# Package 'GCIM'

# February 28, 2025

**Title** The genetic causality inference model(GCIM) is a statistical method for detecting the causal direction in GxE interaction studies

**Version** 0.0.1.000

**Description** GCIM is a statistical method, which deciphers the causal direction of GxE interaction in complex traits and disease.

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**Encoding** UTF-8

**Roxygen** list(markdown = TRUE)

RoxygenNote 7.3.2.9000

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bp\_dis\_phen

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## **Description**

This dataset contains covariate for a binary outcome information of individuals in the discovery dataset, including various confounders.

#### Usage

```
data(bp_dis_cov)
```

#### **Format**

A data frame with 800 rows and 19 columns:

Family ID Family identification number

Individual ID Individual identification number

Binary Covariate A binary covariate

Confounder 1 Confounder 1 description ...

Confounder 16 Confounder 16 description

bp_dis_phen	A phenotype data from the discovery dataset containing binary pheno-
	type trated as an outcome for the proposed causal directions.

## **Description**

This dataset contains phenotype for the outcome information of individuals in the discovery dataset.

## Usage

```
data(bp_dis_phen)
```

#### **Format**

A data frame with 800 rows and 3 columns:

Family ID Family identification number

Individual ID Individual identification number

**Binary outcome** A binary outcome (1=controls, 2=cases)

bp\_tar\_cov 3

bp_tar_cov	A phenotype data from the target dataset containing binary phenotype trated as exposure for the proposed causal directions.

# Description

This dataset contains covariate information of individuals in the target dataset, including various confounders.

# Usage

```
data(bp_tar_cov)
```

## **Format**

A data frame with 800 rows and 19 columns:

Family ID Family identification number

Individual ID Individual identification number

Binary Covariate A binary covariate

Confounder 1 Confounder 1 description ...

Confounder 16 Confounder 16 description

bp_tar_phen	A phenotype data from the target dataset containing binary phenotype
	trated as outcome for the proposed causal directions.

## **Description**

This dataset contains phenotype for the outcome information of individuals in the target dataset,

# Usage

```
data(bp_tar_phen)
```

#### **Format**

A data frame with 800 rows and 3 columns:

Family ID Family identification number

Individual ID Individual identification number

Binary outcome A binary outcome (0=controls, 1=cases)

4 br\_dis\_phen

br_dis_cov	A phenotype data file from the discovery dataset, containing the binary
	exposure treated as binary outcomes for the reverse direction.

# Description

This dataset contains phenotype for the outcome information of individuals in the discovery dataset.

## Usage

```
data(br_dis_cov)
```

## **Format**

A data frame with 800 rows and 3 columns:

Family ID Family identification number

Individual ID Individual identification number

Binary outcome A binary outcome (1=controls, 2=cases)

br\_dis\_phen A phenotype data file from the discovery dataset, containing the binary oucome treated as binary exposure for the reverse direction.

## **Description**

This dataset contains phenotype information of individuals in the discovery dataset, including various confounders.

# Usage

```
data(br_dis_phen)
```

#### **Format**

A data frame with 800 rows and 19 columns:

Family ID Family identification number

Individual ID Individual identification number

Binary Covariate A binary covariate

Confounder 1 Confounder 1 description ...

br\_tar\_cov 5

br_tar_cov A phenotype data file from the target dataset, containing the bind exposure treated as an oucome for the reverse causal directions.	ary
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# Description

This dataset contains phenotype data for the outcome information of individuals in the target dataset,

## Usage

```
data(br_tar_cov)
```

## **Format**

A data frame with 800 rows and 3 columns:

Family ID Family identification number

Individual ID Individual identification number

Binary outcome A binary outcome (0=controls, 1=cases)

br\_tar\_phen A phenotype data file from target dataset, containing a binary outcome treated as a binary exposure in the reverse causal directions.

## **Description**

This dataset contains phenotypic data for the covariate information of individuals in the target dataset, including various confounders.

# Usage

```
data(br_tar_phen)
```

#### **Format**

A data frame with 800 rows and 19 columns:

Family ID Family identification number

Individual ID Individual identification number

Binary Covariate A binary covariate

Confounder 1 Confounder 1 description ...

b\_gweis

b_gwas	Perform GWAS for binary covariates.

# Description

Perform GWAS for binary covariates.

