

# Package ‘r2redux’

July 23, 2025

**Title** R2 Statistic

**Version** 1.0.18

**Description** R2 statistic for significance test. Variance and covariance of R2 values used to assess the 95% CI and p-value of the R2 difference.

**License** GPL (>= 3)

**URL** <https://github.com/mommy003/r2redux>

**Encoding** UTF-8

**RoxygenNote** 7.1.2

**NeedsCompilation** no

**Depends** R (>= 2.10)

**LazyData** true

**Suggests** testthat (>= 3.0.0)

**Config/testthat/edition** 3

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|        |                        |
|--------|------------------------|
| cc_trf | <i>cc_trf function</i> |
|--------|------------------------|

---

**Description**

This function transforms the predictive ability (R2) and its standard error (se) between the observed scale and liability scale

**Usage**

cc\_trf(R2, se, K, P)

**Arguments**

|    |                                                                       |
|----|-----------------------------------------------------------------------|
| R2 | R2 or coefficient of determination on the observed or liability scale |
| se | Standard error of R2                                                  |
| K  | Population prevalence                                                 |
| P  | The ratio of cases in the study samples                               |

**Value**

This function will transform the R2 and its s.e between observed scale and liability scale. Output from the command is the lists of outcomes.

|     |                                       |
|-----|---------------------------------------|
| R2l | Transformed R2 on the liability scale |
| se1 | Transformed se on the liability scale |
| R20 | Transformed R2 on the observed scale  |
| se0 | Transformed se on the observed scale  |

**References**

Lee, S. H., Goddard, M. E., Wray, N. R., and Visscher, P. M. A better coefficient of determination for genetic profile analysis. Genetic epidemiology,(2012). 36(3): p. 214-224.

**Examples**

```
#To get the transformed R2

output=cc_trf(0.06, 0.002, 0.05, 0.05)
output

#output$R2l (transformed R2 on the liability scale)
#0.2679337

#output$se1 (transformed se on the liability scale)
#0.008931123

#output$R20 (transformed R2 on the observed scale)
#0.01343616

#output$se0 (transformed se on the observed scale)
#0.000447872
```

---

|      |                                       |
|------|---------------------------------------|
| dat1 | <i>Phenotypes and 10 sets of PGSs</i> |
|------|---------------------------------------|

---

**Description**

A dataset containing phenotypes and multiple PGSs estimated from 10 sets of SNPs according to GWAS p-value thresholds

**Usage**

```
dat1
```

**Format**

A data frame with 1000 rows and 11 variables:

- V1** Phenotype, value
- V2** PGS1, for p value threshold  $\leq 1$
- V3** PGS2, for p value threshold  $\leq 0.5$
- V4** PGS3, for p value threshold  $\leq 0.4$
- V5** PGS4, for p value threshold  $\leq 0.3$
- V6** PGS5, for p value threshold  $\leq 0.2$
- V7** PGS6, for p value threshold  $\leq 0.1$
- V8** PGS7, for p value threshold  $\leq 0.05$
- V9** PGS8, for p value threshold  $\leq 0.01$
- V10** PGS9, for p value threshold  $\leq 0.001$
- V11** PGS10, for p value threshold  $\leq 0.0001$

---

|      |                                      |
|------|--------------------------------------|
| dat2 | <i>Phenotypes and 2 sets of PGSs</i> |
|------|--------------------------------------|

---

**Description**

A dataset containing phenotypes and 2 sets of PGSs estimated from 2 sets of SNPs from regulatory and non-regulatory genomic regions

**Usage**

```
dat2
```

**Format**

A data frame with 1000 rows and 3 variables:

**V1** Phenotype

**V2** PGS1, regulatory region

**V3** PGS2, non-regulatory region

---

|           |                           |
|-----------|---------------------------|
| olkin12_1 | <i>olkin12_1 function</i> |
|-----------|---------------------------|

---

**Description**

olkin12\_1 function

**Usage**

```
olkin12_1(omat, nv)
```

**Arguments**

|      |                                                                                                                                                                                                |
|------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| omat | 3 by 3 matrix having the correlation coefficients between y, x1 and x2, i.e. $\text{omat} = \text{cor}(\text{dat})$ where dat is N by 3 matrix having variables in the order of cbind(y,x1,x2) |
| nv   | Sample size                                                                                                                                                                                    |

**Value**

This function will be used as source code

---

olkin12\_13*olkin12\_13 function*

---

**Description**

olkin12\_13 function

**Usage**

olkin12\_13(omat, nv)

**Arguments**

|      |                                                                                                                                                                       |
|------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| omat | 3 by 3 matrix having the correlation coefficients between y, x1 and x2, i.e. omat=cor(dat) where dat is N by 3 matrix having variables in the order of cbind(y,x1,x2) |
| nv   | Sample size                                                                                                                                                           |

**Value**

This function will be used as source code

---

olkin12\_3*olkin12\_3 function*

---

**Description**

olkin12\_3 function

**Usage**

olkin12\_3(omat, nv)

**Arguments**

|      |                                                                                                                                                                       |
|------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| omat | 3 by 3 matrix having the correlation coefficients between y, x1 and x2, i.e. omat=cor(dat) where dat is N by 3 matrix having variables in the order of cbind(y,x1,x2) |
| nv   | Sample size                                                                                                                                                           |

