with overlapping samples, without data perturbation.

### Usage

```
mr_cML_Overlap(
   b_exp,
   b_out,
   se_exp,
   se_out,
   K_vec = 0:(length(b_exp) - 2),
   random_start = 0,
   maxit = 100,
   random_seed = 0,
   n,
   rho = 0
)
```

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#### **Arguments**

b\_exp
 b\_out
 Vector of estimated effects for exposure.
 b\_out
 Vector or estimated effects for outcome.
 vector of standard errors for exposure.
 vector of standard errors for outcome.

K\_vec Sets of candidate K's, the constraint parameter representing number of invalid

IVs.

random\_start Number of random start points for cML, default is 0.

maxit Maximum number of iterations for each optimization.

random\_seed Random seed, an integer. Default is 0, which does not set random seed; user

could specify a positive integer as random seed to get replicable results.

n Sample size.

rho Correlation between GWAS summary statistics due to overlapping samples.

#### Value

A list contains full results of cML methods. MA\_BIC\_theta, MA\_BIC\_se, MA\_BIC\_p: Estimate of theta, its standard error and p-value from cML-MA-BIC. Similarly for BIC\_theta, BIC\_se, BIC\_p from cML-BIC. BIC\_invalid is the set of invalid IVs selected by cML-BIC, BIC\_vec is the BIC vector.

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