## Usage

```
b_gwas(plink_path, dis_snp, bp_dis_cov)
```

# Arguments

plink\_path Path to the PLINK executable application.

dis\_snp Prefix for binary files for the discovery dataset.

bp\_dis\_cov File path for covariate data in the discovery dataset.

temp\_dir Directory to save output files.

#### Value

None. Results are saved to files.

b_gweis	Perform GWEIS for binary outcome variables.	
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# Description

This function performs genome-wide-by-environemnt interaction studies (GWEIS) and processes the results to generate files for downstream analysis.

## Usage

```
b_gweis(plink_path, dis_snp, bp_dis_phen, bp_dis_cov)
```

# **Arguments**

plink_path	Path to the PLINK executable application.
dis_snp	Prefix for binary files for the discovery dataset.
bp_dis_phen	File path for the phenotype data in the discovery dataset.
bp_dis_cov	File path for covariate data in the discovery dataset.
temp_dir	Directory to save output files.

## Value

None. Results are saved to files.

dis\_snp.bim 7

dis\_snp.bim

PLINK .bim File for SNP Information

#### **Description**

This dataset follows the standard PLINK .bim format and contains SNP-related information for the discovery dataset, including chromosome ID, SNP ID, and allele details.

## Usage

```
data(dis_snp.bim)
```

#### **Format**

A data frame with 6 columns:

**Column 1** Chromosome ID (integer)

Column 2 SNP ID (character)

Column 3 Position in centimorgans (numeric)

Column 4 Base-pair coordinate (integer)

Column 5 Minor Allele (character)

Column 6 Reference Allele (character)

dis\_snp.fam

PLINK .fam File for Family and Phenotype Information

## **Description**

This dataset follows the standard PLINK .fam format and contains family structure and phenotype information for individuals in the discovery dataset.

## Usage

```
data(dis_snp.fam)
```

#### **Format**

A data frame with 6 columns:

Column 1 Family ID (character or integer)

Column 2 Individual ID (character or integer)

**Column 3** Father's ID (character or integer; 0 if missing)

Column 4 Mother's ID (character or integer; 0 if missing)

**Column 5** Sex (integer; 1 = male, 2 = female, 0 = unknown)

**Column 6** Phenotype value (numeric; 1 = control, 2 = case, -9 = missing)

8 dis\_snp.ped

dis\_snp.map

PLINK .map File for SNP Information

#### **Description**

This dataset follows the standard PLINK .map file format and contains genetic marker information, including chromosome, SNP ID, position in centimorgans, and base-pair coordinates.

## Usage

```
data(dis_snp.map)
```

#### **Format**

A data frame with 4 columns:

Column 1 Chromosome ID (integer)

Column 2 SNP ID (character)

Column 3 Position in centimorgans (numeric; typically 0 if unknown)

Column 4 Base-pair coordinate (integer; position on the chromosome in base pairs)

dis\_snp.ped

PLINK .ped File for Genotype and Sample Information

# Description

This dataset follows the standard PLINK .ped file format. It contains family, individual, parental, sex, phenotype, and genotype information for each sample.

# Usage

```
data(dis_snp.ped)
```

#### **Format**

A data frame with 6 required columns, followed by genotype data:

Column 1 Family ID (character)

Column 2 Individual ID (character)

Column 3 Paternal ID (0 if unknown, character)

Column 4 Maternal ID (0 if unknown, character)

**Column 5** Sex (1 = male, 2 = female, 0 = unknown)

**Column 6** Phenotype value (1 = control, 2 = case, -9 = missing)

**Columns 7+** Genotype data in pairs of alleles for each SNP (e.g., A T, G G, coded as separate columns).

gcim\_b

gcim_b	Perform regression analysis for GCIM with binary outcome.

#### **Description**

Perform regression analysis for GCIM with binary outcome.

#### Usage

```
gcim_b(bp_tar_phen, bp_tar_cov, Add_PRS, Int_PRS, Cov_PRS, confounders)
```

#### **Arguments**

bp\_tar\_phen File path for the target phenotype data.
bp\_tar\_cov File path for the target covariate data.
Additive Scaled additive PRS values.
Interaction Scaled interaction PRS values.
Covariate Scaled covariate PRS values.

Confounders Data frame of additional confounders.

#### Value

Summary of the regression model.

gcim\_q Perform regression analysis for GCIM with quantitative outcome.