**Value**

This function will be used as source code

---

olkin12\_34

*olkin12\_34 function*


---

**Description**

olkin12\_34 function

**Usage**

olkin12\_34(omat, nv)

**Arguments**

|      |                                                                                                                                                                       |
|------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| omat | 3 by 3 matrix having the correlation coefficients between y, x1 and x2, i.e. omat=cor(dat) where dat is N by 3 matrix having variables in the order of cbind(y,x1,x2) |
| nv   | Sample size                                                                                                                                                           |

**Value**
This function will be used as source code

---

olkin1\_2

*olkin1\_2 function*


---

**Description**

olkin1\_2 function

**Usage**

olkin1\_2(omat, nv)

**Arguments**

|      |                                                                                                                                                                       |
|------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| omat | 3 by 3 matrix having the correlation coefficients between y, x1 and x2, i.e. omat=cor(dat) where dat is N by 3 matrix having variables in the order of cbind(y,x1,x2) |
| nv   | Sample size                                                                                                                                                           |

**Value**

This function will be used as source code

olkin\_beta1\_2

*olkin\_beta1\_2 function***Description**

This function derives Information matrix for  $\beta_1^2$  and  $\beta_2^2$  where  $\beta_1$  and  $\beta_2$  are regression coefficients from a multiple regression model, i.e.  $y = x_1 * \beta_1 + x_2 * \beta_2 + e$ , where  $y$ ,  $x_1$  and  $x_2$  are column-standardised, (i.e. in the context of correlation coefficients, see Olkin and Finn 1995).

**Usage**

```
olkin_beta1_2(omat, nv)
```

**Arguments**

|      |                                                                                                                                                                                                                                  |
|------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| omat | 3 by 3 matrix having the correlation coefficients between $y$ , $x_1$ and $x_2$ , i.e. $\text{omat} = \text{cor}(\text{dat})$ where $\text{dat}$ is $N$ by 3 matrix having variables in the order of $\text{cbind}(y, x_1, x_2)$ |
| nv   | Sample size                                                                                                                                                                                                                      |

**Value**

This function will give information (variance-covariance) matrix of  $\beta_1^2$  and  $\beta_2^2$ . To get information (variance-covariance) matrix of  $\beta_1^2$  and  $\beta_2^2$ . Where  $\beta_1$  and  $\beta_2$  are regression coefficients from a multiple regression model. The outputs are listed as follows.

|        |                                                            |
|--------|------------------------------------------------------------|
| info   | 2x2 information (variance-covariance) matrix               |
| var1   | Variance of $\beta_1^2$                                    |
| var2   | Variance of $\beta_2^2$                                    |
| var1_2 | Variance of difference between $\beta_1^2$ and $\beta_2^2$ |

**References**

Olkin, I. and Finn, J.D. Correlations redux. Psychological Bulletin, 1995. 118(1): p. 155.

**Examples**

```
#To get information (variance-covariance) matrix of beta1_2 and beta2_2 where
#beta1 and 2 are regression coefficients from a multiple regression model.
dat=dat1
omat=cor(dat)[1:3,1:3]
#omat
#1.0000000 0.1958636 0.1970060
#0.1958636 1.0000000 0.9981003
#0.1970060 0.9981003 1.0000000
```

```

nv=length(dat$V1)
output=olkin_beta1_2(omat,nv)
output

#output$info (2x2 information (variance-covariance) matrix)
#0.04146276 0.08158261
#0.08158261 0.16111124

#output$var1 (variance of beta1_2)
#0.04146276

#output$var2 (variance of beta2_2)
#0.1611112

#output$var1_2 (variance of difference between beta1_2 and beta2_2)
#0.03940878

```

---

|                |                                |
|----------------|--------------------------------|
| olkin_beta_inf | <i>olkin_beta_inf function</i> |
|----------------|--------------------------------|

---

## Description

This function derives Information matrix for beta1 and beta2 where beta1 and 2 are regression coefficients from a multiple regression model, i.e.  $y = x1 * \beta1 + x2 * \beta2 + e$ , where y, x1 and x2 are column-standardised (see Olkin and Finn 1995).

## Usage

```
olkin_beta_inf(omat, nv)
```

## Arguments

|      |                                                                                                                                                                           |
|------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| omat | 3 by 3 matrix having the correlation coefficients between y, x1 and x2, i.e. $omat = cor(dat)$ where dat is N by 3 matrix having variables in the order of cbind(y,x1,x2) |
| nv   | Sample size                                                                                                                                                               |

## Value

This function will generate information (variance-covariance) matrix of beta1 and beta2. The outputs are listed as follows.

|        |                                                |
|--------|------------------------------------------------|
| info   | 2x2 information (variance-covariance) matrix   |
| var1   | Variance of beta1                              |
| var2   | Variance of beta2                              |
| var1_2 | Variance of difference between beta1 and beta2 |

## References

Olkin, I. and Finn, J.D. Correlations redux. Psychological Bulletin, 1995. 118(1): p. 155.

