

# GSMR

Generalised  
Summary-data-  
based Mendelian  
Randomisation

GCTA

SMR

GSMR

OSCA

GCTB

Program in CTG

CTG forum

---

# Overview

The **gsmr** R-  
package

implements  
the GSMM  
(Generalised  
Summary-  
data-based  
Mendelian  
Randomisation)  
method to

test for  
putative  
causal  
association  
between a  
risk factor and  
a disease  
using

summary-  
level data  
from genome-  
wide  
association  
studies  
(GWAS) (Zhu  
et al. 2018)

Nat.

Commun.).

The R

package is

developed by

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Molecular

Bioscience,

the University

of

Queensland.

Bug reports or

questions:

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**Note:** The

GSMR

method has

also been

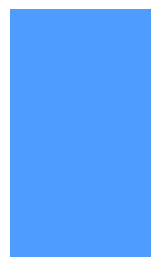
implemented

in the GCTA



software

(GCTA-  
GSMR)



**Citation**

Zhu, Z. et

al. (2018)

Causal

associations  
between risk  
factors and  
common  
diseases  
inferred from  
GWAS  
summary

data. Nat.

Commun. 9,

224

(<https://www.nature.com/doi/10.1038/017-02317-2>).

**Source**

**code**

[gsmr\\_1.0.9.tar.gz](#)

Note: We  
included a  
new HEIDI-  
outlier method  
(as part of the  
GSMR

analysis) in  
gsmr v1.0.7.  
However, the  
new HEIDI-  
outlier method  
is currently  
under  
development

and subject to  
changes  
during the  
method  
development.

From the

GSMR R

package ( $\geq$ )

version 1.0.8),  
we changed  
the default  
back to the  
original HEIDI-  
outlier method  
described in  
Zhu et

al. (2018

Nature

Communications)

and added a

temporary

flag

(‘gsmr2\_beta’)

to test the



new method.

The command

to use this

flag can be

found in the

tutorial below.

The new

HEIDI-outlier

method in  
gsmr ( $\geq$   
version 1.0.8)  
has been  
tested by  
extensive  
simulations  
and real data

analyses. We  
will make a  
formal release  
in our next  
GSMR paper.

Sample data  
are available  
in

[test\\_data.zip](#).

This

document has

been

integrated in

the gsmr R-

package, we

can check it

by the  
standard  
command “?  
function\_name”  
in R.

# Installation

The **gsmr**

requires R  $\geq$   
2.15, you can  
install it in R  
by:

```
# gsmr req  
quires the  
R-package(  
s)  
install.pa
```

```
packages(c('
survey')));
# install
gsmr
install.pa
ckages("ht
tp://cnsge
nomics.com
/software/
gsmr/stati
c/gsmr_1.0
0 + on all
```

```
1.9.tar.gz  
, repos=NUL  
L, type="so  
urce")
```



# Update log

V1.0.9

(gmr\_1.0.9.tar.gz



PDF, 18

Jun. 2019):

Change the

flag

‘gsmr\_beta’

to

‘gsmr2\_beta’.

V1.0.8

(gmr\_1.0.8.tar.gz

PDF, 21

Jan. 2019):

Added a flag

‘gsmr\_beta’

to use a

testing

version of the

HEIDI-outlier  
method.

V1.0.7

([gmr\\_1.0.7.tar.gz](#)

[PDF](#), 9

Oct. 2018):

Added a

multi-SNP-

based HEIDI-  
outlier test in  
the HEIDI-  
outlier  
analysis.

V1.0.6

[\(gmr\\_1.0.6.tar.gz](#)

[PDF, 23](#)

Jan. 2018):

Added a

function to

remove SNPs

in high LD.

V1.0.5

([gmr\\_1.0.5.tar.gz](#)

[PDF](#), 13

Dec. 2017):  
Improved the  
approximation  
of the  
sampling  
covariance  
matrix.

V1.0.4

([gsmr\\_1.0.4.tar.gz](https://github.com/chr17t233/gsmr_1.0.4.tar.gz);

PDF, 6

Nov. 2017):

Added the bi-

directional

GSMR

analysis. The

HEIDI-outlier

analysis has  
been  
integrated in  
the GSMR  
analysis by  
default.

V1.0.3

([gsmr\\_1.0.3.tar.gz](#))



PDF, 12

Oct. 2017):

Added more  
example data.

