

# Package ‘hJAM’

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**Type** Package

**Title** Hierarchical Joint Analysis of Marginal Summary Statistics

**Version** 1.0.0

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**Description** Provides functions to implement a hierarchical approach which is designed to perform joint analysis of summary statistics using the framework of Mendelian Randomization or transcriptome analysis. Reference: Lai Jiang, Shujing Xu, Nicholas Mancuso, Paul J. Newcombe, David V. Conti (2020). ``A Hierarchical Approach Using Marginal Summary Statistics for Multiple Intermediates in a Mendelian Randomization or Transcriptome Analysis." <bioRxiv><doi:10.1101/2020.02.03.924241>.

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**LazyData** true

**RoxygenNote** 6.1.1

**Suggests** knitr, rmarkdown

**VignetteBuilder** knitr

**URL** <https://github.com/lailylajiang/hJAM>

**BugReports** <https://github.com/lailylajiang/hJAM/issues>

**Imports** ggplot2, ggpubr, dplyr, reshape2

**NeedsCompilation** no

**Repository** CRAN

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## Contents

betas.Gy . . . . .	2
conditional_A . . . . .	2
get_cond_A . . . . .	3

get_cond_alpha . . . . .	4
Gl . . . . .	5
hJAM_egger . . . . .	5
hJAM_lnreg . . . . .	7
marginal_A . . . . .	8
output.format . . . . .	8
print.hJAM_egger . . . . .	9
print.hJAM_lnreg . . . . .	9
SNPs_heatmap . . . . .	10
SNPs_info . . . . .	10
SNPs_scatter_plot . . . . .	11

<b>Index</b>	<b>12</b>
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betas.Gy	<i>Example beta list of hJAM</i>
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### Description

Example beta list of hJAM

### Usage

betas.Gy

### Format

The betas.Gy is the beta vector in the hJAM model: the association estimates between 210 SNPs and myocardial infarction. The summary data was collected from UK Biobank (n=459,324).

### References

Sudlow C, Gallacher J, Allen N, et al. UK biobank: an open access resource for identifying the causes of a wide range of complex diseases of middle and old age. PLoS Med 2015; 12: e1001779.

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conditional_A	<i>Example conditional A matrix of hJAM</i>
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### Description

Example conditional A matrix of hJAM

### Usage

conditional\_A

**Format**

The conditional\_A is the conditional estimates alpha matrix in the hJAM model: the association estimates between 210 SNPs and body mass index (BMI) and type 2 diabetes (T2D). The summary data was collected from GIANT consortium (n=339,224) and DIAGRAM+GERA+UKB (n=659316) for BMI and T2D, respectively. We converted it from marginal\_A, using get\_cond\_A function in hJAM package.

**References**

1. Locke AE, Kahali B, Berndt SI, et al. Genetic studies of body mass index yield new insights for obesity biology. *Nature* 2015; 518: 197-206.
2. Xue A, Wu Y, Zhu Z, et al. Genome-wide association analyses identify 143 risk variants and putative regulatory mechanisms for type 2 diabetes. *Nat Commun* 2018; 9: 2941.

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get_cond_A	<i>Compute conditional Z matrix</i>
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**Description**

The get\_cond\_A function is to get the conditional A matrix by using marginal A matrix

**Usage**

```
get_cond_A(marginal_A, G1, N.Gx, ridgeTerm = FALSE)
```

**Arguments**

marginal_A	the marginal effects of SNPs on the exposures (Gx).
G1	the reference panel (G1), such as 1000 Genome
N.Gx	the sample size of each Gx. It can be a scalar or a vector. If there are multiple X's from different Gx, it should be a vector including the sample size of each Gx. If all alphas are from the same Gx, it could be a scalar.
ridgeTerm	ridgeTerm = TRUE when the matrix L is singular. Matrix L is obtained from the cholesky decomposition of $G0'G0$ . Default as FALSE.

**Value**

A matrix with conditional estimates which are converted from marginal estimates using the JAM model.

**Author(s)**

Lai Jiang

**Examples**

```
data(Gl)
data(betas.Gy)
data(marginal_A)
get_cond_A(marginal_A = marginal_A, Gl = Gl, N.Gx = c(339224, 659316), ridgeTerm = TRUE)
```

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get_cond_alpha	<i>Compute conditional alphas</i>
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**Description**

The `get_cond_alpha` function is to compute the conditional alpha vector for each X. If only one X in the model, please use `get_cond_alpha` instead of `get_cond_A`. A sub-step in the `get_cond_A` function.

**Usage**

```
get_cond_alpha(alphas, Gl, N.Gx, ridgeTerm = FALSE)
```

**Arguments**

alphas	the marginal effects of SNPs on one exposure (Gx).
Gl	the reference panel (Gl), such as 1000 Genome
N.Gx	the sample size of the Gx. It can be a scalar.
ridgeTerm	ridgeTerm = TRUE when the matrix L is singular. Matrix L is obtained from the cholesky decomposition of $G_0'G_0$ . Default as FALSE

**Value**

A vector with conditional estimates which are converted from marginal estimates using the JAM model.