## Examples

```
#To get information (variance-covariance) matrix of beta1 and beta2 where
#beta1 and 2 are regression coefficients from a multiple regression model.
dat=dat1
omat=cor(dat)[1:3,1:3]
#omat
#1.0000000 0.1958636 0.1970060
#0.1958636 1.0000000 0.9981003
#0.1970060 0.9981003 1.0000000

nv=length(dat$V1)
output=olkin_beta_inf(omat,nv)
output

#output$info (2x2 information (variance-covariance) matrix)
#0.2531406 -0.2526212
#-0.2526212 0.2530269

#output$var1 (variance of beta1)
#0.2531406

#output$var2 (variance of beta2)
#0.2530269

#output$var1_2 (variance of difference between beta1 and beta2)
#1.01141
```

---

|                  |                                  |
|------------------|----------------------------------|
| olkin_beta_ratio | <i>olkin_beta_ratio function</i> |
|------------------|----------------------------------|

---

## Description

This function derives variance of  $\beta_1^2 / R^2$  where  $\beta_1$  and 2 are regression coefficients from a multiple regression model, i.e.  $y = x_1 * \beta_1 + x_2 * \beta_2 + e$ , where  $y$ ,  $x_1$  and  $x_2$  are column-standardised (see Olkin and Finn 1995).

## Usage

```
olkin_beta_ratio(omat, nv)
```

## Arguments

|      |                                                                                                                                                                                                                            |
|------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| omat | 3 by 3 matrix having the correlation coefficients between $y$ , $x_1$ and $x_2$ , i.e. $\text{omat}=\text{cor}(\text{dat})$ where $\text{dat}$ is N by 3 matrix having variables in the order of $\text{cbind}(y,x_1,x_2)$ |
| nv   | sampel size                                                                                                                                                                                                                |

**Value**

This function will generate the variance of the proportion, i.e.  $\text{beta1}_2/R^2$ .The outputs are listed as follows.

ratio\_var            Variance of ratio

**References**

Olkin, I. and Finn, J.D. Correlations redux. Psychological Bulletin, 1995. 118(1): p. 155.

**Examples**

```
#To get information (variance-covariance) matrix of beta1 and beta2 where
#beta1 and 2 are regression coefficients from a multiple regression model.
dat=dat2
omat=cor(dat)[1:3,1:3]
#omat
#1.0000000 0.1497007 0.136431
#0.1497007 1.0000000 0.622790
#0.1364310 0.6227900 1.000000

nv=length(dat$V1)
output=olkin_beta_ratio(omat,nv)
output

#r2redux output

#output$ratio_var (Variance of ratio)
#0.08042288
```

---

|                    |                    |
|--------------------|--------------------|
| <i>r2_beta_var</i> | <i>r2_beta_var</i> |
|--------------------|--------------------|

---

**Description**

This function estimates  $\text{var}(\text{beta1}^2)$  and  $\text{var}(\text{beta2}^2)$ , and beta1 and 2 are regression coefficients from a multiple regression model, i.e.  $y = x1 * \text{beta1} + x2 * \text{beta2} + e$ , y, x1 and x2 are column-standardised (see Olkin and Finn 1995). y is N by 1 matrix having the dependent variable, x1 is N by 1 matrix having the ith explanatory variable. x2 is N by 1 matrix having the jth explanatory variable. v1 and v2 indicates the ith and jth column in the data (v1 or v2 should be a single interger between 1 - M, see Arguments below).

**Usage**

```
r2_beta_var(dat, v1, v2, nv)
```

**Arguments**

|     |                                                                                      |
|-----|--------------------------------------------------------------------------------------|
| dat | N by (M+1) matrix having variables in the order of cbind(y,x)                        |
| v1  | This can be set as v1=1, v1=2, v1=3 or any value between 1 - M based on combination  |
| v2  | This can be set as v2=1, v2=2, v2=3, or any value between 1 - M based on combination |
| nv  | Sample size                                                                          |

**Value**

This function will estimate the variance of  $\beta_1^2$  and  $\beta_2^2$ , and the covariance between  $\beta_1^2$  and  $\beta_2^2$ , i.e. the information matrix of squared regression coefficients.  $\beta_1$  and  $\beta_2$  are regression coefficients from a multiple regression model, i.e.  $y = x_1 * \beta_1 + x_2 * \beta_2 + e$ , where  $y$ ,  $x_1$  and  $x_2$  are column-standardised. The outputs are listed as follows.

|                |                                                      |
|----------------|------------------------------------------------------|
| beta1_sq       | beta1_sq                                             |
| beta2_sq       | beta2_sq                                             |
| var1           | Variance of beta1_sq                                 |
| var2           | Variance of beta2_sq                                 |
| var1_2         | Variance of difference between beta1_sq and beta2_sq |
| cov            | Covariance between beta1_sq and beta2_sq             |
| upper_beta1_sq | upper limit of 95% CI for beta1_sq                   |
| lower_beta1_sq | lower limit of 95% CI for beta1_sq                   |
| upper_beta2_sq | upper limit of 95% CI for beta2_sq                   |
| lower_beta2_sq | lower limit of 95% CI for beta2_sq                   |

**References**

Olkin, I. and Finn, J.D. Correlations redux. Psychological Bulletin, 1995. 118(1): p. 155.