## **Description**

Perform regression analysis for GCIM with quantitative outcome.

## Usage

```
gcim_q(qp_tar_phen, qp_tar_cov, Add_PRS, Int_PRS, Cov_PRS, confounders)
```

## **Arguments**

bp\_tar\_phen File path for the target phenotype data.
bp\_tar\_cov File path for the target covariate data.

Additive Scaled additive PRS values.

Interaction Scaled interaction PRS values.

Covariate Scaled covariate PRS values.

Confounders Data frame of additional confounders.

# Value

Summary of the regression model.

10 qp\_dis\_cov

prs\_scores

Compute Polygenic Risk Scores (PRS).

## **Description**

Compute Polygenic Risk Scores (PRS).

## Usage

```
prs_scores(plink_path, tar_snp)
```

## **Arguments**

plink\_path Path to the PLINK executable application.
tar\_snp Prefix for binary files for the target dataset.
temp\_dir Directory to save output files.

## Value

A list containing scaled PRS values for additive, interaction, and covariate scores.

qp\_dis\_cov

A phenotype data from the discovery dataset containing quantitative phenotype trated as exposure for the proposed causal directions.

# **Description**

This dataset contains covariate information for individuals in the discovery dataset, including various confounders.

# Usage

```
data(qp_dis_cov)
```

## **Format**

A data frame with 800 rows and 19 columns:

Family ID Family identification number

Individual ID Individual identification number

quantitative Covariate A quantitative covariate

Confounder 1 Confounder 1 description ...

qp\_dis\_phen 11

qp_dis_phen	A phenotype data from the discovery dataset containing quantitative phenotype trated as an outcome for the proposed causal directions.

# Description

This dataset contains phenotype for the outcome information of individuals in the discovery dataset,

## Usage

```
data(qp_dis_phen)
```

## **Format**

A data frame with 800 rows and 3 columns:

Family ID Family identification number

Individual ID Individual identification number

quantitative outcome A quantitative outcome #'

qp\_tar\_covA phenotype data from the target dataset containing quantitative phenotype trated as exposure for the proposed causal directions.

## **Description**

This dataset contains covariate information of individuals in the target dataset, including various confounders.

# Usage

```
data(qp_tar_cov)
```

# Format

A data frame with 800 rows and 19 columns:

Family ID Family identification number

Individual ID Individual identification number

quantitative Covariate A quantitative covariate

Confounder 1 Confounder 1 description ...

12 qr\_dis\_cov

1 71 7	e target dataset containing quantitative phe- for the proposed causal directions.
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# Description

This dataset contains phenotype for the outcome information of individuals in the target dataset.

## Usage

```
data(qp_tar_phen)
```

#### **Format**

A data frame with 800 rows and 3 columns:

Family ID Family identification number

Individual ID Individual identification number

quantitative outcome A qunatitative outcome #'

qr\_dis\_cov A phenotype data file from the discovery dataset, containing the quantitative exposure treated as an outcomes for the reverse direction.

## **Description**

This dataset contains phenotype for the outcome information of individuals in the discovery dataset.

# Usage

```
data(qr_dis_cov)
```

#### **Format**

A data frame with 800 rows and 3 columns:

Family ID Family identification number

Individual ID Individual identification number

quantitative outcome A quantitative outcome #'

qr\_dis\_phen 13

qr_dis_phen	A phenotype data file from the discovery dataset, containing the quantitative outcome treated as an exposure for the reverse direction.

# Description

This dataset contains covariate information of individuals in the discovery dataset, including various confounders.

# Usage

```
data(qr_dis_phen)
```

## **Format**

A data frame with 800 rows and 19 columns:

Family ID Family identification number

Individual ID Individual identification number

quantitative Covariate A quantitative covariate

Confounder 1 Confounder 1 description ...

Confounder 16 Confounder 16 description

qr\_tar\_cov A phenotype data file from the target dataset, containing the quantitative exposure treated as an outcomes for the reverse direction.

# Description

This dataset contains phenotype for the outcome information of individuals in the target dataset.

## Usage

```
data(qr_tar_cov)
```

#### **Format**

A data frame with 800 rows and 3 columns:

Family ID Family identification number

Individual ID Individual identification number

quantitative outcome A qunatitative outcome #'

 $q_{\underline{g}was}$ 

qr_tar_phen A phenotype data file from the target dataset, containing the quantitative outcome treated as an exposure for the reverse direction.
--

# Description

This dataset contains covariate information of individuals in the target dataset, including various confounders.