Removed the  
initial versions  
(8 Nov 2016).

# Tutorial

The GSMR  
analysis only  
requires  
summary-  
level data  
from GWAS.

Here is an  
example,  
where the risk  
factor ( $x$ ) is  
LDL  
cholesterol  
(LDL-c) and  
the disease ( $y$ )

is coronary  
artery disease  
(CAD). GWAS  
summary data  
for both LDL-  
c and CAD  
are available  
in the public

domain

(Global Lipids

Genetics

Consortium et

al. 2013,

Nature

Genetics;

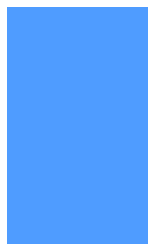
Nikpay, M. et

al. 2015,  
Nature  
Genetics).



**1.**

**Prepare  
data for  
GSMR**



# analysis

## 1.1 Load the GWAS summary data

```
library("gsmr")
data("gsmr")
head(gsmr_data)
```

```
##
```

```
SNP a1 a2
```

```
a1 freq
```



at\_freq

bzx bzx\_se

bzx\_pval

bzx\_n

bzy

## 1 rs109

03129 A

G 0.450019

47 -0.0328

0.0037 3.0

30e-17 169

920.0 0.0

08038

## 2 rs127

48152 T

C 0.080877

58 0.0499

0.0066 3.2

09e-12 172

987.5 0.0

13671

## 3 rs112

06508 A

G 0.143969

88 0.0434

0.0055 2.2

56e-14 172

239.0 0.0

30222

## 4 rs112

06510 C

T 0.191289

11 -0.0831

0.0050 2.3

80e-53 172

012 0 0 0

012.0 -0.0

74519

## 5 rs107

88994 T

C 0.183954

30 0.0687

0.0049 8.8

67e-41 172

941.9 0.0

38267

## 6 rs5

29787 G

```
C 0.197130
99 -0.0553
0.0052 8.7
46e-24 161
969.0 0.0
01707
##          bz
y_se      b
zy_pval   b
zy_n
## 1 0.009
2442 0.384
```

5651000 18

4305

## 2 0.018

5515 0.461

1690000 18

4305

## 3 0.014

1781 0.033

0400000 18

4305

## 4 0.013

0400000 18

3438 0.000

0000234 18

4305

## 5 0.011

8752 0.001

2711000 18

4305

## 6 0.013

5491 0.899

7431000 18

4305

```
dim(gsmr_data)
```

```
## [1] 188  
12
```

This is the  
input format



for the GSMMR  
analysis. In  
this data set,  
there are 188  
near-  
independent  
SNPs  
associated

with LDL-c at  
a genome-  
wide  
significance  
level (i.e.  $p < 5e-8$ ).

- SNP: the genetic

# instrument

- a1: effect allele
- a2: the other allele
- a1\_freq: frequency of a1
- bzx: the

effect size  
of  $a_1$  on  
risk factor

- $bzx\_se$ :  
standard  
error of  $bzx$
- $bzx\_pval$ : p  
value for  
 $bzx$


- `bzx_n`: per-SNP sample size of GWAS for the risk factor
- `bzy`: the effect size

of  $a_1$  on  
disease

- $bzy\_se$ :  
standard  
error of  $bzy$
- $bzy\_pval$ : p  
value for  
 $bzy$
- $bzy\_n$ : per-

SNP  
sample  
size of  
GWAS for  
the disease

**1.2 Estimate  
the LD  
correlation  
matrix**



```
# Save the genetic variants and effect alleles in a text file using R  
write.table(gsmr_data[,c(1,2)], "gsmr_ex
```



```
ample_snps
.allele",
col.names=
F, row.names=
F, quote
=F)
# Extract
the genotype data from a GWAS
dataset using GCTA
```

```
gcta64 --b  
file gsmr_  
example --  
extract gs  
mr_example  
_snps.alle  
le --updat  
e-ref-alle  
le gsmr_ex  
ample_snps  
.allele --
```

```
recode --o  
ut gsmr_ex  
ample
```