**Examples**

```
#To get the 95% CI of beta1_sq and beta2_sq
#beta1 and beta2 are regression coefficients from a multiple regression model,
#i.e.  $y = x_1 * \beta_1 + x_2 * \beta_2 + e$ , where  $y$ ,  $x_1$  and  $x_2$  are column-standardised.

dat=dat2
nv=length(dat$V1)
v1=c(1)
v2=c(2)
output=r2_beta_var(dat,v1,v2,nv)
output
#r2redux output
#output$beta1_sq (beta1_sq)
#0.01118301
```

```

#output$beta2_sq (beta2_sq)
#0.004980285

#output$var1 (variance of beta1_sq)
#7.072931e-05

#output$var2 (variance of beta2_sq)
#3.161929e-05

#output$var1_2 (variance of difference between beta1_sq and beta2_sq)
#0.000162113

#output$cov (covariance between beta1_sq and beta2_sq)
#-2.988221e-05

#output$upper_beta1_sq (upper limit of 95% CI for beta1_sq)
#0.03037793

#output$lower_beta1_sq (lower limit of 95% CI for beta1_sq)
#-0.00123582

#output$upper_beta2_sq (upper limit of 95% CI for beta2_sq)
#0.02490076

#output$lower_beta2_sq (lower limit of 95% CI for beta2_sq)
#-0.005127546

```

---

r2\_diff

*r2\_diff function*


---

### Description

This function estimates  $\text{var}(R^2(y \sim x[,v1]) - R^2(y \sim x[,v2]))$  where  $R^2$  is the R squared value of the model,  $y$  is  $N$  by  $1$  matrix having the dependent variable, and  $x$  is  $N$  by  $M$  matrix having  $M$  explanatory variables.  $v1$  or  $v2$  indicates the  $i$ th column in the  $x$  matrix ( $v1$  or  $v2$  can be multiple values between  $1 - M$ , see Arguments below)

### Usage

```
r2_diff(dat, v1, v2, nv)
```

### Arguments

|     |                                                                                                                   |
|-----|-------------------------------------------------------------------------------------------------------------------|
| dat | $N$ by $(M+1)$ matrix having variables in the order of <code>cbind(y,x)</code>                                    |
| v1  | This can be set as <code>v1=c(1)</code> or <code>v1=c(1,2)</code>                                                 |
| v2  | This can be set as <code>v2=c(2)</code> , <code>v2=c(3)</code> , <code>v2=c(1,3)</code> or <code>v2=c(3,4)</code> |
| nv  | Sample size                                                                                                       |

**Value**

This function will estimate significant difference between two PGS (either dependent or independent and joint or single). To get the test statistics for the difference between  $R2(y \sim x[,v1])$  and  $R2(y \sim x[,v2])$ . (here we define  $R2\_1 = R2(y \sim x[,v1])$  and  $R2\_2 = R2(y \sim x[,v2])$ ). The outputs are listed as follows.

|                     |                                                                     |
|---------------------|---------------------------------------------------------------------|
| rsq1                | R2_1                                                                |
| rsq2                | R2_2                                                                |
| var1                | Variance of R2_1                                                    |
| var2                | variance of R2_2                                                    |
| var_diff            | Variance of difference between R2_1 and R2_2                        |
| r2_based_p          | two tailed P-value for significant difference between R2_1 and R2_2 |
| r2_based_p_one_tail | one tailed P-value for significant difference                       |
| mean_diff           | Differences between R2_1 and R2_2                                   |
| upper_diff          | Upper limit of 95% CI for the difference                            |
| lower_diff          | Lower limit of 95% CI for the difference                            |

**Examples**

#To get the test statistics for the difference between  $R2(y \sim x[,1])$  and  $R2(y \sim x[,2])$ . (here we define  $R2\_1 = R2(y \sim x[,1])$  and  $R2\_2 = R2(y \sim x[,2])$ )

```
dat=dat1
nv=length(dat$V1)
v1=c(1)
v2=c(2)
output=r2_diff(dat,v1,v2,nv)
output

#r2redux output

#output$rsq1 (R2_1)
#0.03836254

#output$rsq2 (R2_2)
#0.03881135

#output$var1 (variance of R2_1)
#0.0001436128

#output$var2 (variance of R2_2)
#0.0001451358

#output$var_diff (variance of difference between R2_1 and R2_2)
#5.678517e-07

#output$r2_based_p (two tailed p-value for significant difference)
```

```

#0.5514562

#output$r2_based_p_one_tail(one tailed p-value for significant difference)
#0.2757281

#output$mean_diff (differences between R2_1 and R2_2)
#-0.0004488044

#output$upper_diff (upper limit of 95% CI for the difference)
#0.001028172

#output$lower_diff (lower limit of 95% CI for the difference)
#-0.001925781

#output$$p$nested
#1

#output$$p$nonnested
#0.5514562

#output$$p$LRT
#1

#To get the test statistics for the difference between  $R^2(y \sim x[,1] + x[,2])$  and
 $R^2(y \sim x[,2])$ . (here  $R2\_1 = R^2(y \sim x[,1] + x[,2])$  and  $R2\_2 = R^2(y \sim x[,1])$ )

dat=dat1
nv=length(dat$V1)
v1=c(1,2)
v2=c(1)
output=r2_diff(dat,v1,v2,nv)

#r2redux output

#output$rsq1 (R2_1)
#0.03896678

#output$rsq2 (R2_2)
#0.03836254

#output$var1 (variance of R2_1)
#0.0001473686

#output$var2 (variance of R2_2)
#0.0001436128

#output$var_diff (variance of difference between R2_1 and R2_2)
#2.321425e-06

#output$r2_based_p (p-value for significant difference between R2_1 and R2_2)
#0.4366883

#output$mean_diff (differences between R2_1 and R2_2)

