

TwoSampleMR

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2022-11-23

Setup environment

```
# install.packages("TwoSampleMR", repos = c("https://mrcieu.r-universe.dev", "https://cloud.r-project.org/"))
# ip("MRCIEU/TwoSampleMR")
library(TwoSampleMR)
library(EnsDb.Hsapiens.v75)
library(locuszoomr)
library(tidyverse)
library(magrittr)
library(patchwork)

theme_set(theme_bw(base_size = 8))

set.seed(666)

load("rf.rdata")
```

Read and prep data

```
eqtl = read.delim("data/sumstats/2022-10-12.STARNET.eQTL.MP.chr15.CPRA_b37.tsv.gz", comment.char = "#")
mqtl = read.delim("data/sumstats/Cruchaga2022.mQTL.CSF.X100001948.chr15.CPRA_b37.tsv.gz", comment.char = "#")
gwas = read.delim("data/sumstats/Bellenguez2022.chr15.CPRA_b37.tsv.gz", comment.char = "#") %>%
```

LACTB

```
GENE = "ENSG00000103642" # LACTB

eqtl.gene = eqtl %>% filter(TRAIT == GENE)

mqtl.gene = mqt1 %>% filter(ID %in% eqtl.gene$ID)
gwas.gene = gwas %>% filter(ID %in% eqtl.gene$ID)
```

Format and harmonise data for MR

```
eqtl.gene.ld_clump = ieugwasr::ld_clump(eqtl.gene %>% select(rsid = ID, pval = P), bfile = "c
```

Clumping gVL5KT, 6600 variants, using: data/ldref/1000G.EUR.CPRA_b38.chr15

Removing 6585 of 6600 variants due to LD with other variants or absence from LD reference panel

```
eqtl.gene.exposure = format_data(eqtl.gene %>%
  filter(ID %in% eqtl.gene.ld_clump$rsid) %>%
  select(SNP = ID,
    beta = BETA,
    se = SE,
    effect_allele = ALT,
    other_allele = REF,
    eaf = AF,
    Phenotype = TRAIT,
    chr = CHROM,
    position = POS,
    sample_size = N,
    pval = P,
    gene = TRAIT),
  type="exposure")
```

```
mqtl.gene.ld_clump = ieugwasr::ld_clump(mqt1.gene %>% select(rsid = ID, pval = P), bfile = "c
```

Clumping 7SxXqj, 6213 variants, using: data/ldref/1000G.EUR.CPRA_b38.chr15

Removing 6204 of 6213 variants due to LD with other variants or absence from LD reference panel

```

mqt1.gene.exposure = format_data(mqt1.gene %>%
  filter(ID %in% mqt1.gene.ld_clump$rsid) %>%
  select(SNP = ID,
    beta = BETA,
    se = SE,
    effect_allele = ALT,
    other_allele = REF,
    eaf = AF,
    Phenotype = TRAIT,
    chr = CHROM,
    position = POS,
    sample_size = N,
    pval = P),
  type="exposure")

```

```

mqt1.gene.outcome = format_data(mqt1.gene %>%
  select(SNP = ID,
    beta = BETA,
    se = SE,
    effect_allele = ALT,
    other_allele = REF,
    eaf = AF,
    Phenotype = TRAIT,
    chr = CHROM,
    position = POS,
    sample_size = N,
    pval = P),
  type="outcome")

```

```

gwas.gene.outcome = format_data(gwas.gene %>%
  select(SNP = ID,
    beta = BETA,
    se = SE,
    effect_allele = ALT,
    other_allele = REF,
    eaf = AF,
    Phenotype = TRAIT,
    chr = CHROM,
    position = POS,
    sample_size = N,
    ncase = N_CASES,
    ncontrol = N_CTRLs),
  type="outcome")

```

```

pval = P,
gene = TRAIT),
type="outcome")

```

Generating sample size from ncase and ncontrol

```

dat = harmonise_data(exposure_dat = eqtl.gene.exposure,
                     outcome_dat = gwas.gene.outcome)

```

Harmonising ENSG00000103642 (E3aY79) and AD (5rt0Eu)

Analyse data and print/plot results

```

(res = mr(dat))

```

Analysing 'E3aY79' on '5rt0Eu'

	id.exposure	id.outcome	outcome	exposure	method	nsnp
1	E3aY79	5rt0Eu	AD	ENSG00000103642	MR Egger	15
2	E3aY79	5rt0Eu	AD	ENSG00000103642	Weighted median	15
3	E3aY79	5rt0Eu	AD	ENSG00000103642	Inverse variance weighted	15
4	E3aY79	5rt0Eu	AD	ENSG00000103642	Simple mode	15
5	E3aY79	5rt0Eu	AD	ENSG00000103642	Weighted mode	15

	b	se	pval
1	0.007503	0.002400	0.0080258
2	0.005276	0.001288	0.0000419
3	0.002863	0.001541	0.0631032
4	-0.003801	0.004243	0.3854475
5	0.004797	0.001743	0.0156014

```

mr_heterogeneity(dat)

```

	id.exposure	id.outcome	outcome	exposure	method	Q
1	E3aY79	5rt0Eu	AD	ENSG00000103642	MR Egger	19.1
2	E3aY79	5rt0Eu	AD	ENSG00000103642	Inverse variance weighted	27.1

	Q_df	Q_pval
1	13	0.11999
2	14	0.01871

```
mr_pleiotropy_test(dat)
```

	id.exposure	id.outcome	outcome	exposure	egger_intercept	se
1	E3aY79	5rt0Eu	AD	ENSG00000103642	-0.02274	0.00975
					pval	
1					0.03639	

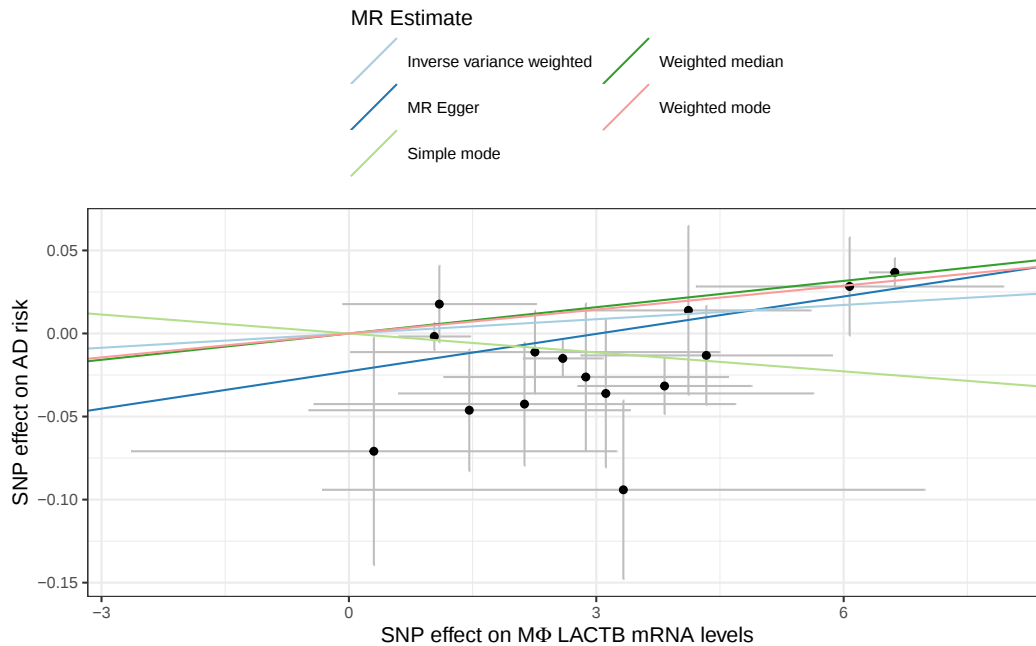
```
mr_leaveoneout(dat)
```

	exposure	outcome	id.exposure	id.outcome	samplesize	SNP
1	ENSG00000103642	AD	E3aY79	5rt0Eu	485999	15:62208259:g:a
2	ENSG00000103642	AD	E3aY79	5rt0Eu	485999	15:62218106:a:t
3	ENSG00000103642	AD	E3aY79	5rt0Eu	485999	15:62221882:g:a
4	ENSG00000103642	AD	E3aY79	5rt0Eu	485999	15:62268638:t:c
5	ENSG00000103642	AD	E3aY79	5rt0Eu	485999	15:62429972:g:c
6	ENSG00000103642	AD	E3aY79	5rt0Eu	485999	15:62520456:t:g
7	ENSG00000103642	AD	E3aY79	5rt0Eu	485999	15:62648840:c:t
8	ENSG00000103642	AD	E3aY79	5rt0Eu	485999	15:62676645:c:t
9	ENSG00000103642	AD	E3aY79	5rt0Eu	485999	15:62768090:t:c
10	ENSG00000103642	AD	E3aY79	5rt0Eu	485999	15:62930647:c:t
11	ENSG00000103642	AD	E3aY79	5rt0Eu	485999	15:62979292:g:c
12	ENSG00000103642	AD	E3aY79	5rt0Eu	485999	15:63141567:g:a
13	ENSG00000103642	AD	E3aY79	5rt0Eu	485999	15:63353203:c:a
14	ENSG00000103642	AD	E3aY79	5rt0Eu	485999	15:63863320:g:a
15	ENSG00000103642	AD	E3aY79	5rt0Eu	485999	15:63902855:g:a
16	ENSG00000103642	AD	E3aY79	5rt0Eu	485999	All
	b	se	p			
1	0.002925	0.001585	0.06492			
2	0.002930	0.001543	0.05765			
3	0.002943	0.001592	0.06449			
4	0.003010	0.001488	0.04312			
5	0.002956	0.001550	0.05657			
6	0.002953	0.001604	0.06568			
7	0.002859	0.001605	0.07489			
8	0.002950	0.001573	0.06072			
9	0.003600	0.001433	0.01199			
10	0.002869	0.001566	0.06699			
11	0.002765	0.001637	0.09123			
12	-0.004302	0.002118	0.04223			
13	0.003019	0.001597	0.05868			
14	0.003534	0.001508	0.01906			

```
15 0.002826 0.001589 0.07532
16 0.002863 0.001541 0.06310
```

```
p1 = mr_scatter_plot(res, dat)[[1]] +
  xlab(expression(paste("SNP effect on M", Phi, " LACTB mRNA levels"))) +
  ylab("SNP effect on AD risk")

p1
```



```
ggsave(str_interp("${res$exposure[1]}.${res$outcome[1]}.pdf"), plot = p1, width = 10.5, height = 10.5)
```

```
dat = harmonise_data(exposure_dat = eqtl.gene.exposure,
  outcome_dat = mqt1.gene.outcome)
```