Note: the two  
steps above  
guarantee  
that the LD  
correlations

are calculated based on the effect alleles for the SNP effects.

```
# Estimate LD correlation matrix using R
```

```
x using R
snpcoeff_
id = scan(
"gsnr_exam
ple.xmat.g
z", what="
", nlines=
1)

snpcoeff
= read.tab
le("gsnr_e
xample.xma
```

```
t.gz", header=F, skip=2)
```

```
# Match the SNP genotype data with the summary data  
cnp_id = D
```

```
snp_id = r  
reduce(intersect, list(gsmr_data  
a$SNP, snp  
_coeff_id)  
)  
gsmr_data  
= gsmr_data  
a[match(snp  
_id, gsmr  
_data$SNP)
```

```
,]  
snp_order  
= match(snp  
p_id, snp_  
coeff_id)  
snp_coeff_  
id = snp_c  
oeff_id[snp  
p_order]  
snp_coeff  
= snp_coef  
f[, snp_or
```



```
der]
```

```
# Calculate the LD correlation matrix
```

```
ldrho = cor(snp_coef)
```

```
# Check th
```

e size of  
the correl  
ation matr  
ix and dou  
ble-check  
if the ord  
er of the  
SNPs in th  
e LD corre  
lation mat  
rix is con  
sistent wi

th that in  
the GWAS s  
ummary dat  
a

```
colnames(ldrho) = rownames(ldrho) = snp_  
coeff_id
```

```
dim(ldrho)
```

```
## [1] 188
```

```
188
```

```
# Show the  
first 5 ro  
ws and col  
umns of th  
e matrix  
ldrho[1:5,  
1:5]
```

```
##
```

```
rs10003120
```

rs10903129

rs12748152

rs11206508

rs11206510

rs10788994

## rs10903

129 1.000

000000 -0.

0045378845

0.00806662

1 -0.01372

112 -0.023

4447102

## rs12748

152 -0.004

537884 1.

0000000000

-0.0066871

81 0.0044

5927 0.00

03629201

## rs11206

508 0.008

066621 -0.

0066871806

1.0000000000

0 -0.21125

757 0.051

2593434

## rs11206

510 -0.013

721120 0.

0044592696

-0.2112575

67 1.00000

0000 0 10



0000 -0.10

42706205

## rs10788

994 -0.023

444710 0.

0003629201

0.05125934

3 -0.18427

062 1.000

0000000

Note: all the analyses implemented in this R-package only require the summary data (e.g. “gsmr\_data”)

and the LD  
correlation  
matrix  
(e.g. “ldrho”)  
listed above.

**2.**

**Standardiza**

This is an optional process. If the risk factor was not standardised in GWAS, the effect sizes

can be scaled  
using the  
method  
below. Note  
that this  
process  
requires allele  
frequencies,

z-statistics  
and sample  
size. After  
scaling,  $b_{zx}$  is  
interpreted as  
the per-allele  
effect of a  
SNP on the

exposure in  
standard  
deviation  
units.

```
snpfreq =  
gsmr_data$a1_freq  
# allele frequencies
```

```
of the SNP  
s  
bzx = gsmr  
_data$bzx  
# effects  
of the ins  
truments o  
n risk fac  
tor  
bzx_se = g  
smr_data$b  
zx_co
```



```
zx_se  
# standard  
errors of  
bzx  
bzx_n = gs  
mr_data$bz  
x_n  
# GWAS sam  
ple size f  
or the ris  
k factor  
std_zx = s
```

```
td_effect(  
  snpfreq, b  
  zx, bzx_se  
  , bzx_n)  
# perform  
standardis  
ation  
gsmr_data$  
std_bzx =  
std_zx$b  
# standard  
ized bzx
```

```
gsmr_data$  
std_bzx_se  
= std_zx$s  
e # sta  
ndardized  
bzx_se  
head(gsmr_  
data)
```

```
##
```

```
SNP a1 a2
a1_freq
bzx bzx_se
bzx_pval
bzx_n
bzy
## 1 rs109
03129 A
G 0.450019
47 -0.0328
0.0037 3.0
30e-17 169
```

920.0 0.0

08038

## 2 rs127

48152 T

C 0.080877

58 0.0499

0.0066 3.2

09e-12 172

987.5 0.0

13671

## 3 rs112

06500

A

06508 A

G 0.143969

88 0.0434

0.0055 2.2

56e-14 172

239.0 0.0

30222

## 4 rs112

06510 C

T 0.191289

11 -0.0831

0.0050 2.3

```
80e-53  172
812.0   -0.0
74519
## 5   rs107
88994   T
C  0.183954
30     0.0687
0.0049  8.8
67e-41  172
941.9   0.0
38267
## 6     rs5
```