```

```

#0.0006042383

#output$upper_diff (upper limit of 95% CI for the difference)
#0.00488788

#output$lower_diff (lower limit of 95% CI for the difference)
#-0.0005576171

#Note: If the directions are not consistent, for instance, if one correlation
#is positive (R_1) and another is negative (R_2), or vice versa, it is crucial
#to approach the interpretation of the comparative test with caution.
#It's important to note that R^2 alone does not provide information about the
#direction or sign of the relationships between predictors and the response variable.

#When faced with multiple predictors common between two models, for example,
#y = any_cov1 + any_cov2 + ... + any_covN + e vs.
#y = PRS + any_cov1 + any_cov2 +...+ any_covN + e

#A more streamlined approach can be adopted by consolidating the various
#predictors into a single predictor (see R code below).

#R
#dat=dat1
#here let's assume, we wanted to test one PRS (dat$V2)
#with 5 covariates (dat$V7 to dat$V11)
#mod1 <- lm(dat$V1~dat$V2 + dat$V7+ dat$V8+ dat$V9+ dat$V10+ dat$V11)
#merged_predictor1 <- mod1$fitted.values
#mod2 <- lm(dat$V1~ dat$V7+ dat$V8+ dat$V9+ dat$V10+ dat$V11)
#merged_predictor2 <- mod2$fitted.values
#dat=data.frame(dat$V1,merged_predictor1,merged_predictor2)

#the comparison can be equivalently expressed as:
#y = merged_predictor1 + e vs.
#y = merged_predictor2 + e

#This comparison can be simply achieved using the r2_diff function, e.g.

#To get the test statistics for the difference between R2(y~x[,1]) and
#R2(y~x[,2]). (here x[,1]= merged_predictor2 (from full model),
#and x[,2]= merged_predictor1(from reduced model))
#v1=c(1)
#v2=c(2)
#output=r2_diff(dat,v1,v2,nv)
#note that the merged predictor from the full model (v1) should be the first.

#str(output)
#List of 11
#$ rsq1 : num 0.0428
#$ rsq2 : num 0.042
#$ var1 : num 0.0.000158
#$ var2 : num 0.0.000156

```

```

#$ var_diff          : num 2.87e-06
#$ r2_based_p        : num 0.658
#$ r2_based_p_one_tail: num 0.329
#$ mean_diff         : num 0.000751
#$ upper_diff        : num 0.00407
#$ lower_diff        : num -0.00257
#$ p                 :List of 3
#..$ nested         : num 0.386
#..$ nonnested       : num 0.658
#..$ LRT             : num 0.376

```

#Importantly note that in this case, merged\_predictor1 is nested within merged\_predictor2 (see mod1 vs. mod2 above). Therefore, this is a nested model comparison. So, output\$p\$nested (0.386) should be used instead of output\$p\$nonnested (0.658).  
 #Note that r2\_based\_p is the same as output\$p\$nonnested (0.658) here.

##For this scenario, alternatively, the outcome variable (y) can be preadjusted with covariate(s), following the procedure in R:

```

#mod <- lm(y ~ any_cov1 + any_cov2 + ... + any_covN)
#y_adj=scale(mod$residuals)
#then, the comparative significance test can be approximated by using
#the following model y_adj = PRS (r2_var(dat, v1, nv))

```

```

#R
#dat=dat1
#mod <- lm(dat$V1~dat$V7+ dat$V8+ dat$V9+ dat$V10+ dat$V11)
#y_adj=scale(mod$residuals)
#dat=data.frame(y_adj,dat$V2)
#v1=c(1)
#output=r2_var(dat, v1, nv)

#str(output)
#$ var          : num 2e-06
#$ LRT_p        :Class 'logLik' : 0.98 (df=2)
#$ r2_based_p: num 0.977
#$ rsq          : num 8.21e-07
#$ upper_r2     : num 0.00403
#$ lower_r2     : num -0.000999

```

#In another scenario where the same covariates, but different PRS1 and PRS2 are compared,  
 #y = PRS1 + any\_cov1 + any\_cov2 + ... + any\_covN + e vs.  
 #y = PRS2 + any\_cov1 + any\_cov2 + ... + any\_covN + e