Harmonising ENSG00000103642 (E3aY79) and CSF_X100001948 (v0F42P)

```
(res = mr(dat))
```

Analysing 'E3aY79' on 'v0F42P'

	id.exposure	id.outcome	outcome	exposure		
1	E3aY79	vOF42P	CSF_X100001948	ENSG000000103642		
2	E3aY79	vOF42P	CSF_X100001948	ENSG000000103642		
3	E3aY79	vOF42P	CSF_X100001948	ENSG000000103642		
4	E3aY79	vOF42P	CSF_X100001948	ENSG000000103642		
5	E3aY79	vOF42P	CSF_X100001948	ENSG000000103642		
		method	nsnp	b	se	pval
1		MR Egger	13	-0.008821	0.0011344	0.000008548731961660662186
2		Weighted median	13	-0.006950	0.0007417	0.000000000000000000007246
3		Inverse variance weighted	13	-0.006062	0.0007953	0.000000000000000024924979491
4		Simple mode	13	-0.002544	0.0016503	0.149119095292512604533641
5		Weighted mode	13	-0.007523	0.0006328	0.000000053670470060982310

```
mr_heterogeneity(dat)
```

	id.exposure	id.outcome	outcome	exposure	
1	E3aY79	vOF42P	CSF_X100001948	ENSG000000103642	
2	E3aY79	vOF42P	CSF_X100001948	ENSG000000103642	
		method	Q	Q_df	Q_pval
1		MR Egger	25.96	11	0.006571402
2		Inverse variance weighted	45.98	12	0.000006983

```
mr_pleiotropy_test(dat)
```

	id.exposure	id.outcome	outcome	exposure	egger_intercept
1	E3aY79	vOF42P	CSF_X100001948	ENSG000000103642	0.0139
		se	pval		
1		0.004773	0.01413		

```
mr_leaveoneout(dat)
```

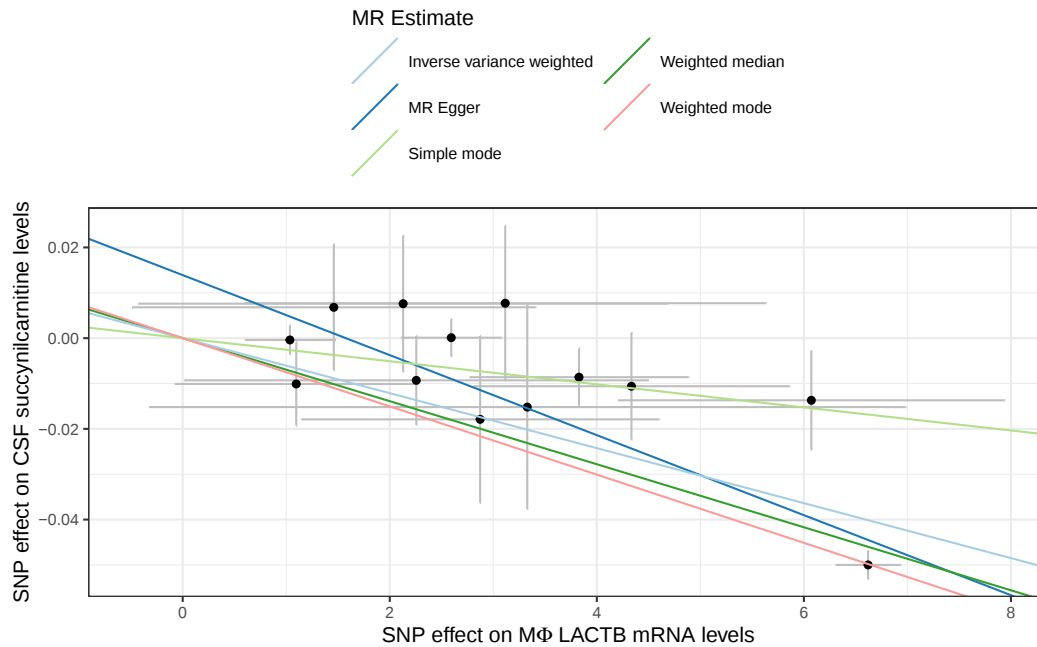
	exposure	outcome	id.exposure	id.outcome	samplesize
1	ENSG000000103642	CSF_X100001948	E3aY79	vOF42P	NA
2	ENSG000000103642	CSF_X100001948	E3aY79	vOF42P	NA
3	ENSG000000103642	CSF_X100001948	E3aY79	vOF42P	NA
4	ENSG000000103642	CSF_X100001948	E3aY79	vOF42P	NA
5	ENSG000000103642	CSF_X100001948	E3aY79	vOF42P	NA
6	ENSG000000103642	CSF_X100001948	E3aY79	vOF42P	NA
7	ENSG000000103642	CSF_X100001948	E3aY79	vOF42P	NA
8	ENSG000000103642	CSF_X100001948	E3aY79	vOF42P	NA

9	ENSG00000103642	CSF_X100001948	E3aY79	v0F42P	NA
10	ENSG00000103642	CSF_X100001948	E3aY79	v0F42P	NA
11	ENSG00000103642	CSF_X100001948	E3aY79	v0F42P	NA
12	ENSG00000103642	CSF_X100001948	E3aY79	v0F42P	NA
13	ENSG00000103642	CSF_X100001948	E3aY79	v0F42P	NA
14	ENSG00000103642	CSF_X100001948	E3aY79	v0F42P	NA

	SNP	b	se	p
1	15:62208259:g:a	-0.006062	0.0008324	0.000000000000032815606033
2	15:62218106:a:t	-0.006082	0.0008199	0.000000000000011910055833
3	15:62221882:g:a	-0.006079	0.0008325	0.000000000000028288758719
4	15:62268638:t:c	-0.006068	0.0008318	0.000000000000029868612309
5	15:62429972:g:c	-0.006094	0.0008149	0.000000000000007525744255
6	15:62520456:t:g	-0.006162	0.0008061	0.000000000000002095786625
7	15:62676645:c:t	-0.006109	0.0008107	0.000000000000004843344437
8	15:62768090:t:c	-0.006310	0.0008021	0.00000000000000364390023
9	15:62979292:g:c	-0.006268	0.0008077	0.00000000000000849284729
10	15:63141567:g:a	-0.001523	0.0008172	0.06237707688136712169680
11	15:63353203:c:a	-0.006145	0.0008235	0.000000000000008518687468
12	15:63863320:g:a	-0.006494	0.0006947	0.00000000000000000000889
13	15:63902855:g:a	-0.006055	0.0008304	0.000000000000030651940511
14	All	-0.006062	0.0007953	0.00000000000002492497949

```
p2 = mr_scatter_plot(res, dat)[[1]] +
  xlab(expression(paste("SNP effect on M", Phi, " LACTB mRNA levels"))) +
  ylab("SNP effect on CSF succinylcarnitine levels")

p2
```



```
ggsave(str_interp("${res$exposure[1]}.${res$outcome[1]}.pdf"), plot = p2, width = 10.5, height = 10.5)
```

```
dat = harmonise_data(exposure_dat = mqt1.gene.exposure,
                     outcome_dat = gwas.gene.outcome)
```

Harmonising CSF_X100001948 (JfjjnJ) and AD (5rt0Eu)

Removing the following SNPs for being palindromic with intermediate allele frequencies:
15:62148640:a:t

```
(res = mr(dat))
```

Analysing 'JfjjnJ' on '5rt0Eu'

	id.exposure	id.outcome	outcome	exposure	method	nsnp
1	JfjjnJ	5rt0Eu	AD CSF_X100001948		MR Egger	8
2	JfjjnJ	5rt0Eu	AD CSF_X100001948		Weighted median	8
3	JfjjnJ	5rt0Eu	AD CSF_X100001948	Inverse variance weighted		8
4	JfjjnJ	5rt0Eu	AD CSF_X100001948	Simple mode		8
5	JfjjnJ	5rt0Eu	AD CSF_X100001948	Weighted mode		8

	b	se	pval
1	-0.8805	0.4005	0.070238964
2	-0.8684	0.1780	0.000001062
3	-0.8873	0.2028	0.000012128
4	-1.5549	0.6158	0.039505462
5	-0.8809	0.1803	0.001780223

```
mr_heterogeneity(dat)
```

	id.exposure	id.outcome	outcome	exposure	method	Q
1	JfjjnJ	5rt0Eu	AD	CSF_X100001948	MR Egger	11.7
2	JfjjnJ	5rt0Eu	AD	CSF_X100001948	Inverse variance weighted	11.7
	Q_df	Q_pval				
1	6	0.06902				
2	7	0.11086				

```
mr_pleiotropy_test(dat)
```

	id.exposure	id.outcome	outcome	exposure	egger_intercept	se	pval
1	JfjjnJ	5rt0Eu	AD	CSF_X100001948	-0.0002445	0.01199	0.9844

```
mr_leaveoneout(dat)
```

