

# Package ‘GxEprs’

August 10, 2023

**Title** Genotype-by-environment (GxE) Interaction in Polygenic Risk Score Models for Quantitative and Binary Traits

**Version** 1.0

**Description** A novel PRS model is introduced to enhance the prediction accuracy by utilising GxE effects. This package performs Genome Wide Association Studies (GWAS) and Genome Wide Environment Interaction Studies (GWEIS) using a discovery dataset. The package has the ability to obtain polygenic risk scores (PRSs) for a target sample. Finally it predicts the risk values of each individual in the target sample. Users have the choice of using existing models (Li et al., 2015)<doi.org/10.1093/annonc/mdu565>, (Pandis et al., 2013)<doi.org/10.1093/ejo/cjt054>, (Peyrot et al., 2018)<doi.org/10.1016/j.biopsych.2017.09.009> and (Song et al., 2022)<doi.org/10.1038/s41467-022-32407-9>, as well as newly proposed models for genomic risk prediction (refer to the URL for more details).

**URL** <https://github.com/DoviniJ/GxEprs>

**License** GPL (>=3)

**Encoding** UTF-8

**Roxygen** list(markdown = TRUE)

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**LazyData** true

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Bcov_discovery	<i>Covariate data file of the discovery dataset when the outcome is binary This contains covariate information of the individuals in the discovery dataset following confounders</i>
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## Description

Covariate data file of the discovery dataset when the outcome is binary This contains covariate information of the individuals in the discovery dataset following confounders

## Usage

```
Bcov_discovery
```

## Format

A dataframe with 7916 rows and 18 columns

**Column 1** Family ID

**Column 2** Individual ID

**Column 3** Standardized covariate

**Column 4** Square of the standardized covariate

**Column 5** Confounder 1

**Column 6** Confounder 2

**Column 7** Confounder 3

**Column 8** Confounder 4

**Column 9** Confounder 5

**Column 10** Confounder 6

**Column 11** Confounder 7

**Column 12** Confounder 8

**Column 13** Confounder 9

**Column 14** Confounder 10

**Column 15** Confounder 11

**Column 16** Confounder 12

**Column 17** Confounder 13

**Column 18** Confounder 14

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Bcov_target	<i>Covariate data file of the target dataset when the outcome is binary This contains covariate information of the individuals in the target dataset following confounders</i>
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**Description**

Covariate data file of the target dataset when the outcome is binary This contains covariate information of the individuals in the target dataset following confounders

**Usage**

```
Bcov_target
```

**Format**

A dataframe with 1939 rows and 18 columns

**Column 1** Family ID

**Column 2** Individual ID

**Column 3** Standardized covariate

**Column 4** Square of the standardized covariate

**Column 5** Confounder 1

**Column 6** Confounder 2

**Column 7** Confounder 3

**Column 8** Confounder 4

**Column 9** Confounder 5

**Column 10** Confounder 6

**Column 11** Confounder 7

**Column 12** Confounder 8

**Column 13** Confounder 9

**Column 14** Confounder 10

**Column 15** Confounder 11

**Column 16** Confounder 12

**Column 17** Confounder 13

**Column 18** Confounder 14

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Bphe_discovery	<i>Phenotype data file of the discovery dataset when the outcome is binary This contains phenotype information of the individuals in the discovery dataset</i>
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### Description

Phenotype data file of the discovery dataset when the outcome is binary This contains phenotype information of the individuals in the discovery dataset

### Usage

Bphe\_discovery

### Format

A dataframe with 7916 rows and 3 columns

**Column 1** Family ID

**Column 2** Individual ID

**Column 3** Phenotype (1=controls, 2=cases)

---

Bphe_target	<i>Phenotype data file of the target dataset when the outcome is binary This contains phenotype information of the individuals in the target dataset</i>
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### Description

Phenotype data file of the target dataset when the outcome is binary This contains phenotype information of the individuals in the target dataset

### Usage

Bphe\_target

### Format

A dataframe with 1939 rows and 3 columns

**Column 1** Family ID

**Column 2** Individual ID

**Column 3** Phenotype (0=controls, 1=cases)

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`DummyData.bim`*PLINK .bim file*

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**Description**

PLINK .bim file

**Usage**`DummyData.bim`**Format**

This follows PLINK general format

**Column 1** Chromosome ID**Column 2** SNP ID**Column 3** Position of centimorgans**Column 4** Base-pair coordinate**Column 5** Minor Allele**Column 6** Reference Allele

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`DummyData.fam`*PLINK .fam file*

