

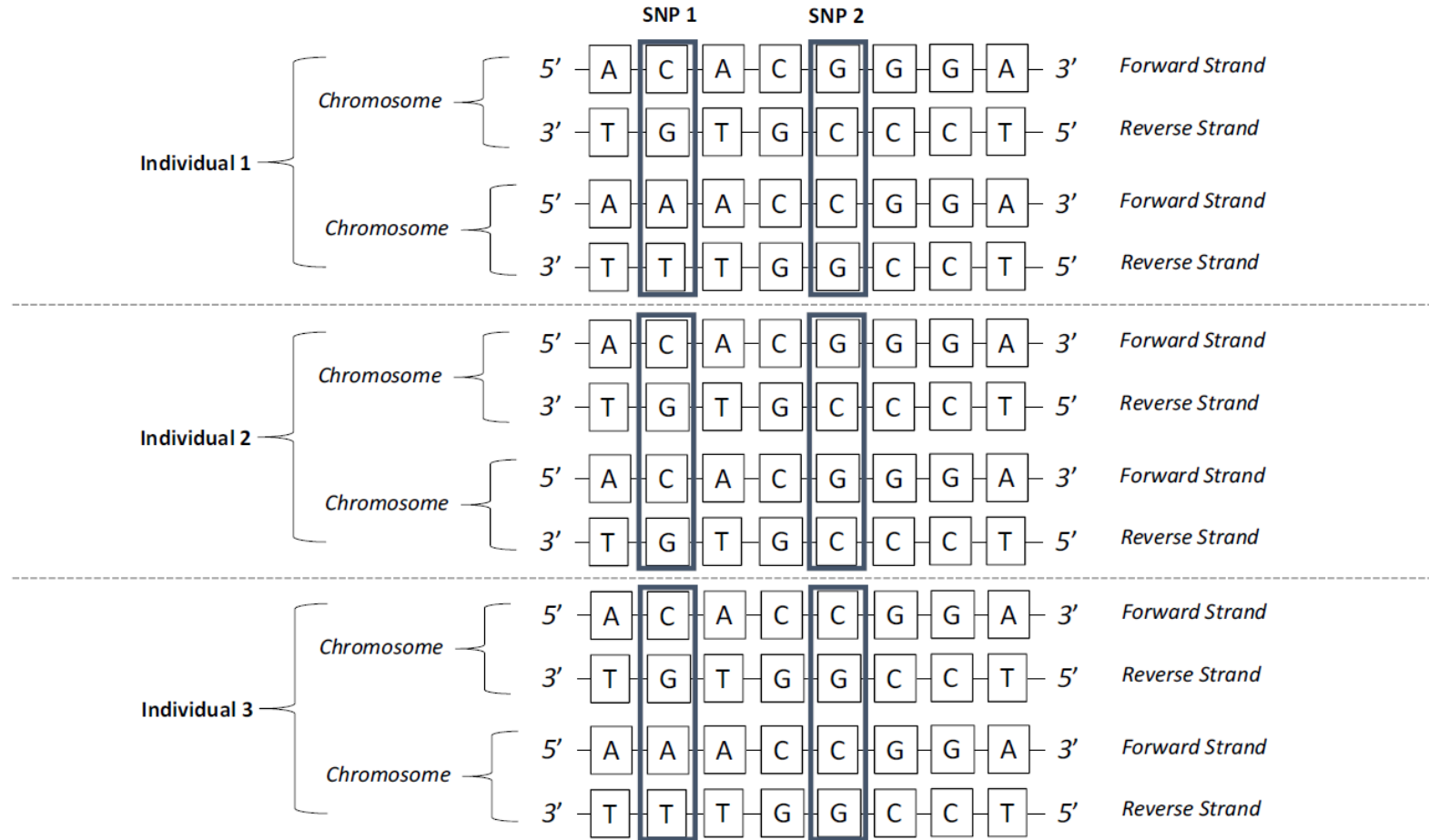
# Mendelian randomization: Practical 2

Does BMI causally affect Coronary Heart Disease?

- Web utilities and software packages exist to carry out two sample MR analyses quickly and efficiently
- This practical is not meant to illustrate the most efficient way to perform an MR study!
- This practical is designed to show you what goes on “under the hood” of these black boxes and to get you familiar with some of the data cleaning and interpretation issues when performing two sample Mendelian randomization. We will also get you to run some of the MR sensitivity analyses too.