	exposure	outcome	id.exposure	id.outcome	samplesize	SNP
1	CSF_X100001948	AD	JfjjnJ	5rt0Eu	487511	15:62455571:c:t
2	CSF_X100001948	AD	JfjjnJ	5rt0Eu	487511	15:62561062:c:t
3	CSF_X100001948	AD	JfjjnJ	5rt0Eu	487511	15:62926987:t:c
4	CSF_X100001948	AD	JfjjnJ	5rt0Eu	487511	15:62929201:c:t
5	CSF_X100001948	AD	JfjjnJ	5rt0Eu	487511	15:62979292:g:c
6	CSF_X100001948	AD	JfjjnJ	5rt0Eu	487511	15:63138257:c:t
7	CSF_X100001948	AD	JfjjnJ	5rt0Eu	487511	15:63142564:a:g
8	CSF_X100001948	AD	JfjjnJ	5rt0Eu	487511	15:63518986:g:c
9	CSF_X100001948	AD	JfjjnJ	5rt0Eu	487511	All
	b	se	p			
1	-0.9288	0.1956	0.000002043			
2	-0.9065	0.1960	0.000003737			
3	-0.8666	0.2073	0.000029091			
4	-0.8857	0.2227	0.000069647			
5	-0.8811	0.2168	0.000048266			
6	-0.8044	0.1842	0.000012591			

```

7 -0.9891 0.5258 0.059959714
8 -0.9167 0.2076 0.000010031
9 -0.8873 0.2028 0.000012128

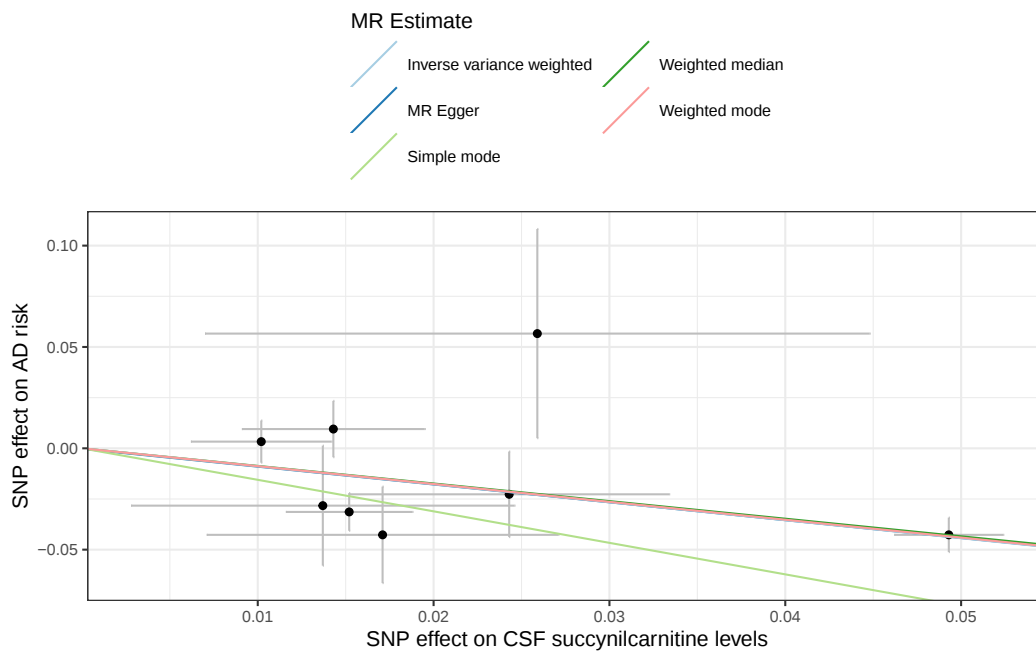
```

```

p3 = mr_scatter_plot(res, dat)[[1]] +
  xlab("SNP effect on CSF succinylcarnitine levels") +
  ylab("SNP effect on AD risk")

```

```
p3
```



```

ggsave(str_interp("${res$exposure[1]}.${res$outcome[1]}.pdf"), plot = p3, width = 10.5, height = 10.5)

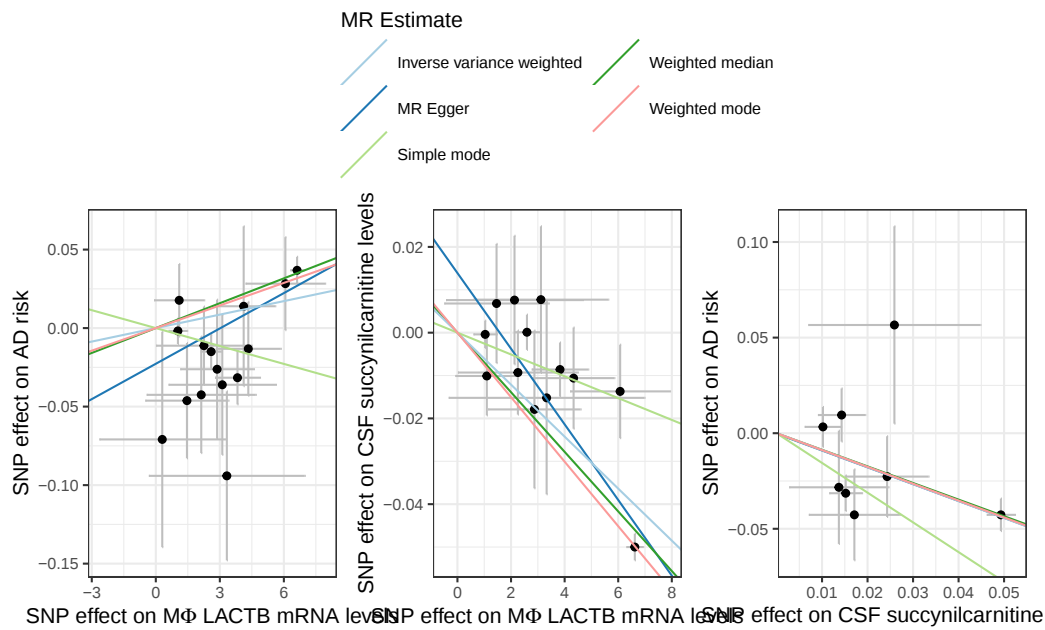
```

```

p <- p1 + p2 + p3 + plot_layout(guides = "collect") & theme(legend.position = 'top')

```

```
p
```



```
ggsave("lactb_succinylcarnitine_ad.mr_plot.pdf", plot = p, width = 7.5, height = 4.5, units = "in")
```

Locuszoom plots

```
gwas.loc <- locus(data = gwas, gene = "LACTB", flank = 5e5, ens_db = EnsDb.Hsapiens.v75, chr = 15)
```

rs2729835, LACTB, chromosome 15, position 62913999 to 63934260

8147 SNPs/datapoints

```
summary(gwas.loc)
```

Gene LACTB

Chromosome 15, position 62,913,999 to 63,934,260

8147 SNPs/datapoints

23 gene transcripts

11 protein_coding, 5 antisense, 4 lincRNA, 2 miRNA, 1 pseudogene

Ensembl version: 75

Organism: Homo sapiens

Genome build: GRCh37

```
gwas.loc <- link_LD(gwas.loc, token = "8656d0cbaeac")
```

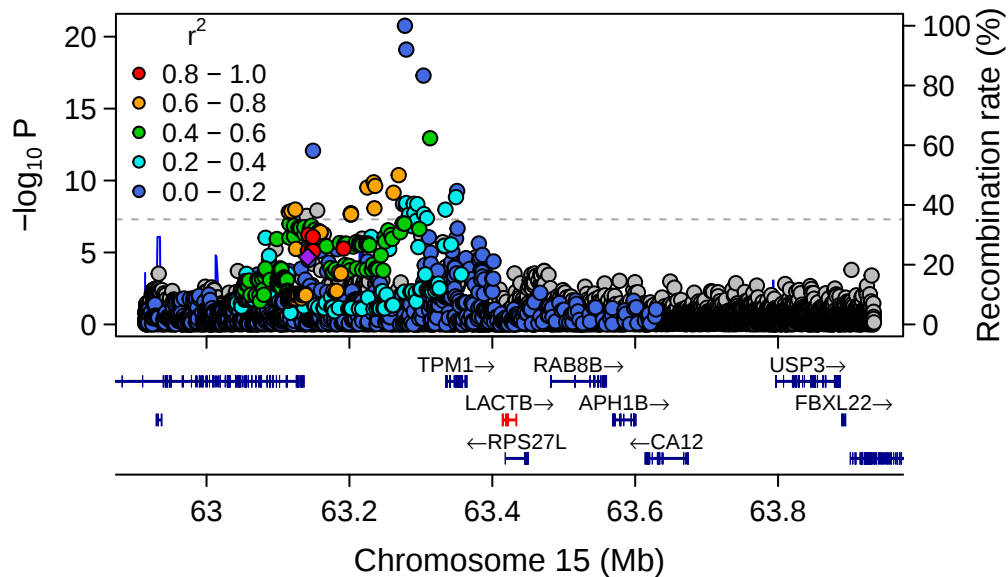
LDlink server is working...

Matched 1219 SNPs (6.87 secs)

```
gwas.loc <- link_recomb(gwas.loc)
```

Retrieving recombination data from UCSC

```
locus_plot(gwas.loc, highlight = "LACTB", filter_gene_biotype = 'protein_coding')
```



```
eqtl.gene.loc <- locus(data = eqtl.gene, gene = "LACTB", flank = 5e5, ens_db = EnsDb.Hsapiens)
```

rs2729835, LACTB, chromosome 15, position 62913999 to 63934260

3355 SNPs/datapoints

```
summary(eqtl.gene.loc)
```

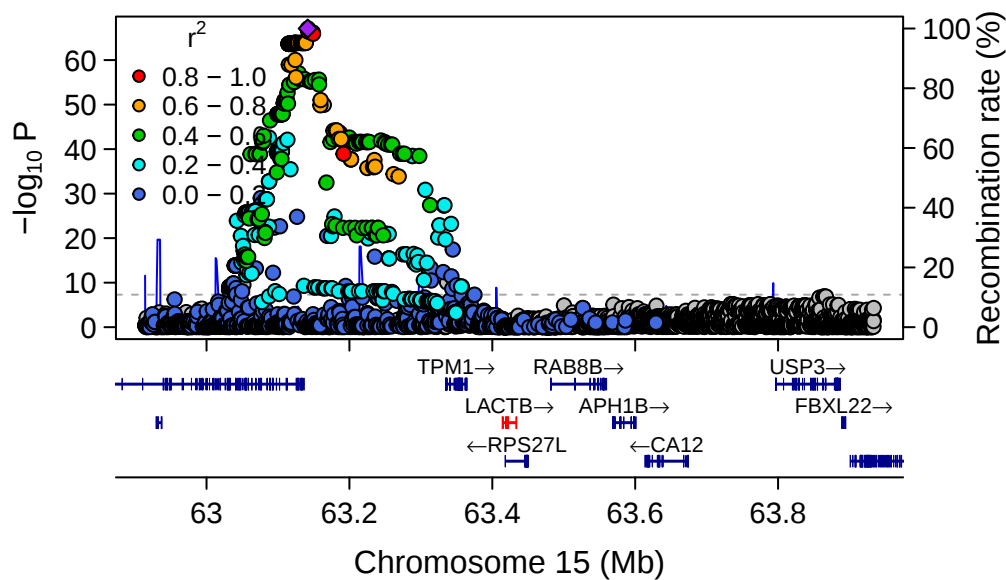
Gene LACTB
Chromosome 15, position 62,913,999 to 63,934,260
3355 SNPs/datapoints
23 gene transcripts
11 protein_coding, 5 antisense, 4 lincRNA, 2 miRNA, 1 pseudogene
Ensembl version: 75
Organism: Homo sapiens
Genome build: GRCh37

```
eqtl.gene.loc <- link_LD(eqtl.gene.loc, token = "8656d0cbaeac")
```