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**Description**

PLINK .fam file

**Usage**`DummyData.fam`**Format**

This follows PLINK general format

**Column 1** Family ID**Column 2** Individual ID**Column 3** Father's ID**Column 4** Mother's ID**Column 5** Sex**Column 6** Phenotype value

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DummyData.map	<i>PLINK .map file</i>
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**Description**

PLINK .map file

**Usage**

DummyData.map

**Format**

This follows PLINK general format

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DummyData.ped	<i>PLINK .ped file</i>
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**Description**

PLINK .ped file

**Usage**

DummyData.ped

**Format**

This follows PLINK general format

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GWAS_binary	<i>GWAS_binary function This function performs GWAS using plink2 and outputs the GWAS summary statistics with additive SNP effects. Users may save the output in a user-specified file (see example).</i>
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**Description**

GWAS\_binary function This function performs GWAS using plink2 and outputs the GWAS summary statistics with additive SNP effects. Users may save the output in a user-specified file (see example).

**Usage**

GWAS\_binary(plink\_path, b\_file, Bphe\_discovery, Bcov\_discovery, thread = 20)

**Arguments**

<code>plink_path</code>	Path to the PLINK executable application
<code>b_file</code>	Prefix of the binary files, where all .fam, .bed and .bim files have a common prefix
<code>Bphe_discovery</code>	Name (with file extension) of the phenotype file containing family ID, individual ID and phenotype of the discovery dataset as columns, without heading
<code>Bcov_discovery</code>	Name (with file extension) of the covariate file containing family ID, individual ID, standardized covariate, square of standardized covariate, and/or confounders of the discovery dataset as columns, without heading
<code>thread</code>	Number of threads used

**Value**

This function will perform GWAS and output

`B_out.trd.sum`  
GWAS summary statistics with additive SNP effects

**Examples**

```
## Not run:
x <- GWAS_binary(plink_path, DummyData, Bphe_discovery, Bcov_discovery,
thread = 20)
sink("B_out.trd.sum") #to create a file in the working directory
write.table(x[c("ID", "A1", "OR")], sep = " ",
row.names = FALSE, quote = FALSE) #to write the output
sink() #to save the output
head(x) #to obtain the head of GWAS summary statistics of additive SNP effects
x$CHROM #to extract the chromosome number
x$POS #to extract the base pair position
x$ID #to extract the SNP ID
x$REF #to extract the reference allele
x$ALT #to extract the alternate allele
x$A1 #to extract the minor allele
x$OBS_CT #to extract the number of allele observations
x$OR #to extract the odds ratios of the SNP effects
x$LOG_OR_SE #to extract the standard errors of log odds
x$Z_STAT #to extract the test statistics
x$P #to extract the p values

## End(Not run)
```

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GWAS_quantitative	<i>GWAS_quantitative function This function performs GWAS using plink2 and outputs the GWAS summary statistics with additive SNP effects. Users may save the output in a user-specified file (see example).</i>
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## Description

GWAS\_quantitative function This function performs GWAS using plink2 and outputs the GWAS summary statistics with additive SNP effects. Users may save the output in a user-specified file (see example).

## Usage

```
GWAS_quantitative(
  plink_path,
  b_file,
  Qphe_discovery,
  Qcov_discovery,
  thread = 20
)
```

## Arguments

plink_path	Path to the PLINK executable application
b_file	Prefix of the binary files, where all .fam, .bed and .bim files have a common prefix
Qphe_discovery	Name (with file extension) of the phenotype file containing family ID, individual ID and phenotype of the discovery dataset as columns, without heading
Qcov_discovery	Name (with file extension) of the covariate file containing family ID, individual ID, standardized covariate, square of standardized covariate, and/or confounders of the discovery dataset as columns, without heading
thread	Number of threads used

## Value

This function will perform GWAS and output

Q_out.trd.sum	GWAS summary statistics with additive SNP effects
---------------	---

## Examples

```
## Not run:
x <- GWAS_quantitative(plink_path, DummyData, Qphe_discovery, Qcov_discovery,
  thread = 20)
sink("Q_out.trd.sum") #to create a file in the working directory
write.table(x[c("ID", "A1", "BETA")], sep = " ",
  row.names = FALSE, quote = FALSE) #to write the output
sink() #to save the output
head(x) #to obtain the head of GWAS summary statistics of additive SNP effects
x$CHROM #to extract the chromosome number
x$POS #to extract the base pair position
x$ID #to extract the SNP ID
x$REF #to extract the reference allele
x$ALT #to extract the alternate allele
x$A1 #to extract the minor allele
x$OBS_CT #to extract the number of allele observations
x$BETA #to extract the SNP effects
```



```

x$SE #to extract the standard errors of the SNP effects
x$T_STAT #to extract the test statistics
x$P #to extract the p values

## End(Not run)