#following approach can be employed (see R code below).

```

#R
#dat=dat1

```

```

#here let's assume dat$V2 as PRS1, dat$V3 as PRS2 and dat$V7 to dat$V11 as covariates
#mod1 <- lm(dat$V1~dat$V2 + dat$V7+ dat$V8+ dat$V9+ dat$V10+ dat$V11)
#merged_predictor1 <- mod1$fitted.values
#mod2 <- lm(dat$V1~dat$V3 + dat$V7+ dat$V8+ dat$V9+ dat$V10+ dat$V11)
#merged_predictor2 <- mod2$fitted.values
#dat=data.frame(dat$V1,merged_predictor2,merged_predictor1)

#the comparison can be equivalently expressed as:
#y = merged_predictor1 + e    vs.
#y = merged_predictor2 + e

#This comparison can be simply achieved using the r2_diff function, e.g.

#To get the test statistics for the difference between R2(y~x[,1]) and
#R2(y~x[,2]). (here x[,1]= merged_predictor2, and x[,2]= merged_predictor1)
#v1=c(1)
#v2=c(2)
#output=r2_diff(dat,v1,v2,nv)

#str(output)
#List of 11
#$ rsq1          : num 0.043
#$ rsq2          : num 0.0428
#$ var1          : num 0.000159
#$ var2          : num 0.000158
#$ var_diff      : num 2.6e-07
#$ r2_based_p    : num 0.657
#$ r2_based_p_one_tail: num 0.328
#$ mean_diff     : num 0.000227
#$ upper_diff    : num 0.00123
#$ lower_diff    : num 0.000773
#$ p             :List of 3
#..$ nested     : num 0.634
#..$ nonnested  : num 0.657
#..$ LRT        : num 0.627

#Importantly note that in this case, merged_predictor1 and merged_predictor2
#are not nested to each other (see mod1 vs. mod2 above).
#Therefore, this is nonnested model comparison.
#So, output$p$nonnested (0.657) should be used instead of
#output$p$nested (0.634). Note that r2_based_p is the same
#as output$p$nonnested (0.657) here.

#For the above non-nested scenario, alternatively, the outcome variable (y)
#can be preadjusted with covariate(s), following the procedure in R:
#mod <- lm(y ~ any_cov1 + any_cov2 + ... + any_covN)
#y_adj=scale(mod$residuals)

#R
#dat=dat1
#mod <- lm(dat$V1~dat$V7+ dat$V8+ dat$V9+ dat$V10+ dat$V11)
#y_adj=scale(mod$residuals)

```

```

#dat=data.frame(y_adj,dat$V3,dat$V2)

#the comparison can be equivalently expressed as:
#y_adj = PRS1 + e   vs.
#y_adj = PRS2 + e
#then, the comparative significance test can be approximated by using r2_diff function
#To get the test statistics for the difference between R2(y~x[,1]) and
#R2(y~x[,2]). (here x[,1]= PRS1 and x[,2]= PRS2)
#v1=c(1)
#v2=c(2)
#output=r2_diff(dat,v1,v2,nv)

#str(output)
#List of 11
#$ rsq1          : num 5.16e-05
#$ rsq2          : num 4.63e-05
#$ var1          : num 2.21e-06
#$ var2          : num 2.18e-06
#$ var_diff      : num 1.31e-09
#$ r2_based_p    : num 0.884
#$ r2_based_p_one_tail: num 0.442
#$ mean_diff     : num 5.28e-06
#$ upper_diff    : num 7.63e-05
#$ lower_diff    : num -6.57e-05
#$ p             :List of 3
#..$ nested     : num 0.942
#..$ nonnested  : num 0.884
#..$ LRT        : num 0.942

```

---

r2\_enrich\_beta

*r2\_enrich\_beta*


---

## Description

This function estimates  $\text{var}(\beta_1^2/R^2)$ ,  $\beta_1$  and  $R^2$  are regression coefficient and the coefficient of determination from a multiple regression model, i.e.  $y = x_1 * \beta_1 + x_2 * \beta_2 + e$ , where  $y$ ,  $x_1$  and  $x_2$  are column-standardised (see Olkin and Finn 1995).  $y$  is N by 1 matrix having the dependent variable, and  $x_1$  is N by 1 matrix having the  $i$ th explanatory variables.  $x_2$  is N by 1 matrix having the  $j$ th explanatory variables.  $v_1$  and  $v_2$  indicates the  $i$ th and  $j$ th column in the data ( $v_1$  or  $v_2$  should be a single interger between 1 - M, see Arguments below).

## Usage

```
r2_enrich_beta(dat, v1, v2, nv, exp1)
```

## Arguments

**dat**                      N by (M+1) matrix having variables in the order of `cbind(y,x)`

|      |                                                                                       |
|------|---------------------------------------------------------------------------------------|
| v1   | These can be set as v1=1, v1=2, v1=3 or any value between 1 - M based on combination  |
| v2   | These can be set as v2=1, v2=2, v2=3, or any value between 1 - M based on combination |
| nv   | Sample size                                                                           |
| exp1 | The expectation of the ratio (e.g. ratio of # SNPs in genomic partitioning)           |

### Value

This function will estimate  $\text{var}(\beta_1^2/R^2)$ ,  $\beta_1$  and  $R^2$  are regression coefficient and the coefficient of determination from a multiple regression model, i.e.  $y = x_1 * \beta_1 + x_2 * \beta_2 + e$ , where  $y$ ,  $x_1$  and  $x_2$  are column-standardised. The outputs are listed as follows.

|                    |                                                                              |
|--------------------|------------------------------------------------------------------------------|
| beta1_sq           | beta1_sq                                                                     |
| beta2_sq           | beta2_sq                                                                     |
| ratio1             | beta1_sq/R^2                                                                 |
| ratio2             | beta2_sq/R^2                                                                 |
| ratio_var1         | variance of ratio 1                                                          |
| ratio_var2         | variance of ratio 2                                                          |
| upper_ratio1       | upper limit of 95% CI for ratio 1                                            |
| lower_ratio1       | lower limit of 95% CI for ratio 1                                            |
| upper_ratio2       | upper limit of 95% CI for ratio 2                                            |
| lower_ratio2       | lower limit of 95% CI for ratio 2                                            |
| enrich_p1          | two tailed P-value for beta1_sq/R^2 is significantly different from exp1     |
| enrich_p1_one_tail | one tailed P-value for beta1_sq/R^2 is significantly different from exp1     |
| enrich_p2          | P-value for beta2_sq/R^2 is significantly different from (1-exp1)            |
| enrich_p2_one_tail | one tailed P-value for beta2_sq/R^2 is significantly different from (1-exp1) |

### References

Olkin, I. and Finn, J.D. Correlations redux. Psychological Bulletin, 1995. 118(1): p. 155.