Matched 1087 SNPs (0.000451 secs)

```
eqtl.gene.loc <- link_recomb(eqtl.gene.loc)
```

```
locus_plot(eqtl.gene.loc, highlight = "LACTB", filter_gene_biotype = 'protein_coding')
```



```
mqt1.loc <- locus(data = eqtl, gene = "LACTB", flank = 5e5, ens_db = EnsDb.Hsapiens.v75, chr
```

rs2729835, LACTB, chromosome 15, position 62913999 to 63934260

76622 SNPs/datapoints

```
summary(mqt1.loc)
```

Gene LACTB

Chromosome 15, position 62,913,999 to 63,934,260

76622 SNPs/datapoints

23 gene transcripts

11 protein_coding, 5 antisense, 4 lincRNA, 2 miRNA, 1 pseudogene

Ensembl version: 75

Organism: Homo sapiens

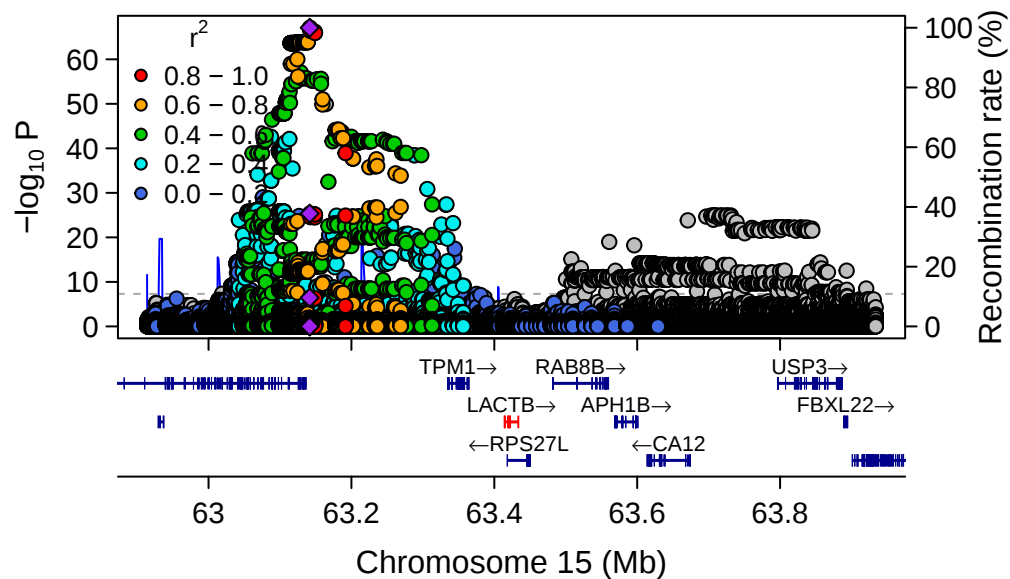
Genome build: GRCh37

```
mqt1.loc <- link_LD(mqt1.loc, token = "8656d0cbaeac")
```

Matched 20563 SNPs (0.00403 secs)

```
mqt1.loc <- link_recomb(mqt1.loc)
```

```
locus_plot(mqt1.loc, highlight = "LACTB", filter_gene_biotype = 'protein_coding')
```



APH1B

```
GENE = "ENSG00000138613" # APH1B

eqtl.gene = eqtl %>% filter(TRAIT == GENE)

mqtl.gene = mqt1 %>% filter(ID %in% eqtl.gene$ID)
gwas.gene = gwas %>% filter(ID %in% eqtl.gene$ID)
```

Format and harmonise data for MR

```
eqtl.gene.ld_clump = ieugwasr::ld_clump(eqtl.gene %>% select(rsid = ID, pval = P), bfile = "o
```

Clumping dHbOLF, 6472 variants, using: data/ldref/1000G.EUR.CPRA_b38.chr15

Removing 6453 of 6472 variants due to LD with other variants or absence from LD reference panel

```
eqtl.gene.exposure = format_data(eqtl.gene %>%
  filter(ID %in% eqtl.gene.ld_clump$rsid) %>%
  select(SNP = ID,
    beta = BETA,
    se = SE,
    effect_allele = ALT,
    other_allele = REF,
    eaf = AF,
    Phenotype = TRAIT,
    chr = CHROM,
    position = POS,
    sample_size = N,
    pval = P,
    gene = TRAIT),
  type="exposure")
```

```
mqt1.gene.ld_clump = ieugwasr::ld_clump(mqt1.gene %>% select(rsid = ID, pval = P), bfile = "C
```

Clumping uLTF71, 6097 variants, using: data/ldref/1000G.EUR.CPRA_b38.chr15

Removing 6087 of 6097 variants due to LD with other variants or absence from LD reference panel

```
mqt1.gene.exposure = format_data(mqt1.gene %>%
  filter(ID %in% mqt1.gene.ld_clump$rsid) %>%
  select(SNP = ID,
    beta = BETA,
    se = SE,
    effect_allele = ALT,
    other_allele = REF,
    eaf = AF,
    Phenotype = TRAIT,
    chr = CHROM,
    position = POS,
    sample_size = N,
    pval = P),
  type="exposure")
```

```
mqt1.gene.outcome = format_data(mqt1.gene %>%
  select(SNP = ID,
    beta = BETA,
```

```

        se = SE,
        effect_allele = ALT,
        other_allele = REF,
        eaf = AF,
        Phenotype = TRAIT,
        chr = CHROM,
        position = POS,
        sample_size = N,
        pval = P),
    type="outcome")

```

```

gwas.gene.outcome = format_data(gwas.gene %>%
    select(SNP = ID,
           beta = BETA,
           se = SE,
           effect_allele = ALT,
           other_allele = REF,
           eaf = AF,
           Phenotype = TRAIT,
           chr = CHROM,
           position = POS,
           sample_size = N,
           ncase = N_CASES,
           ncontrol = N_CTRLs,
           pval = P,
           gene = TRAIT),
    type="outcome")

```

Generating sample size from ncase and ncontrol

```

dat = harmonise_data(exposure_dat = eqtl.gene.exposure,
                    outcome_dat = gwas.gene.outcome)

```

Harmonising ENSG00000138613 (mLJtA1) and AD (mwJnAA)

Analyse data and print/plot results

```

(res = mr(dat))

```

Analysing 'mLJtA1' on 'mwJnAA'

	id.exposure	id.outcome	outcome	exposure	method	nsnp
1	mLJtA1	mwJnAA	AD	ENSG000000138613	MR Egger	19
2	mLJtA1	mwJnAA	AD	ENSG000000138613	Weighted median	19
3	mLJtA1	mwJnAA	AD	ENSG000000138613	Inverse variance weighted	19
4	mLJtA1	mwJnAA	AD	ENSG000000138613	Simple mode	19
5	mLJtA1	mwJnAA	AD	ENSG000000138613	Weighted mode	19

	b	se	pval
1	-0.02877396	0.017004	0.1089
2	-0.00758644	0.010150	0.4548
3	0.00002654	0.007999	0.9974
4	-0.01693756	0.014170	0.2475
5	-0.00909930	0.008696	0.3093

`mr_heterogeneity(dat)`

	id.exposure	id.outcome	outcome	exposure	method
1	mLJtA1	mwJnAA	AD	ENSG000000138613	MR Egger
2	mLJtA1	mwJnAA	AD	ENSG000000138613	Inverse variance weighted

	Q	Q_df	Q_pval
1	18.62	17	0.3505
2	22.52	18	0.2096

`mr_pleiotropy_test(dat)`

	id.exposure	id.outcome	outcome	exposure	egger_intercept	se
1	mLJtA1	mwJnAA	AD	ENSG000000138613	0.03138	0.01664

	pval
1	0.07646

`mr_leaveoneout(dat)`

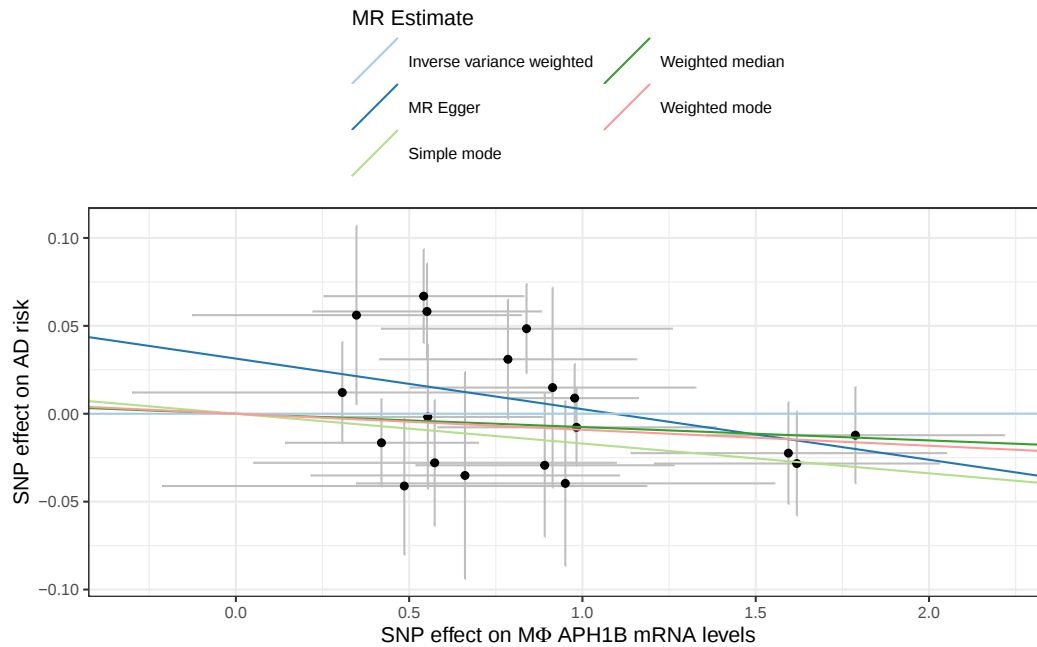
	exposure	outcome	id.exposure	id.outcome	samplesize	SNP
1	ENSG000000138613	AD	mLJtA1	mwJnAA	487511	15:62311651:t:c
2	ENSG000000138613	AD	mLJtA1	mwJnAA	487511	15:62456877:c:t
3	ENSG000000138613	AD	mLJtA1	mwJnAA	487511	15:62592045:t:c
4	ENSG000000138613	AD	mLJtA1	mwJnAA	487511	15:62595386:c:t
5	ENSG000000138613	AD	mLJtA1	mwJnAA	487511	15:62687961:a:g
6	ENSG000000138613	AD	mLJtA1	mwJnAA	487511	15:62780067:c:t