```

---

GWEIS_binary	<i>GWEIS_binary function This function performs GWEIS using plink2 and outputs the GWEIS summary statistics with additive SNP effects and interaction SNP effects. Users may save the outputs in separate user-specified files (see examples).</i>
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## Description

GWEIS\_binary function This function performs GWEIS using plink2 and outputs the GWEIS summary statistics with additive SNP effects and interaction SNP effects. Users may save the outputs in separate user-specified files (see examples).

## Usage

```
GWEIS_binary(plink_path, b_file, Bphe_discovery, Bcov_discovery, thread = 20)
```

## Arguments

plink_path	Path to the PLINK executable application
b_file	Prefix of the binary files, where all .fam, .bed and .bim files have a common prefix
Bphe_discovery	Phenotype file containing family ID, individual ID and phenotype of the discovery dataset as columns, without heading
Bcov_discovery	Covariate file containing family ID, individual ID, standardized covariate, square of standardized covariate, and/or confounders of the discovery dataset as columns, without heading
thread	Number of threads used

## Value

This function will perform GWEIS and output

B_out.sum	GWEIS summary statistics with additive and interaction SNP effects
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## Examples

```

## Not run:
x <- GWEIS_binary(plink_path, DummyData, Bphe_discovery, Bcov_discovery,
thread = 20)
sink("B_out.add.sum") #to create a file in the working directory
write.table(x[c("ID", "A1", "ADD_OR")], sep = " ",
row.names = FALSE, quote = FALSE) #to write the output
sink() #to save the output
sink("B_out.gxe.sum") #to create a file in the working directory

```

```

write.table(x[c("ID", "A1", "INTERACTION_OR")], sep = " ",
row.names = FALSE, quote = FALSE) #to write the output
sink() #to save the output
head(x) #to extract the head of all columns in GWEIS summary statistics of
additive and interaction SNP effects
x$CHROM #to extract the chromosome number
x$POS #to extract the base pair position
x$ID #to extract the SNP ID
x$REF #to extract the reference allele
x$ALT #to extract the alternate allele
x$A1 #to extract the minor allele
x$OBS_CT #to extract the number of allele observations
x$ADD_OR #to extract the odds ratios of additive SNP effects
x$ADD_LOG_OR_SE #to extract the standard errors of log odds of
additive SNP effects
x$ADD_Z_STAT #to extract the test statistics of additive SNP effects
x$ADD_P #to extract the p values of additive SNP effects
x$INTERACTION_OR #to extract the odds ratios of the SNP effects of
interaction SNP effects
x$INTERACTION_LOG_OR_SE #to extract the standard errors of log odds
of interaction SNP effects
x$INTERACTION_Z_STAT #to extract the test statistics of interaction
SNP effects
x$INTERACTION_P #to extract the p values of interaction SNP effects

## End(Not run)

```

---

GWEIS\_quantitative *GWEIS\_quantitative function This function performs GWEIS using plink2 and outputs the GWEIS summary statistics with additive SNP effects and interaction SNP effects separately. It is recommended to save the outputs in separate user-specified files (see examples).*

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## Description

GWEIS\_quantitative function This function performs GWEIS using plink2 and outputs the GWEIS summary statistics with additive SNP effects and interaction SNP effects separately. It is recommended to save the outputs in separate user-specified files (see examples).

## Usage

```

GWEIS_quantitative(
  plink_path,
  b_file,
  Qphe_discovery,
  Qcov_discovery,
  thread = 20
)

```

## Arguments

plink\_path      Path to the PLINK executable application

b_file	Prefix of the binary files, where all .fam, .bed and .bim files have a common prefix
Qphe_discovery	Phenotype file containing family ID, individual ID and phenotype of the discovery dataset as columns, without heading
Qcov_discovery	Covariate file containing family ID, individual ID, standardized covariate, square of standardized covariate, and/or confounders of the discovery dataset as columns, without heading
thread	Number of threads used

### Value

This function will perform GWEIS and output

Q\_out.sum      GWEIS summary statistics with additive and interaction SNP effects