29787 G

C 0.197130

99 -0.0553

0.0052 8.7

46e-24 161

969.0 0.0

01707

## bz

y\_se b

zy\_pval b

zy\_n s



td\_bzx st

d\_bzx\_se

## 1 0.009

2442 0.384

5651000 18

4305 -0.03

055942 0.0

03447252

## 2 0.018

5515 0.461

1690000 18

4305 0.04

713698 0.0

06234550

## 3 0.014

1781 0.033

0400000 18

4305 0.03

829018 0.0

04852442

## 4 0.013

3438 0.000

0000234 18

4305 -0 07

4305 0.07

181919 0.0

04321251

## 5 0.011

8752 0.001

2711000 18

4305 0.06

149455 0.0

04386074

## 6 0.013

5491 0.899

7431000 18

4305 -0.04

695042 0.0

04414868

**3.**

**GSMR**

**analysis**

This is the

main analysis  
of this R-  
package. It  
uses SNPs  
associated  
with the risk  
factor (e.g. at  
 $p < 5e-8$ ) as

the  
instruments to  
test for  
putative  
causal effect  
of the risk  
factor on the  
disease. The

analysis

involves a

step that uses

the **HEIDI-**

**outlier**

approach to

remove SNPs

that have

effects on  
both the risk  
factor and the  
disease  
because of  
pleiotropy.

```
bzx = gsmr  
_data$std_
```



```
bzx      # S
NP effects
on the risk factor
bzx_se = gsmr_data$
td_bzx_se
# standard
errors of
bzx
bzx_pval =
gsmr_data$
```

```
bzx_pval
# p-values
for bzx
bzy = gsmr
_data$bzy
# SNP effects on the
disease
bzy_se = g
smr_data$b
zy_se      #
```

```
Standard errors of bzy
bzy_pval = gsmr_data$bzy_pval
# p-values for bzy
n_ref = 7703 # Sample size of the ref
```

reference sam  
ple

gwas\_thres

h =  $5e-8$

# GWAS thr

eshold to

select SNP

s as the i

nstruments

for the GS

MR analysi

s

```
single_snp  
_heidi_thr  
esh = 0.01  
# p-value  
threshold  
for single  
-SNP-based  
HEIDI-outl  
ier analys  
is  
multi_snp_
```

```
heidi_thre  
sh = 0.01  
# p-value  
threshold  
for multi-  
SNP-based  
HEIDI-outl  
ier analys  
is  
nsnps_thre  
sh = 10  
# the mini
```

minimum number  
of instruments required for the  
GSMR analysis

heidi\_outlier\_flag =  
**T** # flag for HEIDI  
I-outlier  
analysis

and cys13

ld\_r2\_thre

sh = 0.05

# LD r2 th

reshold to

remove SNP

s in high

LD

ld\_fdr\_thr

esh = 0.05

# FDR thre

shold to r



remove the  
chance cor  
relations  
between th  
e SNP inst  
ruments  
gsmr2\_beta  
= 0 #  
0 – the or  
iginal HEI  
DI-outlier  
method; 1

– the new  
HEIDI-outlier method  
that is currently under development

```
gsmr_results = gsmr(  
    bzx, bzx_se,  
    bzx_pval,  
    bzy, bz
```

l, bzy, bz  
y\_se, bzy\_  
pval, ldrh  
o, snp\_coe  
ff\_id, n\_r  
ef, heidi\_  
outlier\_fl  
ag, gwas\_t  
hresh, sin  
gle\_snp\_he  
idi\_thresh  
, multi\_sn

```
p_heidi_th  
resh, nsnp  
s_thresh,  
ld_r2_thre  
sh, ld_fdr  
_thresh, g  
smr2_beta)  
# GSMM ana  
lysis  
filtered_i  
ndex=gsmr_  
results$us
```

```
ed_index  
cat("The e  
stimated e  
ffect of t  
he exposur  
e on outco  
me: ", gsmr  
_results$br  
xy)
```

```
## The estimated effect of the exposure on outcome:  
0.4322395
```

```
cat("Standard  
error  
of bxy: ",  
gsmr_results$  
bxy_se)
```

```
## Standard  
error of  
bxy: 0.02  
210985
```



```
cat("P-value for bxy  
: ", gsmr_  
results$bxy_  
pval)
```