# Usage

```
data(qr_tar_phen)
```

#### **Format**

A data frame with 800 rows and 19 columns:

Family ID Family identification number

Individual ID Individual identification number

quantitative Covariate A quantitative covariate

Confounder 1 Confounder 1 description ...

Confounder 16 Confounder 16 description

q\_gwas

Perform GWAS for quantitative covariates.

# Description

Perform GWAS for quantitative covariates.

# Usage

```
q_gwas(plink_path, dis_snp, qp_dis_cov)
```

## **Arguments**

plink_path	Path to the PLINK executable application.
dis_snp	Prefix for binary files for the discovery dataset.
qp_dis_cov	File path for covariate data in the discovery dataset.
temp_dir	Directory to save output files.

#### Value

None. Results are saved to files.

q\_gweis 15

q_gweis	Perform GWEIS for quantitative outcome var	riables.
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# Description

This function performs genome-wide interaction studies (GWEIS) and processes the results to generate files for downstream analysis.

## Usage

```
q_gweis(plink_path, dis_snp, qp_dis_phen, qp_dis_cov)
```

## **Arguments**

plink_path	Path to the PLINK executable application.
dis_snp	Prefix for binary files for the discovery dataset.
qp_dis_phen	File path for the phenotype data in the discovery dataset.
qp_dis_cov	File path for covariate data in the discovery dataset.
temp_dir	Directory to save output files.

#### Value

None. Results are saved to files.

```
tar_snp.bim PLINK.bim file for SNP information
```

# **Description**

This dataset follows the standard PLINK .bim format and contains SNP-related information for the target dataset, including chromosome ID, SNP ID, and allele details.

# Usage

```
data(tar_snp.bim)
```

#### **Format**

A data frame with 6 columns:

```
Column 1 Chromosome ID (integer)
```

Column 2 SNP ID (character)

**Column 3** Position in centimorgans (numeric)

Column 4 Base-pair coordinate (integer)

Column 5 Minor Allele (character)

Column 6 Reference Allele (character)

16 tar\_snp.map

tar\_snp.fam

PLINK .fam file for family and phenotype information

#### **Description**

This dataset follows the standard PLINK .fam format and contains family structure and phenotype information for individuals in the target dataset.

## Usage

```
data(tar_snp.fam)
```

#### **Format**

A data frame with 6 columns:

Column 1 Family ID (character or integer)

Column 2 Individual ID (character or integer)

**Column 3** Father's ID (character or integer; 0 if missing)

**Column 4** Mother's ID (character or integer; 0 if missing)

**Column 5** Sex (integer; 1 = male, 2 = female, 0 = unknown)

**Column 6** Phenotype value (numeric; 1 = control, 2 = case, -9 = missing)

tar\_snp.map

PLINK .map file for SNP information

#### **Description**

This dataset follows the standard PLINK .map file format and contains genetic marker information, including chromosome, SNP ID, position in centimorgans, and base-pair coordinates.

## Usage

```
data(tar_snp.map)
```

## **Format**

A data frame with 4 columns:

Column 1 Chromosome ID (integer)

Column 2 SNP ID (character)

Column 3 Position in centimorgans (numeric; typically 0 if unknown)

Column 4 Base-pair coordinate (integer; position on the chromosome in base pairs)

tar\_snp.ped 17

tar\_snp.ped

PLINK .ped file for genotype and sample information

# **Description**

This dataset follows the standard PLINK .ped file format. It contains family, individual, parental, sex, phenotype, and genotype information for each sample.

# Usage

```
data(tar_snp.ped)
```

#### **Format**

A data frame with 6 required columns, followed by genotype data:

Column 1 Family ID (character)

Column 2 Individual ID (character)

**Column 3** Paternal ID (0 if unknown, character)

Column 4 Maternal ID (0 if unknown, character)

**Column 5** Sex (1 = male, 2 = female, 0 = unknown)

**Column 6** Phenotype value (1 = control, 2 = case, -9 = missing)

**Columns 7+** Genotype data in pairs of alleles for each SNP (e.g., A T, C, G, coded as separate columns).

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