### Examples

```
## Not run:
x <- GWEIS_quantitative (plink_path, DummyData, Qphe_discovery, Qcov_discovery,
thread = 20)
sink("Q_out.add.sum") #to create a file in the working directory
write.table(x[c("ID", "A1", "ADD_BETA")], sep = " ",
row.names = FALSE, quote = FALSE) #to write the output
sink() #to save the output
sink("Q_out.gxe.sum") #to create a file in the working directory
write.table(x[c("ID", "A1", "INTERACTION_BETA")], sep = " ",
row.names = FALSE, quote = FALSE) #to write the output
sink() #to save the output
head(x) #to extract the head of all columns in GWEIS summary statistics of
additive and interaction SNP effects
x$CHROM #to extract the chromosome number
x$POS #to extract the base pair position
x$ID #to extract the SNP ID
x$REF #to extract the reference allele
x$ALT #to extract the alternate allele
x$A1 #to extract the minor allele
x$OBS_CT #to extract the number of allele observations
x$ADD_BETA #to extract the additive SNP effects
x$ADD_SE #to extract the standard errors of the
additive SNP effects
x$ADD_T_STAT #to extract the test statistics of additive
SNP effects
x$ADD_P #to extract the p values of additive SNP effects
x$INTERACTION_BETA #to extract the interaction SNP effects
x$INTERACTION_SE #to extract the standard errors of the
interaction SNP effects
x$INTERACTION_T_STAT #to extract the test statistics of
interaction SNP effects
x$INTERACTION_P #to extract the p values of interaction
SNP effects

## End(Not run)
```

---

PRS_binary	<i>PRS_binary function This function uses plink2 and outputs Polygenic Risk Scores (PRSs) of all the individuals, using pre-generated GWAS and/or GWEIS summary statistics. Note that the input used in this function can be generated by using GWAS_binary and/or GWEIS_binary functions. Users may save the output in a user-specified file (see examples).</i>
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## Description

PRS\_binary function This function uses plink2 and outputs Polygenic Risk Scores (PRSs) of all the individuals, using pre-generated GWAS and/or GWEIS summary statistics. Note that the input used in this function can be generated by using GWAS\_binary and/or GWEIS\_binary functions. Users may save the output in a user-specified file (see examples).

## Usage

```
PRS_binary(plink_path, b_file, summary_input)
```

## Arguments

plink_path	Path to the PLINK executable application
b_file	Prefix of the binary files, where all .fam, .bed and .bim files have a common prefix
summary_input	Pre-generated GWAS and/or GWEIS summary statistics

## Value

This function will output

prs.sscore	PRSs for each individual
------------	--------------------------

## Examples

```
## Not run:
a <- GWAS_binary(plink_path, DummyData, Bphe_discovery, Bcov_discovery)
trd <- a[c("ID", "A1", "OR")]
b <- GWEIS_binary(plink_path, DummyData, Bphe_discovery, Bcov_discovery)
add <- b[c("ID", "A1", "ADD_OR")]
gxe <- b[c("ID", "A1", "INTERACTION_OR")]
x <- PRS_binary(plink_path, DummyData, summary_input = trd)
sink("B_trd.sscore") #to create a file in the working directory
write.table(x, sep = " ", row.names = FALSE, quote = FALSE) #to write the output
sink() #to save the output
head(x) #to read the head of all columns in the output
x$FID #to extract the family ID's of full dataset
x$IID #to extract the individual ID's of full dataset
x$PRS #to extract the polygenic risk scores of full dataset
y <- PRS_binary(plink_path, DummyData, summary_input = add)
sink("B_add.sscore") #to create a file in the working directory
write.table(y, sep = " ", row.names = FALSE, quote = FALSE) #to write the output
sink() #to save the output
```

```

z <- PRs_binary(plink_path, DummyData, summary_input = gxe)
sink("B_gxe.sscore") #to create a file in the working directory
write.table(z, sep = " ", row.names = FALSE, quote = FALSE) #to write the output
sink() #to save the output

## End(Not run)

```

---

PRs_quantitative	<i>PRs_quantitative function This function uses plink2 and outputs Polygenic Risk Scores (PRSs) of all the individuals, using pre-generated GWAS and/or GWEIS summary statistics. Note that the input used in this function can be generated by using GWAS_quantitative and/or GWEIS_quantitative functions. Users may save the output in a user-specified file (see examples).</i>
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## Description

PRs\_quantitative function This function uses plink2 and outputs Polygenic Risk Scores (PRSs) of all the individuals, using pre-generated GWAS and/or GWEIS summary statistics. Note that the input used in this function can be generated by using GWAS\_quantitative and/or GWEIS\_quantitative functions. Users may save the output in a user-specified file (see examples).