7	ENSG00000138613	AD	mLJtA1	mwJnAA	487511	15:62794527:c:t
8	ENSG00000138613	AD	mLJtA1	mwJnAA	487511	15:62822417:c:t
9	ENSG00000138613	AD	mLJtA1	mwJnAA	487511	15:62979292:g:c
10	ENSG00000138613	AD	mLJtA1	mwJnAA	487511	15:63164189:c:t
11	ENSG00000138613	AD	mLJtA1	mwJnAA	487511	15:63203962:c:t
12	ENSG00000138613	AD	mLJtA1	mwJnAA	487511	15:63273445:t:a
13	ENSG00000138613	AD	mLJtA1	mwJnAA	487511	15:63414875:a:t
14	ENSG00000138613	AD	mLJtA1	mwJnAA	487511	15:63564573:g:t
15	ENSG00000138613	AD	mLJtA1	mwJnAA	487511	15:63901140:g:a
16	ENSG00000138613	AD	mLJtA1	mwJnAA	487511	15:64008168:c:t
17	ENSG00000138613	AD	mLJtA1	mwJnAA	487511	15:64035151:g:a
18	ENSG00000138613	AD	mLJtA1	mwJnAA	487511	15:64053387:c:t
19	ENSG00000138613	AD	mLJtA1	mwJnAA	487511	15:64063833:g:a
20	ENSG00000138613	AD	mLJtA1	mwJnAA	487511	All

	b	se	p
1	0.00092932	0.008664	0.9146
2	0.00067406	0.008172	0.9343
3	-0.00035967	0.008015	0.9642
4	0.00005741	0.008270	0.9945
5	-0.00337940	0.007715	0.6613
6	0.00037103	0.008192	0.9639
7	0.00092112	0.008183	0.9104
8	0.00259991	0.008810	0.7679
9	0.00318750	0.008726	0.7149
10	-0.00131227	0.008771	0.8811
11	0.00060715	0.008209	0.9410
12	-0.00262957	0.007228	0.7160
13	0.00193277	0.009253	0.8345
14	0.00085777	0.008235	0.9170
15	-0.00107957	0.008186	0.8951
16	0.00069680	0.008058	0.9311
17	-0.00019107	0.008273	0.9816
18	-0.00020376	0.008223	0.9802
19	-0.00222237	0.007412	0.7643
20	0.00002654	0.007999	0.9974

```
p1 = mr_scatter_plot(res, dat)[[1]] +
  xlab(expression(paste("SNP effect on M", Phi, " APOB mRNA levels"))) +
  ylab("SNP effect on AD risk")
```

```
p1
```



```
ggsave(str_interp("${res$exposure[1]}.${res$outcome[1]}.pdf"), plot = p1, width = 10.5, height = 10.5)
```

```
dat = harmonise_data(exposure_dat = eqtl.gene.exposure,
                     outcome_dat = mqt1.gene.outcome)
```

Harmonising ENSG00000138613 (mLJtA1) and CSF_X100001948 (UjcIe9)

```
(res = mr(dat))
```

Analysing 'mLJtA1' on 'UjcIe9'

	id.exposure	id.outcome		outcome	exposure	
1	mLJtA1	UjcIe9	CSF_X100001948	ENSG00000138613		
2	mLJtA1	UjcIe9	CSF_X100001948	ENSG00000138613		
3	mLJtA1	UjcIe9	CSF_X100001948	ENSG00000138613		
4	mLJtA1	UjcIe9	CSF_X100001948	ENSG00000138613		
5	mLJtA1	UjcIe9	CSF_X100001948	ENSG00000138613		
		method	nsnp	b	se	pval
1		MR Egger	19	0.004992	0.008471	0.56338
2		Weighted median	19	0.003132	0.004295	0.46588
3		Inverse variance weighted	19	0.005930	0.003604	0.09988

4	Simple mode	19	0.005543	0.006263	0.38783
5	Weighted mode	19	0.005543	0.003923	0.17473

mr_heterogeneity(dat)

	id.exposure	id.outcome	outcome	exposure	
1	mLJtA1	UjcIe9	CSF_X100001948	ENSG000000138613	
2	mLJtA1	UjcIe9	CSF_X100001948	ENSG000000138613	
		method	Q	Q_df	Q_pval
1		MR Egger	28.75	17	0.03689
2	Inverse variance weighted		28.78	18	0.05118

mr_pleiotropy_test(dat)

	id.exposure	id.outcome	outcome	exposure	egger_intercept
1	mLJtA1	UjcIe9	CSF_X100001948	ENSG000000138613	0.001022
	se	pval			
1	0.008304	0.9035			

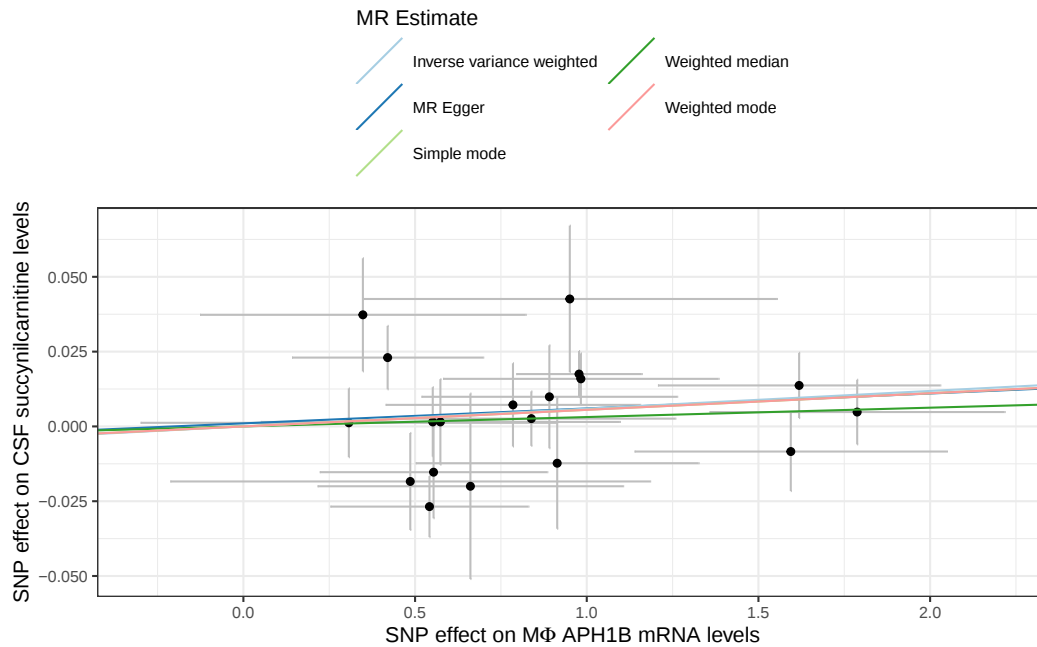
mr_leaveoneout(dat)

	exposure	outcome	id.exposure	id.outcome	samplesize
1	ENSG000000138613	CSF_X100001948	mLJtA1	UjcIe9	NA
2	ENSG000000138613	CSF_X100001948	mLJtA1	UjcIe9	NA
3	ENSG000000138613	CSF_X100001948	mLJtA1	UjcIe9	NA
4	ENSG000000138613	CSF_X100001948	mLJtA1	UjcIe9	NA
5	ENSG000000138613	CSF_X100001948	mLJtA1	UjcIe9	NA
6	ENSG000000138613	CSF_X100001948	mLJtA1	UjcIe9	NA
7	ENSG000000138613	CSF_X100001948	mLJtA1	UjcIe9	NA
8	ENSG000000138613	CSF_X100001948	mLJtA1	UjcIe9	NA
9	ENSG000000138613	CSF_X100001948	mLJtA1	UjcIe9	NA
10	ENSG000000138613	CSF_X100001948	mLJtA1	UjcIe9	NA
11	ENSG000000138613	CSF_X100001948	mLJtA1	UjcIe9	NA
12	ENSG000000138613	CSF_X100001948	mLJtA1	UjcIe9	NA
13	ENSG000000138613	CSF_X100001948	mLJtA1	UjcIe9	NA
14	ENSG000000138613	CSF_X100001948	mLJtA1	UjcIe9	NA
15	ENSG000000138613	CSF_X100001948	mLJtA1	UjcIe9	NA
16	ENSG000000138613	CSF_X100001948	mLJtA1	UjcIe9	NA
17	ENSG000000138613	CSF_X100001948	mLJtA1	UjcIe9	NA
18	ENSG000000138613	CSF_X100001948	mLJtA1	UjcIe9	NA