### Examples

```
#To get the test statistic for the ratio which is significantly
#different from the expectation, this function estimates
#var (beta1^2/R^2), where
#beta1^2 and R^2 are regression coefficients and the
#coefficient of determination from a multiple regression model,
#i.e. y = x1 * beta1 + x2 * beta2 + e, where y, x1 and x2 are
#column-standardised.

dat=dat2
nv=length(dat$V1)
```

```
v1=c(1)
v2=c(2)
expected_ratio=0.04
output=r2_enrich_beta(dat,v1,v2,nv,expected_ratio)
output

#r2redux output

#output$beta1_sq (beta1_sq)
#0.01118301

#output$beta2_sq (beta2_sq)
#0.004980285

#output$ratio1 (beta1_sq/R^2)
#0.4392572

#output$ratio2 (beta2_sq/R^2)
#0.1956205

#output$ratio_var1 (variance of ratio 1)
#0.08042288

#output$ratio_var2 (variance of ratio 2)
#0.0431134

#output$upper_ratio1 (upper limit of 95% CI for ratio 1)
#0.9950922

#output$lower_ratio1 (lower limit of 95% CI for ratio 1)
#-0.1165778

#output$upper_ratio2 upper limit of 95% CI for ratio 2)
#0.6025904

#output$lower_ratio2 (lower limit of 95% CI for ratio 2)
#-0.2113493

#output$enrich_p1 (two tailed P-value for beta1_sq/R^2 is
#significantly different from exp1)
#0.1591692

#output$enrich_p1_one_tail (one tailed P-value for beta1_sq/R^2
#is significantly different from exp1)
#0.07958459

#output$enrich_p2 (two tailed P-value for beta2_sq/R2 is
#significantly different from (1-exp1))
#0.000232035

#output$enrich_p2_one_tail (one tailed P-value for beta2_sq/R2
#is significantly different from (1-exp1))
#0.0001160175
```

r2\_var

*r2\_var function***Description**

This function estimates  $\text{var}(R^2(y \sim x[,v1]))$  where  $R^2$  is the R squared value of the model, where  $R^2$  is the R squared value of the model,  $y$  is  $N$  by  $1$  matrix having the dependent variable, and  $x$  is  $N$  by  $M$  matrix having  $M$  explanatory variables.  $v1$  indicates the  $i$ th column in the  $x$  matrix ( $v1$  can be multiple values between  $1 - M$ , see Arguments below)

**Usage**

```
r2_var(dat, v1, nv)
```

**Arguments**

|                  |                                                                                               |
|------------------|-----------------------------------------------------------------------------------------------|
| <code>dat</code> | $N$ by $(M+1)$ matrix having variables in the order of <code>cbind(y,x)</code>                |
| <code>v1</code>  | This can be set as <code>v1=c(1)</code> , <code>v1=c(1,2)</code> or possibly with more values |
| <code>nv</code>  | Sample size                                                                                   |

**Value**

This function will test the null hypothesis for  $R^2$ . To get the test statistics for  $R^2(y \sim x[,v1])$ . The outputs are listed as follows.

|                         |                                                 |
|-------------------------|-------------------------------------------------|
| <code>rsq</code>        | $R^2$                                           |
| <code>var</code>        | Variance of $R^2$                               |
| <code>r2_based_p</code> | P-value under the null hypothesis, i.e. $R^2=0$ |
| <code>upper_r2</code>   | Upper limit of 95% CI for $R^2$                 |
| <code>lower_r2</code>   | Lower limit of 95% CI for $R^2$                 |

**Examples**

```
#To get the test statistics for R2(y~x[,1])
dat=dat1
nv=length(dat$V1)
v1=c(1)
output=r2_var(dat,v1,nv)
output

#r2redux output

#output$rsq (R2)
#0.03836254

#output$var (variance of R2)
#0.0001436128
```

```

#output$r2_based_p (P-value under the null hypothesis, i.e. R2=0)
#1.188162e-10

#output$upper_r2 (upper limit of 95% CI for R2)
#0.06433782

#output$lower_r2 (lower limit of 95% CI for R2)
#0.01764252

#To get the test statistic for R2(y~x[,1]+x[,2]+x[,3])

dat=dat1
nv=length(dat$V1)
v1=c(1,2,3)
r2_var(dat,v1,nv)

#r2redux output

#output$rsq (R2)
#0.03836254

#output$var (variance of R2)
#0.0001436128

#output$r2_based_p (R2 based P-value)
#1.188162e-10

#output$upper_r2 (upper limit of 95% CI for R2)
#0.06433782

#output$lower_r2 (lower limit of 95% CI for R2)
#0.0176425

#When comparing two independent sets of PGSs
#Let's assume dat1$V1 and dat2$V2 are independent for this example
#(e.g. male PGS vs. female PGS)

nv=length(dat1$V1)
v1=c(1)
output1=r2_var(dat1,v1,nv)
nv=length(dat2$V1)
v1=c(1)
output2=r2_var(dat2,v1,nv)

#To get the difference between two independent sets of PGSs
r2_diff_independent=abs(output1$rsq-output2$rsq)

#To get the variance of the difference between two independent sets of PGSs
var_r2_diff_independent= output1$var+output2$var
sd_r2_diff_independent=sqrt(var_r2_diff_independent)