## Usage

```
PRs_quantitative(plink_path, b_file, summary_input)
```

## Arguments

plink_path	Path to the PLINK executable application
b_file	Prefix of the binary files, where all .fam, .bed and .bim files have a common prefix
summary_input	Pre-generated GWAS and/or GWEIS summary statistics

## Value

This function will output

prs.sscore	PRSs for each individual
------------	--------------------------

## Examples

```

## Not run:
a <- GWAS_quantitative(plink_path, DummyData, Qphe_discovery, Qcov_discovery)
trd <- a[c("ID", "A1", "BETA")]
b <- GWEIS_quantitative(plink_path, DummyData, Qphe_discovery, Qcov_discovery)
add <- b[c("ID", "A1", "ADD_BETA")]
gxe <- b[c("ID", "A1", "INTERACTION_BETA")]
x <- PRs_quantitative(plink_path, DummyData, summary_input = trd)
sink("Q_trd.sscore") #to create a file in the working directory
write.table(x, sep = " ", row.names = FALSE, quote = FALSE) #to write the output
sink() #to save the output
head(x) #to read the head of all columns in the output

```

```

x$FID #to extract the family ID's of full dataset
x$IID #to extract the individual ID's of full dataset
x$PRS #to extract the polygenic risk scores of full dataset
y <- PRS_quantitative(plink_path, DummyData, summary_input = add)
sink("Q_add.sscore") #to create a file in the working directory
write.table(y, sep = " ", row.names = FALSE, quote = FALSE) #to write the output
sink() #to save the output
z <- PRS_quantitative(plink_path, DummyData, summary_input = gxe)
sink("Q_gxe.sscore") #to create a file in the working directory
write.table(z, sep = " ", row.names = FALSE, quote = FALSE) #to write the output
sink() #to save the output

## End(Not run)

```

---

Qcov\_discovery

*Covariate data file of the discovery dataset when the outcome is quantitative This contains covariate information of the individuals in the discovery dataset following confounders*

---

## Description

Covariate data file of the discovery dataset when the outcome is quantitative This contains covariate information of the individuals in the discovery dataset following confounders

## Usage

Qcov\_discovery

## Format

A dataframe with 6426 rows and 18 columns

**Column 1** Family ID

**Column 2** Individual ID

**Column 3** Standardized covariate

**Column 4** Square of the standardized covariate

**Column 5** Confounder 1

**Column 6** Confounder 2

**Column 7** Confounder 3

**Column 8** Confounder 4

**Column 9** Confounder 5

**Column 10** Confounder 6

**Column 11** Confounder 7

**Column 12** Confounder 8

**Column 13** Confounder 9

**Column 14** Confounder 10

**Column 15** Confounder 11

**Column 16** Confounder 12

**Column 17** Confounder 13

**Column 18** Confounder 14

---

Qcov_target	<i>Covariate data file of the target dataset when the outcome is quantitative This contains covariate information of the individuals in the target dataset following confounders</i>
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---

**Description**

Covariate data file of the target dataset when the outcome is quantitative This contains covariate information of the individuals in the target dataset following confounders

**Usage**

```
Qcov_target
```

**Format**

A dataframe with 1579 rows and 18 columns

**Column 1** Family ID

**Column 2** Individual ID

**Column 3** Standardized covariate

**Column 4** Square of the standardized covariate

**Column 5** Confounder 1

**Column 6** Confounder 2

**Column 7** Confounder 3

**Column 8** Confounder 4

**Column 9** Confounder 5

**Column 10** Confounder 6

**Column 11** Confounder 7

**Column 12** Confounder 8

**Column 13** Confounder 9

**Column 14** Confounder 10

**Column 15** Confounder 11

**Column 16** Confounder 12

**Column 17** Confounder 13

**Column 18** Confounder 14

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Qphe_discovery	<i>Phenotype data file of the discovery dataset when the outcome is quantitative This contains phenotype information of the individuals in the discovery dataset</i>
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---

**Description**

Phenotype data file of the discovery dataset when the outcome is quantitative This contains phenotype information of the individuals in the discovery dataset

**Usage**

Qphe\_discovery

**Format**

A dataframe with 6426 rows and 3 columns

**Column 1** Family ID

**Column 2** Individual ID

**Column 3** Phenotype

---

Qphe_target	<i>Phenotype data file of the target dataset when the outcome is quantitative This contains phenotype information of the individuals in the target dataset</i>
-------------	--

---

**Description**

Phenotype data file of the target dataset when the outcome is quantitative This contains phenotype information of the individuals in the target dataset