19	ENSG00000138613	CSF_X100001948	mLJtA1	UjcIe9	NA
20	ENSG00000138613	CSF_X100001948	mLJtA1	UjcIe9	NA
	SNP	b	se	p	
1	15:62311651:t:c	0.004681	0.003819	0.22027	
2	15:62456877:c:t	0.005974	0.003732	0.10941	
3	15:62592045:t:c	0.005650	0.003481	0.10458	
4	15:62595386:c:t	0.006286	0.003631	0.08344	
5	15:62687961:a:g	0.006139	0.003838	0.10970	
6	15:62780067:c:t	0.006064	0.003676	0.09905	
7	15:62794527:c:t	0.005448	0.003579	0.12789	
8	15:62822417:c:t	0.007435	0.003805	0.05067	
9	15:62979292:g:c	0.005377	0.004081	0.18762	
10	15:63164189:c:t	0.004126	0.003790	0.27625	
11	15:63203962:c:t	0.005299	0.003478	0.12758	
12	15:63273445:t:a	0.007230	0.003121	0.02053	
13	15:63414875:a:t	0.006858	0.004178	0.10071	
14	15:63564573:g:t	0.005814	0.003745	0.12048	
15	15:63901140:g:a	0.005844	0.003755	0.11966	
16	15:64008168:c:t	0.006252	0.003608	0.08309	
17	15:64035151:g:a	0.006208	0.003691	0.09262	
18	15:64053387:c:t	0.005942	0.003719	0.11011	
19	15:64063833:g:a	0.005990	0.003741	0.10937	
20	All	0.005930	0.003604	0.09988	

```
p2 = mr_scatter_plot(res, dat)[[1]] +
  xlab(expression(paste("SNP effect on M", Phi, " APH1B mRNA levels")))) +
  ylab("SNP effect on CSF succinylcarnitine levels")

p2
```



```
ggsave(str_interp("${res$exposure[1]}.${res$outcome[1]}.pdf"), plot = p2, width = 10.5, height = 10.5)
```

```
dat = harmonise_data(exposure_dat = mqt1.gene.exposure,
                     outcome_dat = gwas.gene.outcome)
```

Harmonising CSF_X100001948 (1H2bXQ) and AD (mwJnAA)

```
(res = mr(dat))
```

Analysing '1H2bXQ' on 'mwJnAA'

	id.exposure	id.outcome	outcome	exposure	method	nsnp
1	1H2bXQ	mwJnAA	AD	CSF_X100001948	MR Egger	10
2	1H2bXQ	mwJnAA	AD	CSF_X100001948	Weighted median	10
3	1H2bXQ	mwJnAA	AD	CSF_X100001948	Inverse variance weighted	10
4	1H2bXQ	mwJnAA	AD	CSF_X100001948	Simple mode	10
5	1H2bXQ	mwJnAA	AD	CSF_X100001948	Weighted mode	10
	b	se	pval			
1	-0.8343	0.3744	0.056419510			
2	-0.8685	0.1809	0.000001574			
3	-0.9014	0.1946	0.000003615			

```
4 -1.8114 0.5942 0.013824366
5 -0.8596 0.1670 0.000605754
```

```
mr_heterogeneity(dat)
```

	id.exposure	id.outcome	outcome	exposure	method	Q
1	1H2bXQ	mwJnAA	AD	CSF_X100001948	MR Egger	13.83
2	1H2bXQ	mwJnAA	AD	CSF_X100001948	Inverse variance weighted	13.91
	Q_df	Q_pval				
1	8	0.08623				
2	9	0.12547				

```
mr_pleiotropy_test(dat)
```

	id.exposure	id.outcome	outcome	exposure	egger_intercept	se	pval
1	1H2bXQ	mwJnAA	AD	CSF_X100001948	-0.002385	0.01111	0.8355

```
mr_leaveoneout(dat)
```

	exposure	outcome	id.exposure	id.outcome	samplesize	SNP
1	CSF_X100001948	AD	1H2bXQ	mwJnAA	483897	15:62390324:c:t
2	CSF_X100001948	AD	1H2bXQ	mwJnAA	483897	15:62455571:c:t
3	CSF_X100001948	AD	1H2bXQ	mwJnAA	483897	15:62561062:c:t
4	CSF_X100001948	AD	1H2bXQ	mwJnAA	483897	15:62926987:t:c
5	CSF_X100001948	AD	1H2bXQ	mwJnAA	483897	15:62929201:c:t
6	CSF_X100001948	AD	1H2bXQ	mwJnAA	483897	15:62979292:g:c
7	CSF_X100001948	AD	1H2bXQ	mwJnAA	483897	15:63138257:c:t
8	CSF_X100001948	AD	1H2bXQ	mwJnAA	483897	15:63142564:a:g
9	CSF_X100001948	AD	1H2bXQ	mwJnAA	483897	15:63518986:g:c
10	CSF_X100001948	AD	1H2bXQ	mwJnAA	483897	15:64050396:c:t
11	CSF_X100001948	AD	1H2bXQ	mwJnAA	483897	All
	b	se	p			
1	-0.8940	0.2020	0.0000095852			
2	-0.9430	0.1880	0.0000005294			
3	-0.9205	0.1882	0.0000010014			
4	-0.8809	0.1975	0.0000081903			
5	-0.9003	0.2098	0.0000177930			
6	-0.8952	0.2047	0.0000122868			
7	-0.8199	0.1813	0.0000061441			
8	-1.0663	0.4876	0.0287649500			

```

9 -0.9309 0.1975 0.0000024208
10 -0.8947 0.1945 0.0000042094
11 -0.9014 0.1946 0.0000036145

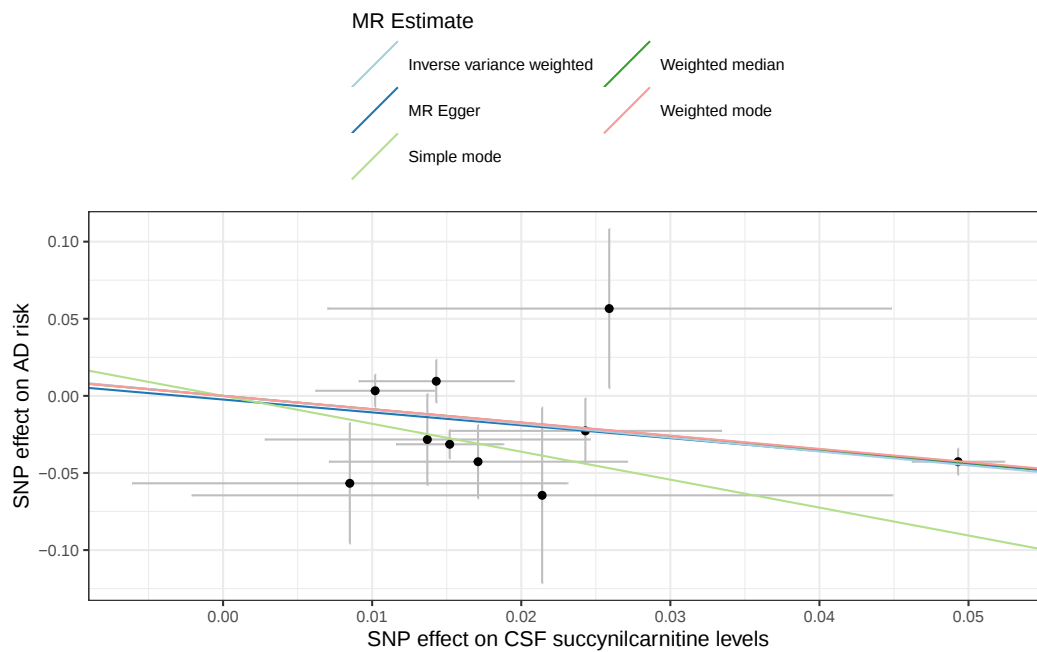
```

```

p3 = mr_scatter_plot(res, dat)[[1]] +
  xlab("SNP effect on CSF succinylcarnitine levels") +
  ylab("SNP effect on AD risk")

```

```
p3
```



```

ggsave(str_interp("${res$exposure[1]}.${res$outcome[1]}.pdf"), plot = p3, width = 10.5, height = 10.5)

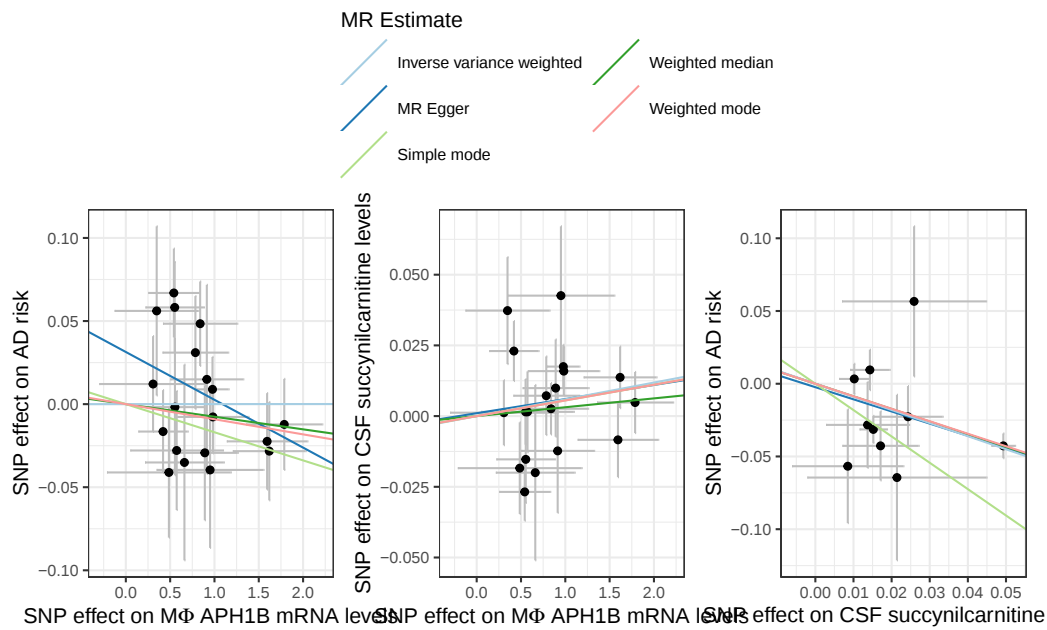
```

```

p <- p1 + p2 + p3 + plot_layout(guides = "collect") & theme(legend.position = 'top')