**Author(s)**

Lai Jiang

**References**

Lai Jiang, Shujing Xu, Nicholas Mancuso, Paul J. Newcombe, David V. Conti (2020). A Hierarchical Approach Using Marginal Summary Statistics for Multiple Intermediates in a Mendelian Randomization or Transcriptome Analysis. *bioRxiv* <https://doi.org/10.1101/2020.02.03.924241>.

**Examples**

```
data(Gl)
data(betas.Gy)
data(marginal_A)
get_cond_alpha(alphas = marginal_A[, 1], Gl = Gl, N.Gx = 339224, ridgeTerm = TRUE)
```

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G1	<i>Example reference data of hJAM</i>
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**Description**

The real data example from hJAM paper

**Usage**

G1

**Format**

The G1 object is a data matrix with 2467 individual of 210 SNPs from 1000 Genome project.

**References**

Consortium GP. A global reference for human genetic variation. Nature 2015; 526: 68.

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hJAM_egger	<i>Fit hJAM with Egger regression</i>
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**Description**

The hJAM\_egger function is to get the results from the hJAM model with Egger regression. It is for detecting potential pleiotropy

**Usage**

```
hJAM_egger(betas.Gy, N.Gy, G1, A, ridgeTerm = FALSE)
```

**Arguments**

betas.Gy	The betas in the paper: the marginal effects of SNPs on the phenotype (Gy)
N.Gy	The sample size of Gy
G1	The reference panel (G1), such as 1000 Genome
A	The A matrix in the paper: the marginal/conditional effects of SNPs on the exposures (Gx)
ridgeTerm	ridgeTerm = TRUE when the matrix L is singular. Matrix L is obtained from the cholesky decomposition of $G0'G0$ . Default as FALSE.

**Value**

An object of the hJAM with egger regression results.

**Exposure** The intermediates, such as the modifiable risk factors in Mendelian Randomization and gene expression in transcriptome analysis.

**numSNP** The number of SNPs that the user use in the instrument set.

**Estimate** The conditional estimates of the associations between intermediates and the outcome.

**StdErr** The standard error of the conditional estimates of the associations between intermediates and the outcome.

**Lower.CI** The lower bound of the 95% confidence interval of the estimates.

**Upper.CI** The upper bound of the 95% confidence interval of the estimates.

**Pvalue** The p value of the estimates with a type-I error equals 0.05.

**Est.Int** The intercept of the regression of intermediates on the outcome.

**StdErr.Int** The standard error of the intercept of the regression of intermediates on the outcome.

**Lower.CI.Int** The lower bound of the 95% confidence interval of the intercept.

**Upper.CI.Int** The upper bound of the 95% confidence interval of the intercept.

**Pvalue.Int** The p value of the intercept with a type-I error equals 0.05.

An object of hJAM with egger regression results.

**Author(s)**

Lai Jiang

**References**

Lai Jiang, Shujing Xu, Nicholas Mancuso, Paul J. Newcombe, David V. Conti (2020). A Hierarchical Approach Using Marginal Summary Statistics for Multiple Intermediates in a Mendelian Randomization or Transcriptome Analysis. *bioRxiv* <https://doi.org/10.1101/2020.02.03.924241>.

**Examples**

```
data(G1)
data(betas.Gy)
data(conditional_A)
hJAM_egger(betas.Gy = betas.Gy, G1 = G1, N.Gy = 459324, A = conditional_A, ridgeTerm = TRUE)
```

---

hJAM_Inreg	<i>Fit hJAM with linear regression</i>
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---

**Description**

The hJAM function is to get the results from the hJAM model using input data

**Usage**

```
hJAM_Inreg(betas.Gy, N.Gy, G1, A, ridgeTerm = FALSE)
```

**Arguments**

betas.Gy	The betas in the paper: the marginal effects of SNPs on the phenotype (Gy)
N.Gy	The sample size of Gy
G1	The reference panel (G1), such as 1000 Genome
A	The A matrix in the paper: the marginal/conditional effects of SNPs on the exposures (Gx)
ridgeTerm	ridgeTerm = TRUE when the matrix L is singular. Matrix L is obtained from the cholesky decomposition of $G0'G0$ . Default as FALSE.

**Value**

An object of the hJAM with linear regression results.

**Exposure** The intermediates, such as the modifiable risk factors in Mendelian Randomization and gene expression in transcriptome analysis.

**numSNP** The number of SNPs that the user use in the instrument set.

**Estimate** The conditional estimates of the associations between intermediates and the outcome.

**StdErr** The standard error of the conditional estimates of the associations between intermediates and the outcome.

**Lower.CI** The lower bound of the 95% confidence interval of the estimates.

**Upper.CI** The upper bound of the 95% confidence interval of the estimates.

**Pvalue** The p value of the estimates with a type-I error equals 0.05.

**Author(s)**

Lai Jiang

**References**

Lai Jiang, Shujing Xu, Nicholas Mancuso, Paul J. Newcombe, David V. Conti (2020). A Hierarchical Approach Using Marginal Summary Statistics for Multiple Intermediates in a Mendelian Randomization or Transcriptome Analysis. *bioRxiv* <https://doi.org/10.1101/2020.02.03.924241>.