**Usage**

Qphe\_target

**Format**

A dataframe with 1579 rows and 3 columns

**Column 1** Family ID

**Column 2** Individual ID

**Column 3** Phenotype



---

summary\_permuted\_binary

*summary\_permuted\_binary function This function outputs the p value of permuted model in the target dataset, using pre-generated Polygenic Risk Scores (PRSs) of all the individuals. Note that the input used in this function can be generated by using PRS\_quantitative function. It is recommended to run this function, if you choose to fit 'PRS\_gxe x E' interaction component (i.e. novel proposed model, Model 5) when generating risk scores. If the 'PRS\_gxe x E' term is significant in Model 5, and insignificant in Model 5\* (permuted p value), consider that the 'PRS\_gxe x E' interaction component is actually insignificant (always give priority to the p value obtained from the permuted model).*

---

## Description

summary\_permuted\_binary function This function outputs the p value of permuted model in the target dataset, using pre-generated Polygenic Risk Scores (PRSs) of all the individuals. Note that the input used in this function can be generated by using PRS\_quantitative function. It is recommended to run this function, if you choose to fit 'PRS\_gxe x E' interaction component (i.e. novel proposed model, Model 5) when generating risk scores. If the 'PRS\_gxe x E' term is significant in Model 5, and insignificant in Model 5\* (permuted p value), consider that the 'PRS\_gxe x E' interaction component is actually insignificant (always give priority to the p value obtained from the permuted model).

## Usage

```
summary_permuted_binary(
  Bphe_target,
  Bcov_target,
  iterations = 1000,
  add_score,
  gxe_score
)
```

## Arguments

Bphe_target	Phenotype file containing family ID, individual ID and phenotype of the target dataset as columns, without heading
Bcov_target	Covariate file containing family ID, individual ID, standardized covariate, square of standardized covariate, and/or confounders of the target dataset as columns, without heading
iterations	Number of iterations used in permutation
add_score	PRSs generated using additive SNP effects of GWEIS summary statistics
gxe_score	PRSs generated using interaction SNP effects of GWEIS summary statistics

## Value

This function will output

B\_permuted\_p the p value of the permuted model

## Examples

```
## Not run:
a <- GWEIS_binary(plink_path, DummyData, Bphe_discovery, Bcov_discovery)
add <- a[c("ID", "A1", "ADD_OR")]
gxe <- a[c("ID", "A1", "INTERACTION_OR")]
p <- PRS_binary(plink_path, DummyData, summary_input = add)
q <- PRS_binary(plink_path, DummyData, summary_input = gxe)
x <- summary_permuted_binary(Bphe_target, Bcov_target, iterations = 1000,
add_score = p, gxe_score = q)
x

## End(Not run)
```

---

summary\_permuted\_quantitative

*summary\_permuted\_quantitative* function This function outputs the p value of permuted model in the target dataset, using pre-generated Polygenic Risk Scores (PRSs) of all the individuals. Note that the input used in this function can be generated by using PRS\_quantitative functions. It is recommended to run this function, if you choose to fit 'PRS\_gxe x E' interaction component (i.e. novel proposed model, Model 4) when generating risk scores. If the 'PRS\_gxe x E' term is significant in Model 4, and insignificant in Model 4\* (permuted p value), consider that the 'PRS\_gxe x E' interaction component is actually insignificant (always give priority to the p value obtained from the permuted model).

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## Description

summary\_permuted\_quantitative function This function outputs the p value of permuted model in the target dataset, using pre-generated Polygenic Risk Scores (PRSs) of all the individuals. Note that the input used in this function can be generated by using PRS\_quantitative functions. It is recommended to run this function, if you choose to fit 'PRS\_gxe x E' interaction component (i.e. novel proposed model, Model 4) when generating risk scores. If the 'PRS\_gxe x E' term is significant in Model 4, and insignificant in Model 4\* (permuted p value), consider that the 'PRS\_gxe x E' interaction component is actually insignificant (always give priority to the p value obtained from the permuted model).