```

```
p
```



```
ggsave("aph1b_succinylcarnitine_ad.mr_plot.pdf", plot = p, width = 7.5, height = 4.5, units = "in")
```

Locuszoom plots

```
gwas.loc <- locus(data = gwas, gene = "APH1B", flank = 5e5, ens_db = EnsDb.Hsapiens.v75, chr = 15)
```

rs2729835, APH1B, chromosome 15, position 63068217 to 64101325

8020 SNPs/datapoints

```
summary(gwas.loc)
```

Gene APH1B

Chromosome 15, position 63,068,217 to 64,101,325

8020 SNPs/datapoints

22 gene transcripts

10 protein_coding, 5 antisense, 4 lincRNA, 2 miRNA, 1 pseudogene

Ensembl version: 75

Organism: Homo sapiens

Genome build: GRCh37

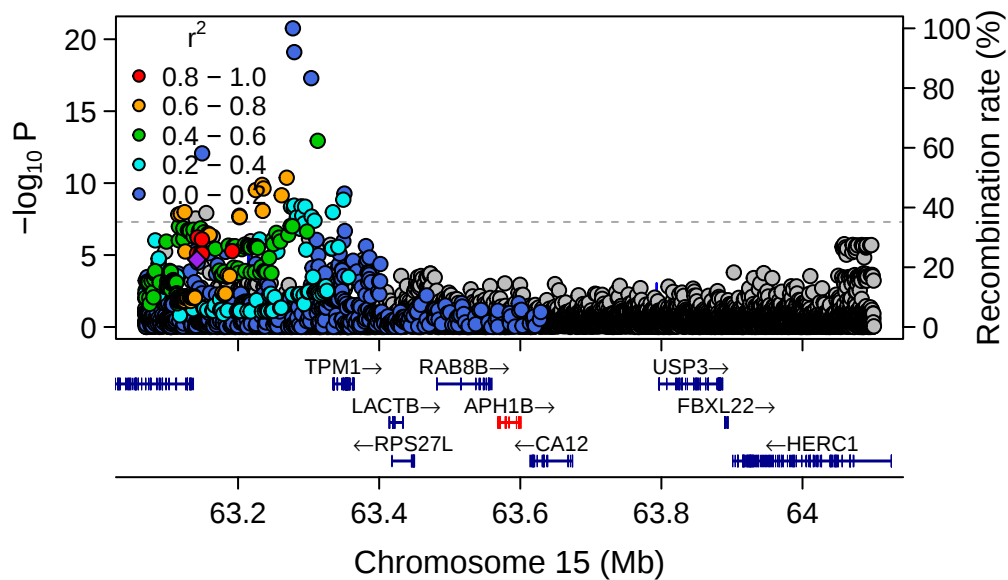
```
gwas.loc <- link_LD(gwas.loc, token = "8656d0cbaeac")
```

Matched 848 SNPs (0.000954 secs)

```
gwas.loc <- link_recomb(gwas.loc)
```

Retrieving recombination data from UCSC

```
locus_plot(gwas.loc, highlight = "APH1B", filter_gene_biotype = 'protein_coding')
```



```
eqtl.gene.loc <- locus(data = eqtl.gene, gene = "APH1B", flank = 5e5, ens_db = EnsDb.Hsapiens)
```

rs2729835, APH1B, chromosome 15, position 63068217 to 64101325

3278 SNPs/datapoints

```
summary(eqtl.gene.loc)
```

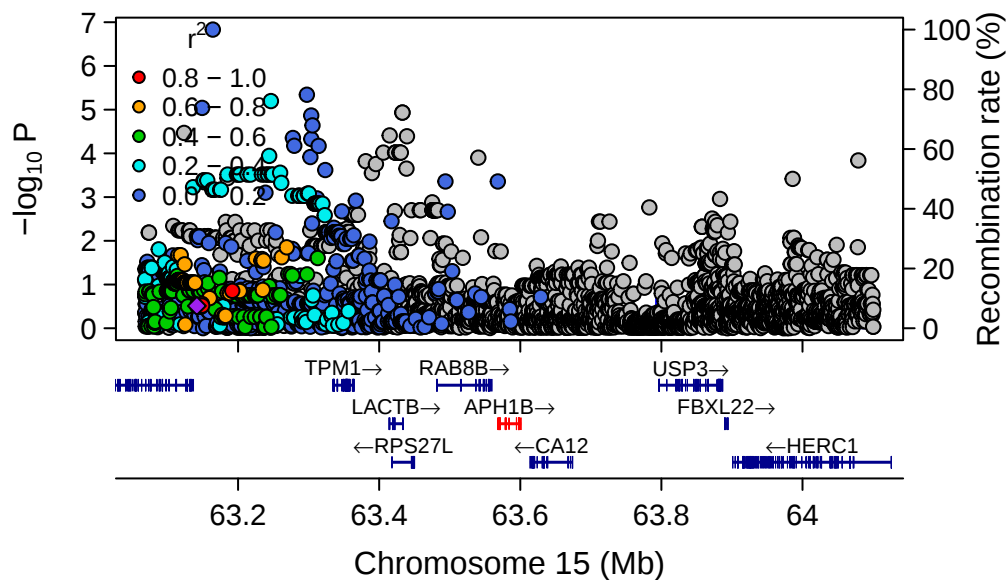
Gene APH1B
Chromosome 15, position 63,068,217 to 64,101,325
3278 SNPs/datapoints
22 gene transcripts
10 protein_coding, 5 antisense, 4 lincRNA, 2 miRNA, 1 pseudogene
Ensembl version: 75
Organism: Homo sapiens
Genome build: GRCh37

```
eqtl.gene.loc <- link_LD(eqtl.gene.loc, token = "8656d0cbaeac")
```

Matched 770 SNPs (0.000434 secs)

```
eqtl.gene.loc <- link_recomb(eqtl.gene.loc)
```

```
locus_plot(eqtl.gene.loc, highlight = "APH1B", filter_gene_biotype = 'protein_coding')
```



```
mqt1.loc <- locus(data = eqtl, gene = "APH1B", flank = 5e5, ens_db = EnsDb.Hsapiens.v75, chr
```

rs2729835, APH1B, chromosome 15, position 63068217 to 64101325

85570 SNPs/datapoints

```
summary(mqtl.loc)
```

Gene APH1B

Chromosome 15, position 63,068,217 to 64,101,325

85570 SNPs/datapoints

22 gene transcripts

10 protein_coding, 5 antisense, 4 lincRNA, 2 miRNA, 1 pseudogene

Ensembl version: 75

Organism: Homo sapiens

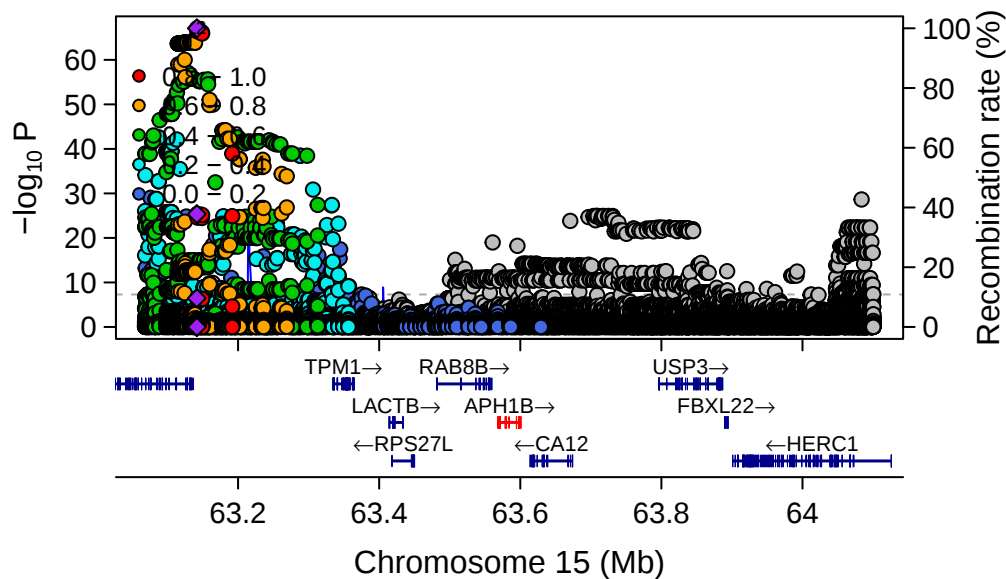
Genome build: GRCh37

```
mqtl.loc <- link_LD(mqtl.loc, token = "8656d0cbaeac")
```

Matched 15208 SNPs (0.00404 secs)

```
mqtl.loc <- link_recomb(mqtl.loc)
```

```
locus_plot(mqtl.loc, highlight = "APH1B", filter_gene_biotype = 'protein_coding')
```



Print environment

```
sessioninfo::session_info()
```

```
- Session info -----
setting  value
version  R version 4.5.2 (2025-10-31)
os       macOS Sequoia 15.7.4
system   aarch64, darwin20
ui       X11
language (EN)
collate  en_US.UTF-8
ctype    en_US.UTF-8
tz       America/New_York
date     2026-02-15
pandoc   3.9 @ /opt/homebrew/bin/ (via rmarkdown)
quarto   1.8.27 @ /usr/local/bin/quarto

- Packages -----
package      * version      date (UTC) lib source
abind         1.4-8         2024-09-12 [1] CRAN (R 4.5.0)
AnnotationDbi * 1.72.0        2025-10-29 [1] Bioconductor 3.22 (R 4.5.1)
AnnotationFilter * 1.34.0        2025-10-29 [1] Bioconductor 3.22 (R 4.5.1)
Biobase       * 2.70.0        2025-10-29 [1] Bioconductor 3.22 (R 4.5.1)
BiocGenerics  * 0.56.0        2025-10-29 [1] Bioconductor 3.22 (R 4.5.1)
BiocIO        1.20.0        2025-10-29 [1] Bioconductor 3.22 (R 4.5.1)
BiocParallel  1.44.0        2025-10-29 [1] Bioconductor 3.22 (R 4.5.1)
Biostrings    2.78.0        2025-10-29 [1] Bioconduc~
bit           4.6.0         2025-03-06 [1] CRAN (R 4.5.0)
bit64         4.6.0-1       2025-01-16 [1] CRAN (R 4.5.0)
bitops        1.0-9         2024-10-03 [1] CRAN (R 4.5.0)
blob          1.3.0         2026-01-14 [1] CRAN (R 4.5.2)
cachem        1.1.0         2024-05-16 [1] CRAN (R 4.5.0)
cigarillo     1.0.0         2025-10-29 [1] Bioconduc~
cli           3.6.5         2025-04-23 [1] CRAN (R 4.5.0)
codetools     0.2-20        2024-03-31 [2] CRAN (R 4.5.2)
coro          1.1.0         2024-11-05 [1] CRAN (R 4.5.0)
cowplot       1.2.0         2025-07-07 [1] CRAN (R 4.5.0)
crayon        1.5.3         2024-06-20 [1] CRAN (R 4.5.0)
curl          7.0.0         2025-08-19 [1] CRAN (R 4.5.0)
data.table    1.18.2.1      2026-01-27 [1] CRAN (R 4.5.2)
```