## P-value  
for bxy:  
4.15454e-8  
5

```
cat("Indexes of the  
SNPs used  
in the GSM  
R analysis  
: ", gsmr_  
results$us  
ed_index[1  
:5], "..."  
)
```

```
## Indexes  
of the SNP  
s used in  
the GSMR a  
nalysis:
```

```
1 2 3 5 6
```

```
...
```

```
cat("Number of SNPs  
with missing  
estimates in the  
summary data:  
", length(gsmr_results$na_snp))
```

```
## Number  
of SNPs wi  
th missing  
estimates  
in the sum  
mary data:  
0
```

```
cat("Number of non-significant  
SNPs: ", length(gsmr_results$weak_snps))
```

## Number  
of non-sig  
nificant S  
NPs: 39

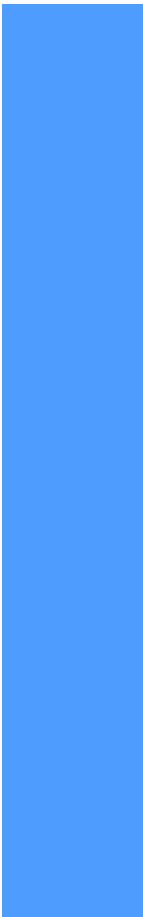


```
cat("Number of SNPs  
in high LD  
( LD rsq >  
", ld_r2_t  
hresh, "):  
", length(  
gsmr_result  
ts$linkage  
_snps))
```

```
## Number  
of SNPs in  
high LD (  
LD rsq > 0  
.05 ): 5
```

```
cat("Number of pleio  
tropic outliers: ",  
length(gsm  
r_results$  
pleio_snps  
))
```

```
## Number  
of pleiotr  
opic outli  
ers: 9
```



## 4. Bi- directional GSMR

# analysis

The script  
below runs bi-  
directional  
GSMR  
analyses,  
i.e. a forward-  
GSMR

analysis as  
described  
above and a  
reverse-  
GSMR  
analysis that  
uses SNPs  
associated

with the  
disease  
(e.g. at  $p < 5e-8$ ) as the  
instruments to  
test for  
putative  
causal effect

of the disease  
on risk factor.

```
gsmr_results = bi_gsmr(bzx, bzx_se, bzx_pval, bzy, bzy_se, bzy_pval, ld_rho, cnp_c
```



```
rno, snp_c  
coeff_id, n  
_ref, heid  
i_outlier_  
flag, gwas  
_thresh, s  
ingle_snp_  
heidi_thre  
sh, multi_  
snp_heidi_  
thresh, ns  
nps_thresh
```

```
, ld_r2_th  
resh, ld_f  
dr_thresh,  
gsmr2_beta  
) # GSM  
R analysis
```

```
cat("Effec  
t of risk  
factor on  
disease: "  
, gsmr resu
```

```
lts$forward_bxy)
```

```
## Effect  
of risk fa  
ctor on di  
sease: 0.  
4322395
```

```
cat("Standard error  
of bxy in  
the forward-GSMR ana-  
lysis: ", gsmr_result  
s$forward_  
bxy_se)
```

```
## Standard error of  
bxy in the  
forward-GS  
MR analysis:  
0.0221  
0985
```

```
cat("P-value of bxy  
in the forward-GSMR  
analysis:  
", gsmr_results$forward_bxy_pval)
```

## P-value  
of bxy in  
the forward-GSMR ana-  
lysis: 4.  
15454e-85

```
cat("Effect  
of disease  
on risk  
factor: ",  
gsmr_results$reverse  
_bxy)
```



```
## Effect  
of disease  
on risk fa  
ctor:    -0.  
02739421
```

```
cat("Standard error  
of bxy in  
the reverse  
e-GSMR ana  
lysis: ", g  
smr_result  
s$reverse_  
bxy_se)
```

```
## Standard error of  
bxy in the  
reverse-GS  
MR analysis:  
0.0095  
51025
```

```
cat("P-value of bxy  
in the reverse-GSMR  
analysis:  
", gsmr_results$reverse_bxy_pval)
```

```
## P-value  
of bxy in  
the revers  
e-GSMR ana  
lysis: 0.  
004128198
```