## Usage

```
summary_permuted_quantitative(
  Qphe_target,
  Qcov_target,
  iterations = 1000,
  add_score,
  gxe_score
)
```

## Arguments

Qphe\_target Phenotype file containing family ID, individual ID and phenotype of the target dataset as columns, without heading

Qcov_target	Covariate file containing family ID, individual ID, standardized covariate, square of standardized covariate, and/or confounders of the target dataset as columns, without heading
iterations	Number of iterations used in permutation
add_score	PRSs generated using additive SNP effects of GWEIS summary statistics
gxe_score	PRSs generated using interaction SNP effects of GWEIS summary statistics

### Value

This function will output

Q\_permuted\_p.txt  
the p value of the permuted model

### Examples

```
## Not run:
a <- GWEIS_quantitative(plink_path, DummyData, Qphe_discovery, Qcov_discovery)
add <- a[c("ID", "A1", "ADD_BETA")]
gxe <- a[c("ID", "A1", "INTERACTION_BETA")]
p <- PRS_quantitative(plink_path, DummyData, summary_input = add)
q <- PRS_quantitative(plink_path, DummyData, summary_input = gxe)
x <- summary_permuted_quantitative(Qphe_target, Qcov_target, iterations = 1000,
add_score = p, gxe_score = q)
x

## End(Not run)
```

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summary\_regular\_binary

*summary\_regular\_binary function This function outputs the summary of regular model and final risk score values of each individual in the target dataset using pre-generated Polygenic Risk Scores (PRSs) of all the individuals. Note that the input used in this function can be generated by using PRS\_binary function.*

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### Description

summary\_regular\_binary function This function outputs the summary of regular model and final risk score values of each individual in the target dataset using pre-generated Polygenic Risk Scores (PRSs) of all the individuals. Note that the input used in this function can be generated by using PRS\_binary function.

### Usage

```
summary_regular_binary(
  Bphe_target,
  Bcov_target,
  add_score = NULL,
  gxe_score = NULL,
  Model
)
```

**Arguments**

Bphe_target	Phenotype file containing family ID, individual ID and phenotype of the target dataset as columns, without heading
Bcov_target	Covariate file containing family ID, individual ID, standardized covariate, square of standardized covariate, and/or confounders of the target dataset as columns, without heading
add_score	PRSs generated using additive SNP effects of GWAS/GWEIS summary statistics
gxe_score	PRSs generated using interaction SNP effects of GWEIS summary statistics
Model	Specify the model number (0: $y = \text{PRS\_trd} + \text{confounders}$ , 1: $y = \text{PRS\_trd} + E + \text{PRS\_trd} \times E + \text{confounders}$ , 2: $y = \text{PRS\_add} + E + \text{PRS\_add} \times E + \text{confounders}$ , 3: $y = \text{PRS\_add} + E + \text{PRS\_gxe} \times E + \text{confounders}$ , 4: $y = \text{PRS\_add} + E + \text{PRS\_gxe} + \text{PRS\_gxe} \times E + \text{confounders}$ , 5: $y = \text{PRS\_add} + E + E^2 + \text{PRS\_gxe} + \text{PRS\_gxe} \times E + \text{confounders}$ , where $y$ is the outcome variable, $E$ is the covariate of interest, $\text{PRS\_trd}$ and $\text{PRS\_add}$ are the polygenic risk scores computed using additive SNP effects of GWAS and GWEIS summary statistics respectively, and $\text{PRS\_gxe}$ is the polygenic risk scores computed using GxE interaction SNP effects of GWEIS summary statistics.)

**Value**

This function will output

Bsummary	the summary of the fitted model
Individual_risk_values	the estimated risk values of individuals in the target sample

**Examples**

```
## Not run:
a <- GWAS_binary(plink_path, DummyData, Bphe_discovery, Bcov_discovery)
trd <- a[c("ID", "A1", "OR")]
b <- GWEIS_binary(plink_path, DummyData, Bphe_discovery, Bcov_discovery)
add <- b[c("ID", "A1", "ADD_OR")]
gxe <- b[c("ID", "A1", "INTERACTION_OR")]
p <- PRS_binary(plink_path, DummyData, summary_input = trd)
q <- PRS_binary(plink_path, DummyData, summary_input = add)
r <- PRS_binary(plink_path, DummyData, summary_input = gxe)
summary_regular_binary(Bphe_target, Bcov_target,
                       add_score = p,
                       Model = 0)
summary_regular_binary(Bphe_target, Bcov_target,
                       add_score = p,
                       Model = 1)
summary_regular_binary(Bphe_target, Bcov_target,
                       add_score = q,
                       Model = 2)
summary_regular_binary(Bphe_target, Bcov_target,
                       add_score = q,
                       gxe_score = r,
                       Model = 3)
summary_regular_binary(Bphe_target, Bcov_target,
                       add_score = q,
```

```

                                gxe_score = r,
                                Model = 4)
x <- summary_regular_binary(Bphe_target, Bcov_target,
                            add_score = q,
                            gxe_score = r,
                            Model = 5)

sink("Bsummary.txt") #to create a file in the working directory
print(x$summary) #to write the output
sink() #to save the output
sink("Individual_risk_values.txt") #to create a file in the working directory
write.table(x$risk.values, sep = " ", row.names = FALSE, col.names = FALSE,
quote = FALSE) #to write the output
sink() #to save the output
x$summary #to obtain the model summary output
x$risk.values #to obtain the predicted risk values of target individuals

## End(Not run)