DBI	1.2.3	2024-06-02	[1]	CRAN (R 4.5.0)
DelayedArray	0.36.0	2025-10-29	[1]	Bioconductor 3.22 (R 4.5.1)
digest	0.6.39	2025-11-19	[1]	CRAN (R 4.5.2)
dplyr	* 1.2.0	2026-02-03	[1]	CRAN (R 4.5.2)
ellmer	0.4.0	2025-11-15	[1]	CRAN (R 4.5.2)
EnsDb.Hsapiens.v75	* 2.99.0	2026-02-13	[1]	Bioconductor
ensemblDb	* 2.34.0	2025-10-29	[1]	Bioconductor 3.22 (R 4.5.1)
evaluate	1.0.5	2025-08-27	[1]	CRAN (R 4.5.0)
farver	2.1.2	2024-05-13	[1]	CRAN (R 4.5.0)
fastmap	1.2.0	2024-05-15	[1]	CRAN (R 4.5.0)
forcats	* 1.0.1	2025-09-25	[1]	CRAN (R 4.5.0)
generics	* 0.1.4	2025-05-09	[1]	CRAN (R 4.5.0)
GenomeInfoDb	1.46.2	2025-12-08	[1]	Bioconductor 3.22 (R 4.5.2)
GenomicAlignments	1.46.0	2025-10-29	[1]	Bioconduc~
GenomicFeatures	* 1.62.0	2025-10-29	[1]	Bioconduc~
GenomicRanges	* 1.62.1	2025-12-08	[1]	Bioconductor 3.22 (R 4.5.2)
gggrid	0.2-0	2022-01-11	[1]	CRAN (R 4.5.0)
ggplot2	* 4.0.2	2026-02-03	[1]	CRAN (R 4.5.2)
ggrepel	0.9.6	2024-09-07	[1]	CRAN (R 4.5.0)
glue	1.8.0	2024-09-30	[1]	CRAN (R 4.5.0)
gtable	0.3.6	2024-10-25	[1]	CRAN (R 4.5.0)
hms	1.1.4	2025-10-17	[1]	CRAN (R 4.5.0)
htmltools	0.5.9	2025-12-04	[1]	CRAN (R 4.5.2)
htmlwidgets	1.6.4	2023-12-06	[1]	CRAN (R 4.5.0)
httr	1.4.8	2026-02-13	[1]	CRAN (R 4.5.2)
httr2	1.2.2	2025-12-08	[1]	CRAN (R 4.5.2)
ieugwasr	1.1.0	2025-07-31	[1]	CRAN (R 4.5.0)
IRanges	* 2.44.0	2025-10-29	[1]	Bioconduc~
jsonlite	2.0.0	2025-03-27	[1]	CRAN (R 4.5.0)
KEGGREST	1.50.0	2025-10-29	[1]	Bioconductor 3.22 (R 4.5.1)
knitr	1.51	2025-12-20	[1]	CRAN (R 4.5.2)
labeling	0.4.3	2023-08-29	[1]	CRAN (R 4.5.0)
lattice	0.22-9	2026-02-09	[1]	CRAN (R 4.5.2)
lazyeval	0.2.2	2019-03-15	[1]	CRAN (R 4.5.0)
LDlinkR	1.4.0	2024-04-10	[1]	CRAN (R 4.5.0)
lifecycle	1.0.5	2026-01-08	[1]	CRAN (R 4.5.2)
locuszoomr	* 0.3.8	2025-03-03	[1]	CRAN (R 4.5.0)
lubridate	* 1.9.5	2026-02-04	[1]	CRAN (R 4.5.2)
magrittr	* 2.0.4	2025-09-12	[1]	CRAN (R 4.5.0)
Matrix	1.7-4	2025-08-28	[2]	CRAN (R 4.5.2)
MatrixGenerics	1.22.0	2025-10-29	[1]	Bioconductor 3.22 (R 4.5.1)
matrixStats	1.5.0	2025-01-07	[1]	CRAN (R 4.5.0)
memoise	2.0.1	2021-11-26	[1]	CRAN (R 4.5.0)

otel	0.2.0	2025-08-29	[1]	CRAN (R 4.5.0)
patchwork	* 1.3.2	2025-08-25	[1]	CRAN (R 4.5.0)
pillar	1.11.1	2025-09-17	[1]	CRAN (R 4.5.0)
pkgconfig	2.0.3	2019-09-22	[1]	CRAN (R 4.5.0)
plotly	4.12.0	2026-01-24	[1]	CRAN (R 4.5.2)
plyr	1.8.9	2023-10-02	[1]	CRAN (R 4.5.0)
png	0.1-8	2022-11-29	[1]	CRAN (R 4.5.0)
ProtGenerics	1.42.0	2025-10-29	[1]	Bioconductor 3.22 (R 4.5.1)
purrr	* 1.2.1	2026-01-09	[1]	CRAN (R 4.5.2)
R6	2.6.1	2025-02-15	[1]	CRAN (R 4.5.0)
ragg	1.5.0	2025-09-02	[1]	CRAN (R 4.5.0)
rappdirs	0.3.4	2026-01-17	[1]	CRAN (R 4.5.2)
RColorBrewer	1.1-3	2022-04-03	[1]	CRAN (R 4.5.0)
Rcpp	1.1.1	2026-01-10	[1]	CRAN (R 4.5.2)
RCurl	1.98-1.17	2025-03-22	[1]	CRAN (R 4.5.0)
readr	* 2.1.6	2025-11-14	[1]	CRAN (R 4.5.2)
restfulr	0.0.16	2025-06-27	[1]	CRAN (R 4.5.0)
rjson	0.2.23	2024-09-16	[1]	CRAN (R 4.5.0)
rlang	1.1.7	2026-01-09	[1]	CRAN (R 4.5.2)
rmarkdown	2.30	2025-09-28	[1]	CRAN (R 4.5.0)
Rsamtools	2.26.0	2025-10-29	[1]	Bioconduc~
RSQLite	2.4.6	2026-02-06	[1]	CRAN (R 4.5.2)
rstudioapi	0.18.0	2026-01-16	[1]	CRAN (R 4.5.2)
rtracklayer	1.70.1	2025-12-20	[1]	https://bioc-release.r-
universe.dev (R 4.5.2)				
S4Arrays	1.10.1	2025-12-08	[1]	Bioconductor 3.22 (R 4.5.2)
S4Vectors	* 0.48.0	2025-10-29	[1]	Bioconduc~
S7	0.2.1	2025-11-14	[1]	CRAN (R 4.5.2)
scales	1.4.0	2025-04-24	[1]	CRAN (R 4.5.0)
Seqinfo	* 1.0.0	2025-10-29	[1]	Bioconduc~
sessioninfo	1.2.3	2025-02-05	[1]	CRAN (R 4.5.0)
SparseArray	1.10.8	2025-12-18	[1]	Bioconductor 3.22 (R 4.5.2)
stringi	1.8.7	2025-03-27	[1]	CRAN (R 4.5.0)
stringr	* 1.6.0	2025-11-04	[1]	CRAN (R 4.5.0)
SummarizedExperiment	1.40.0	2025-10-29	[1]	Bioconduc~
systemfonts	1.3.1	2025-10-01	[1]	CRAN (R 4.5.0)
textshaping	1.0.4	2025-10-10	[1]	CRAN (R 4.5.0)
tibble	* 3.3.1	2026-01-11	[1]	CRAN (R 4.5.2)
tidyr	* 1.3.2	2025-12-19	[1]	CRAN (R 4.5.2)
tidyselect	1.2.1	2024-03-11	[1]	CRAN (R 4.5.0)
tidyverse	* 2.0.0	2023-02-22	[1]	CRAN (R 4.5.0)
timechange	0.4.0	2026-01-29	[1]	CRAN (R 4.5.2)
TwoSampleMR	* 0.6.22	2025-10-25	[1]	https://mrcieu.r-universe.dev (R 4.5.1)

tzdb	0.5.0	2025-03-15	[1]	CRAN (R 4.5.0)
UCSC.utils	1.6.1	2025-12-11	[1]	Bioconductor 3.22 (R 4.5.2)
vctrs	0.7.1	2026-01-23	[1]	CRAN (R 4.5.2)
viridisLite	0.4.3	2026-02-04	[1]	CRAN (R 4.5.2)
withr	3.0.2	2024-10-28	[1]	CRAN (R 4.5.0)
xfun	0.56	2026-01-18	[1]	CRAN (R 4.5.2)
XML	3.99-0.22	2026-02-10	[1]	CRAN (R 4.5.2)
XVector	0.50.0	2025-10-29	[1]	Bioconductor 3.22 (R 4.5.1)
yaml	2.3.12	2025-12-10	[1]	CRAN (R 4.5.2)
zoo	1.8-15	2025-12-15	[1]	CRAN (R 4.5.2)

[1] /Users/marcoe02/.Rlib

[2] /Library/Frameworks/R.framework/Versions/4.5-arm64/Resources/library

* -- Packages attached to the search path.