**Examples**

```
data(G1)
data(betas.Gy)
data(conditional_A)
hJAM_lgreg(betas.Gy = betas.Gy, G1 = G1, N.Gy = 459324, A = conditional_A, ridgeTerm = TRUE)
```

---

marginal_A	<i>Example marginal A matrix of hJAM</i>
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---

**Description**

Example marginal A matrix of hJAM

**Usage**

```
marginal_A
```

**Format**

The `marginal_A` is the marginal estimates alpha matrix in the hJAM model: the association estimates between 210 SNPs and body mass index (BMI) and type 2 diabetes (T2D). The summary data was collected from GIANT consortium (n=339,224) and DIAGRAM+GERA+UKB (n=659316) for BMI and T2D, respectively.

**References**

1. Locke AE, Kahali B, Berndt SI, et al. Genetic studies of body mass index yield new insights for obesity biology. *Nature* 2015; 518: 197-206.
2. Xue A, Wu Y, Zhu Z, et al. Genome-wide association analyses identify 143 risk variants and putative regulatory mechanisms for type 2 diabetes. *Nat Commun* 2018; 9: 2941.

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output.format	<i>Keep the output as three digits</i>
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---

**Description**

Keep the output as three digits

**Usage**

```
output.format(x, ...)
```

**Arguments**

x	input
...	other options you want to put in

**Author(s)**

Lai Jiang

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*print.hJAM\_egger*      *Print out for hJAM\_egger*

---

**Description**

Print out for hJAM\_egger

**Usage**

```
## S3 method for class 'hJAM_egger'  
print(x, ...)
```

**Arguments**

x                    input  
...                  other options you want to put in

**Author(s)**

Lai Jiang

---

*print.hJAM\_lgreg*      *Print out for hJAM\_lgreg*

---

**Description**

Print out for hJAM\_lgreg

**Usage**

```
## S3 method for class 'hJAM_lgreg'  
print(x, ...)
```

**Arguments**

x                    input  
...                  other options you want to put in

**Author(s)**

Lai Jiang

SNPs\_heatmap

*Heatmap for all the SNPs used in the analysis*

---

**Description**

To generate the heatmap of all the SNPs that the user use in the analysis

**Usage**

```
SNPs_heatmap(G1)
```

**Arguments**

G1                    The reference panel (G1) of the SNPs that the user use in the analysis, such as 1000 Genome

**Author(s)**

Lai Jiang

**Examples**

```
data(G1)
t = SNPs_heatmap(G1 = G1)
t
```

---

SNPs\_info

*Example SNPs' information of hJAM*

---

**Description**

Example SNPs' information of hJAM

**Usage**

```
SNPs_info
```

**Format**

The SNPs\_info is the information of the 210 SNPs that we used in this data example. It includes three columns: the rsID, major allele, and minor allele frequency of each SNP. The minor allele frequencies were calculated in the 503 European-ancestry subjects in 1000 Genome project.

**References**

Consortium GP. A global reference for human genetic variation. Nature 2015; 526: 68.

---

SNPs\_scatter\_plot      *Scatter plot for all the SNPs used in the analysis*

---

**Description**

To generate the scatter plot of all the SNPs that the user use in the analysis

**Usage**

```
SNPs_scatter_plot(A, betas.Gy, num_X)
```

**Arguments**

A	The effects of SNPs on the exposures (Gx).
betas.Gy	The betas in the paper: the marginal effects of SNPs on the phenotype (Gy)
num_X	The number of intermediates in the research question.

**Value**

A set of scatter plots with x-axis being the conditional  $\alpha$  estimates for each intermediate and y-axis being the  $\beta$  estimates.

**Author(s)**

Lai Jiang

**Examples**

```
data(conditional_A)
data(betas.Gy)
t = SNPs_scatter_plot(A = conditional_A, betas.Gy = betas.Gy, num_X = 2)
t
```

# Index

## \* datasets

- betas.Gy, [2](#)
- conditional\_A, [2](#)
- Gl, [5](#)
- marginal\_A, [8](#)
- SNPs\_info, [10](#)

betas.Gy, [2](#)

conditional\_A, [2](#)

get\_cond\_A, [3](#)

get\_cond\_alpha, [4](#)

Gl, [5](#)

hJAM\_egger, [5](#)

hJAM\_lnreg, [7](#)

marginal\_A, [8](#)

output.format, [8](#)

print.hJAM\_egger, [9](#)

print.hJAM\_lnreg, [9](#)

SNPs\_heatmap, [10](#)

SNPs\_info, [10](#)

SNPs\_scatter\_plot, [11](#)