```

---

summary\_regular\_quantitative

*summary\_regular\_quantitative function This function outputs the summary of regular model and final risk score values of each individual in the target dataset using pre-generated Polygenic Risk Scores (PRSs) of all the individuals. Note that the input used in this function can be generated by using PRS\_quantitative function.*

---

## Description

summary\_regular\_quantitative function This function outputs the summary of regular model and final risk score values of each individual in the target dataset using pre-generated Polygenic Risk Scores (PRSs) of all the individuals. Note that the input used in this function can be generated by using PRS\_quantitative function.

## Usage

```

summary_regular_quantitative(
  Qphe_target,
  Qcov_target,
  add_score = NULL,
  gxe_score = NULL,
  Model
)

```

## Arguments

Qphe_target	Phenotype file containing family ID, individual ID and phenotype of the target dataset as columns, without heading
Qcov_target	Covariate file containing family ID, individual ID, standardized covariate, square of standardized covariate, and/or confounders of the target dataset as columns, without heading
add_score	PRSs generated using additive SNP effects of GWAS/GWEIS summary statistics

gxe_score	PRSs generated using interaction SNP effects of GWEIS summary statistics
Model	Specify the model number (0: $y = \text{PRS\_trd} + \text{confounders}$ , 1: $y = \text{PRS\_trd} + E + \text{PRS\_trd} \times E + \text{confounders}$ , 2: $y = \text{PRS\_add} + E + \text{PRS\_add} \times E + \text{confounders}$ , 3: $y = \text{PRS\_add} + E + \text{PRS\_gxe} \times E + \text{confounders}$ , 4: $y = \text{PRS\_add} + E + \text{PRS\_gxe} + \text{PRS\_gxe} \times E + \text{confounders}$ , where $y$ is the outcome variable, $E$ is the covariate of interest, $\text{PRS\_trd}$ and $\text{PRS\_add}$ are the polygenic risk scores computed using additive SNP effects of GWAS and GWEIS summary statistics respectively, and $\text{PRS\_gxe}$ is the polygenic risk scores computed using GxE interaction SNP effects of GWEIS summary statistics.)

## Value

This function will output

Qsummary.txt the summary of the fitted model

Individual\_risk\_values.txt  
the estimated risk values of individuals in the target sample

## Examples

```
## Not run:
a <- GWAS_quantitative(plink_path, DummyData, Qphe_discovery, Qcov_discovery)
trd <- a[c("ID", "A1", "BETA")]
b <- GWEIS_quantitative(plink_path, DummyData, Qphe_discovery, Qcov_discovery)
add <- b[c("ID", "A1", "ADD_BETA")]
gxe <- b[c("ID", "A1", "INTERACTION_BETA")]
p <- PRS_quantitative(plink_path, DummyData, summary_input = trd)
q <- PRS_quantitative(plink_path, DummyData, summary_input = add)
r <- PRS_quantitative(plink_path, DummyData, summary_input = gxe)
summary_regular_quantitative(Qphe_target, Qcov_target,
                             add_score = p,
                             Model = 0)
summary_regular_quantitative(Qphe_target, Qcov_target,
                             add_score = p,
                             Model = 1)
summary_regular_quantitative(Qphe_target, Qcov_target,
                             add_score = q,
                             Model = 2)
summary_regular_quantitative(Qphe_target, Qcov_target,
                             add_score = q,
                             gxe_score = r,
                             Model = 3)
x <- summary_regular_quantitative(Qphe_target, Qcov_target,
                                 add_score = q,
                                 gxe_score = r,
                                 Model = 4)

sink("Qsummary.txt") #to create a file in the working directory
print(x$summary) #to write the output
sink() #to save the output
sink("Individual_risk_values.txt") #to create a file in the working directory
write.table(x$risk.values, sep = " ", row.names = FALSE, col.names = FALSE,
           quote = FALSE) #to write the output
sink() #to save the output
x$summary #to obtain the model summary output
x$risk.values #to obtain the predicted risk values of target individuals
```

```
## End (Not run)
```

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