**5.**

**Visualizatio**

```
effect_col  
= colors()  
[75]  
vals = c(b  
zx[filtere  
d_index]-b  
zx_se[filt  
ered_index  
, bzx[fil  
tered_inde  
x]+bzx se[
```

```
filtered_index])
xmin = min
(vals); xmax
= max(v
als)
vals = c(b
zy[filtere
d_index]-b
zy_se[filt
ered_index
1, b-v, [fi]
```

```
], bzy[filtered_index]+bzy_selected_index])  
ymin = min(vals); ymax = max(vals)  
par(mar=c(5, 5, 4, 2))  
plot(bzx[f
```



```
filtered_in  
dex], bzy[  
filtered_i  
ndex], pch  
=20, cex=0  
.8, bty="n  
", cex.axi  
s=1.1, cex  
.lab=1.2,  
co  
l=effect_c  
ol. xlim=c
```

```
(xmin, xmax), ylim=c  
(ymin, ymax),
```

```
xl
```

```
ab=expression( LDL~cholesterol~  
(italic(b[  
zx]))),
```

```
yl
```

```
ab=expression(Corona  
ry~artery~  
disease~(i  
talic(b[zy  
]))))
```

```
abline(0,  
gsmr_results$forward  
_bxy, lwd=  
1.5, lty=2  
, col="dim
```

```
grey" )
```

```
nsnps = length(bzx[filtered_index])
```

```
for( i in 1:nsnps )
```

```
{
```

```
    # x ax
```

```
is
```

```
    xstart
```

```
        xstart = bzx[filtered_index  
= bzx[filtered_index  
[i]] - bzx  
_se[filtered  
ed_index[i  
]]; xend =  
bzx[filter  
ed_index[i  
]] + bzx_s  
e[filtered  
_index[i]]
```

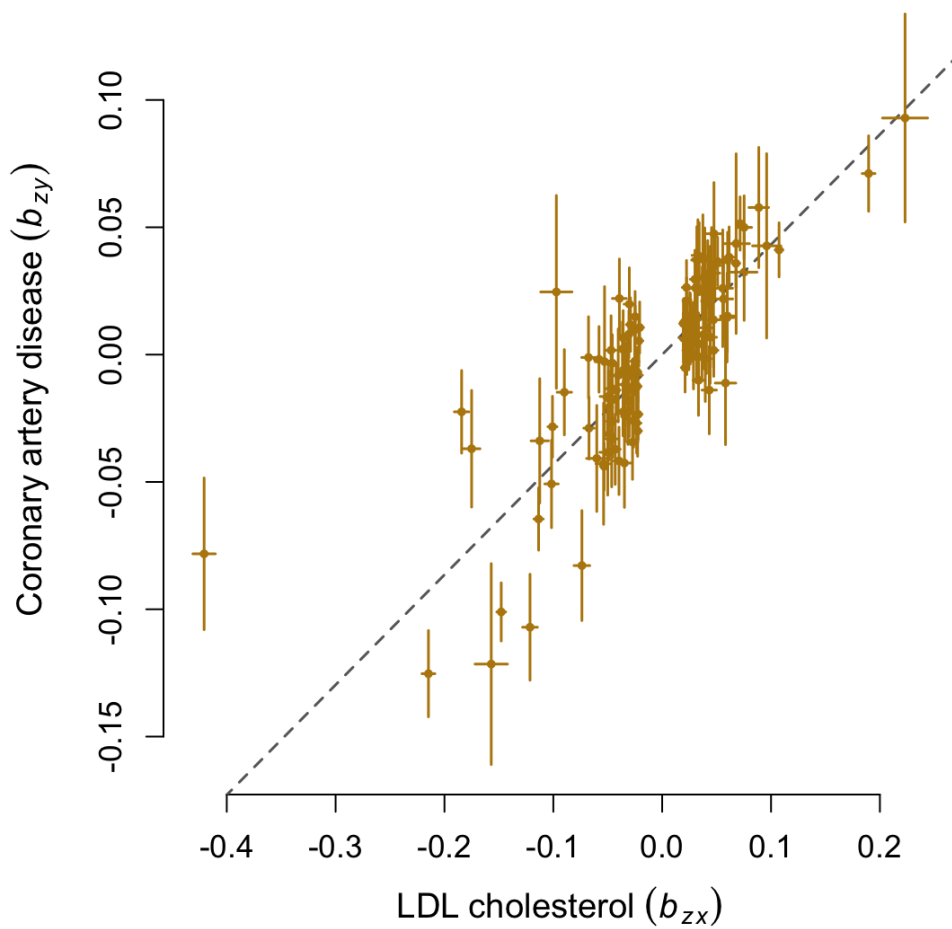
```
        ystart  
= bzy[filter  
ered_index  
[i]]; yend  
= bzy[filter  
ered_index  
[i]]  
  
        segmen  
ts(xstart,  
ystart, xe  
nd, yend,  
lwd=1.5, c
```

```
ol=effect_  
col)  
    # y ax  
is  
    xstart  
= bzx[filter  
ered_index  
[i]]; xend  
= bzx[filter  
ered_index  
[i]]  
    vstart
```

```
        ystart  
= bzy[filter  
ed_index  
[i]] - bzy  
_se[filter  
ed_index[i  
]]; yend =  
bzy[filter  
ed_index[i  
]] + bzy_s  
e[filtered  
_index[i]]
```



```
segments(xstart,  
ystart, xend,  
yend,  
lwd=1.5, col=effect_  
col)  
}
```