```

```
#To get p-value (following eq. 15 in the paper)
chi=r2_diff_independent^2/var_r2_diff_independent
p_value=pchisq(chi,1,lower.tail=FALSE)
#to get 95% CI (following eq. 15 in the paper)
uci=r2_diff_independent+1.96*sd_r2_diff_independent
lci=r2_diff_independent-1.96*sd_r2_diff_independent
```

r\_diff

*r\_diff function*

### Description

This function estimates  $\text{var}(R(y \sim x[,v1]) - R(y \sim x[,v2]))$  where  $R$  is the correlation between  $y$  and  $x$ ,  $y$  is  $N$  by  $1$  matrix having the dependent variable, and  $x$  is  $N$  by  $M$  matrix having  $M$  explanatory variables.  $v1$  or  $v2$  indicates the  $i$ th column in the  $x$  matrix ( $v1$  or  $v2$  can be multiple values between  $1 - M$ , see Arguments below)

### Usage

```
r_diff(dat, v1, v2, nv)
```

### Arguments

|     |                                                                                                                   |
|-----|-------------------------------------------------------------------------------------------------------------------|
| dat | $N$ by $(M+1)$ matrix having variables in the order of <code>cbind(y,x)</code>                                    |
| v1  | This can be set as <code>v1=c(1)</code> or <code>v1=c(1,2)</code>                                                 |
| v2  | This can be set as <code>v2=c(2)</code> , <code>v2=c(3)</code> , <code>v2=c(1,3)</code> or <code>v2=c(3,4)</code> |
| nv  | Sample size                                                                                                       |

### Value

This function will estimate significant difference between two PGS (either dependent or independent and joint or single). To get the test statistics for the difference between  $R(y \sim x[,v1])$  and  $R(y \sim x[,v2])$ . (here we define  $R_1 = R(y \sim x[,v1])$  and  $R_2 = R(y \sim x[,v2])$ ). The outputs are listed as follows.

|                    |                                                                                |
|--------------------|--------------------------------------------------------------------------------|
| r1                 | $R_1$                                                                          |
| r2                 | $R_2$                                                                          |
| var1               | Variance of $R_1$                                                              |
| var2               | variance of $R_2$                                                              |
| var_diff           | Variance of difference between $R_1$ and $R_2$                                 |
| r2_based_p         | P-value for significant difference between $R_1$ and $R_2$ for two tailed test |
| r_based_p_one_tail | P-value for significant difference between $R_1$ and $R_2$ for one tailed test |
| mean_diff          | Differences between $R_1$ and $R_2$                                            |
| upper_diff         | Upper limit of 95% CI for the difference                                       |
| lower_diff         | Lower limit of 95% CI for the difference                                       |

## Examples

```
#To get the test statistics for the difference between R(y~x[,1]) and
#R(y~x[,2]). (here we define R_1=R(y~x[,1])) and R_2=R(y~x[,2]))

dat=dat1
nv=length(dat$V1)
v1=c(1)
v2=c(2)
output=r_diff(dat,v1,v2,nv)
output

#r2redux output

#output$r1 (R_1)
#0.1958636

#output$r2 (R_2)
#0.197006

#output$var1 (variance of R_1)
#0.0009247466

#output$var2 (variance of R_1)
#0.0001451358

#output$var_diff (variance of difference between R_1 and R_2)
#3.65286e-06

#output$r_based_p (two tailed p-value for significant difference between R_1 and R_2)
#0.5500319

#output$r_based_p_one_tail (one tailed p-value
#0.2750159

#output$mean_diff
#-0.001142375 (differences between R2_1 and R2_2)

#output$upper_diff (upper limit of 95% CI for the difference)
#0.002603666

#output$lower_diff (lower limit of 95% CI for the difference)
#-0.004888417

#To get the test statistics for the difference between R(y~x[,1]+[,2]) and
#R(y~x[,2]). (here R_1=R(y~x[,1]+x[,2]) and R_2=R(y~x[,1]))

nv=length(dat$V1)
v1=c(1,2)
v2=c(2)
output=r_diff(dat,v1,v2,nv)
output
```

```
#output$r1  
#0.1974001
```

```
#output$r2  
#0.197006
```

```
#output$var1  
#0.0009235848
```

```
#output$var2  
#0.0009238836
```

```
#output$var_diff  
#3.837451e-06
```

```
#output$r2_based_p  
#0.8405593
```

```
#output$mean_diff  
#0.0003940961
```

```
#output$upper_diff  
#0.004233621
```

```
#output$lower_diff  
#-0.003445429
```

```
#Note: If the directions are not consistent, for instance, if one correlation  
#is positive (R_1) and another is negative (R_2), or vice versa, it is  
#crucial to approach the interpretation of the comparative test with caution.  
#This caution is especially emphasized when applying r_diff()  
#in a nested model comparison involving a joint model
```

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