# Package

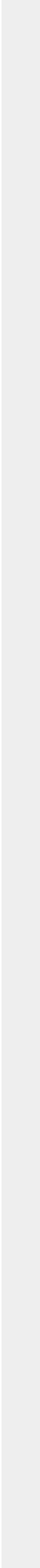
# Document



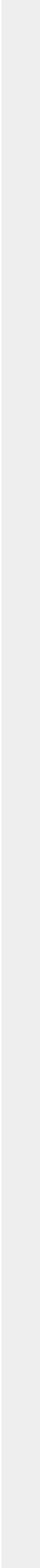
**bi\_gsmr**



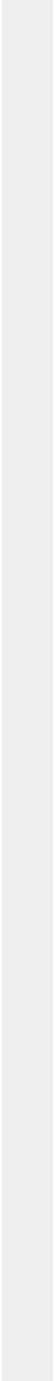
Bi-  
directional  
GSMR  
analysis is  
composed



of a  
forward-  
GSMR  
analysis  
and a  
reverse-  
GSMR  
analysis  
that uses



SNPs  
associated  
with the  
disease  
(e.g. at  $< 5e-8$ ) as  
the  
instruments  
to test for



putative  
causal  
effect of  
the disease  
on the risk  
factor.

**Usage**

```
bi_gsmr(bzx
, bzx_se, b
zx_pval, bz
y, bzy_se,
bzy_pval, l
drho, snpid
, heidi_out
lier_flag=T
, gwas_thre
sh=5e-8, si
ngle_snp_he
```

```
idi_thresh=  
0.01, multi  
_snp_heidi_  
thresh=0.01  
, nsnp_s_thr  
esh=10, ld_  
r2_thresh=0  
.05, ld_fdr  
_thresh=0.0  
5, gsmr2_be  
ta=0)
```



# Arguments

`bxz`

bzx\_se

bzx\_pval

bzy

bzy\_se

bzy\_pvał

ldrho

snpid

n\_ref

heidi\_outlier fla

gwas\_thresh



single\_snp\_heidi.

multi\_snp\_heidi\_.

nsnps\_thresh



ld\_r2\_thresh

ld\_fdr\_thresh

gsmr2\_beta



**Value**

**Estimate of**



causative  
effect of risk  
factor on  
disease  
(forward\_bxy),  
the  
corresponding  
standard error

(forward\_bxy\_se),

p-value

(forward\_bxy\_pva

and SNP

index

(forward\_index),

and estimate

of causative

effect of  
disease on  
risk factor  
(reverse\_bxy),  
the  
corresponding  
standard error  
(reverse\_bxy\_se),

p-value

(reverse\_bxy\_pva

SNP index

(reverse\_index),

SNPs with

missing

values, with

non-

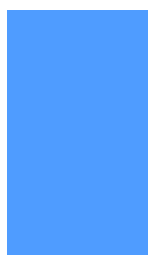
significant p-values and those in LD.

## Examples

```
data("gsmr")  
gsmr_result = bi_gsmr(
```

```
r(gsmr_data  
a$bzx, gsm  
r_data$bzx  
_se, gsmr_  
data$bzx_p  
val, gsmr_  
data$bzy,  
gsmr_data$  
bzy_se, gs  
mr_data$bz  
y_pval, ld  
rho, gsmr_
```

```
data$SNP,  
n_ref, T,  
5e-8, 0.01  
, 0.01, 10  
, 0.05, 0.  
05, 0)
```



**gsmr**



GSMR

(Generalised

Summary-

data-based

Mendelian

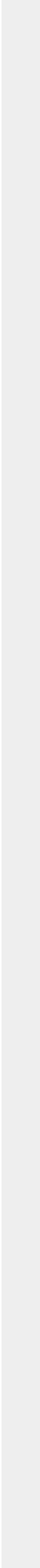
Randomisation

is a flexible

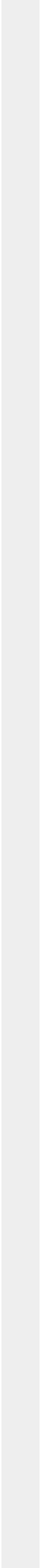
and

powerful





approach  
that utilises  
multiple  
genetic  
instruments  
to test for  
causal  
association  
between a



risk factor  
and  
disease  
using  
summary-  
level data  
from  
independent  
genome-

wide  
association  
studies.

## Usage

```
gsmr(bzx, b  
zx_se, bzx_  
pval, bzy,  
bzy_se, ldr
```

```
ho, snpid,  
heidi_outli  
er_flag=T,  
gwas_thresh  
=5e-8, sing  
le_heidi_th  
resh=0.01,  
multi_heidi  
_thresh=0.0  
1, nsnp_s_th  
resh=10, ld
```

```
_r2_thresh=  
0.05, ld_fd  
r_thresh=0.  
05, gsmr2_b  
eta=0)
```

# Arguments

bxz

bxz\_se

bzx\_pval

bzy

bzy\_se



ldrho

snpid

n\_ref

heidi\_outlier fla

gwas\_thresh

nsnps\_thresh





ld\_r2\_thresh

ld\_fdr\_thresh

gsmr2\_beta









single\_heidi\_thro

multi\_heidi\_thres

**Value**

Estimate of  
causative  
effect of risk  
factor on  
disease ( $b_{xy}$ ),  
the  
corresponding  
standard error

(bxy\_se), p-value

(bxy\_pval),

SNP index

(used\_index),

SNPs with

missing

values, with

non-  
significant p-  
values and  
those in LD.

## Examples

```
data("gsmr")  
gsmr_result
```

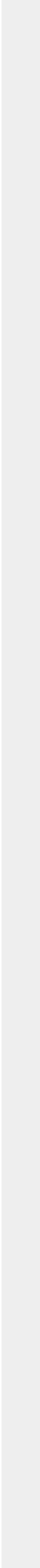


```
t = gsmr(g  
smr_data$b  
zx, gsmr_d  
ata$bzx_se  
, gsmr_dat  
a$bzx_pval  
, gsmr_dat  
a$bzy, gsm  
r_data$bzy  
_se, ldrho  
, gsmr_dat  
a$SNP . n r
```

```
ef, T, 5e-  
8, 0.01, 0  
.01, 10, 0  
.1, 0.05,  
0)
```

---

 **std\_effect**



Standardization  
of SNP  
effect and  
its  
standard  
error using  
z-statistic,  
allele  
frequency



and sample  
size

## Usage

```
std_effect(  
  snp_freq, b  
  , se, n)
```

## Arguments

snp\_freq

vector,

allele

frequen

**b**

vector,  
SNP  
effects  
risk fac

se

vector,  
standar  
errors c

n

vector,  
SNP  
sample  
sizes fo  
GWAS  
the risk  
factor



# Value

Standardised  
effect (b) and  
standard error  
(se)

## Examples

```
data("gsmr
```

```
" )  
std_effect  
s = std_ef  
fect(gsmr_  
data$a1_fr  
eq, gsmr_d  
ata$bzx, g  
smr_data$b  
zx_se, gsm  
r_data$bzx  
_n)
```