# The Issue of Strand

Evans et al (2021) *Behav Genet*



SNP1 F (+) A/C ( AA / AC / CC )  
SNP1 R (-) G/T ( GG / GT / TT )

SNP2 F (+) C/G ( CC / CG / GG )  
SNP1 R (-) G/C ( GG / CG / CC )

# Harmonise exposure and outcome effects

SNP	Exposure GWAS				Outcome GWAS			
	Effect	Effect allele	Other allele	Effect allele frequency	Effect	Effect allele	Other allele	Effect allele frequency
rs12345	0.132	A	G	0.28	0.022	A	G	0.26
rs23456	-0.485	G	T	0.41	<b>0.056</b>	<b>T</b>	<b>G</b>	<b>0.61</b>
rs34567	0.203	G	C	0.11	<b>-0.046</b>	<b>G</b>	<b>C</b>	<b>0.88</b>

↓

SNP	Exposure GWAS				Outcome GWAS			
	Effect	Effect allele	Other allele	Effect allele frequency	Effect	Effect allele	Other allele	Effect allele frequency
rs12345	0.132	A	G	0.28	0.022	A	G	0.26
rs23456	-0.485	G	T	0.41	<b>-0.056</b>	<b>G</b>	<b>T</b>	<b>0.39</b>
rs34567	0.203	G	C	0.11	<b>0.046</b>	<b>G</b>	<b>C</b>	<b>0.12</b>

# Mendelian randomization: Practical 2

# Use your web browser to navigate to: <https://workshop.colorado.edu/rstudio/>

#Login with your username and password

#Click on the “terminal” tab. This will take you to a UNIX like environment where you can copy the files over for this session’s  
#practical exercise

# Now go to your home directory, and move to the directory “MR” you previously created:

```
cd  
cd MR
```

# Copy the PRACTICAL2 directory from David Evans’ Faculty drive into this directory

```
cp -r /faculty/davide/BOULDER2023/PRACTICAL2 .
```

#Move into your newly created PRACTICAL2 directory and print the working directory here

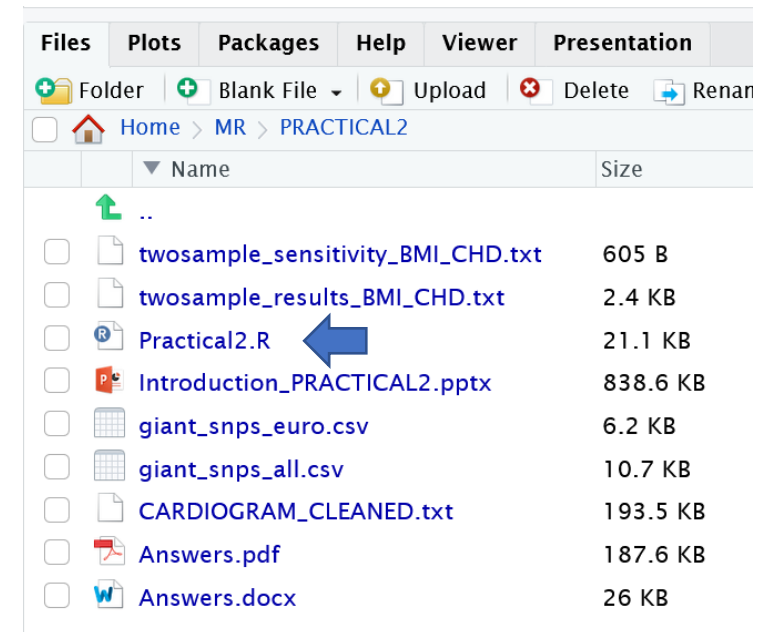
```
cd PRACTICAL2  
pwd
```

#Instructions, commands and questions for this practical are located in the file Practical2.R

#Click on Practical2.R and it will open up

#Remember to set your working directory at the beginning of the prac in R studio e.g.

```
setwd("~/MR/PRACTICAL2")
```



- We have limited time!!!
- DO NOT FOCUS ON THE SYNTAX!!! (just accept that the code does what it says on the tin- go back later and check/run through)
- Run the code in 5 blocks (labelled PART ONE through PART 5)

# Sensitivity Analyses- BMI and CHD

	parameter	estimate	se	lower_CI	upper_CI	p_value
1 IVW	beta	0.287658553	0.086237732	0.11590122	0.459415882	0.001318512
2 Weighted_median	beta	0.379652982	0.117839188	0.08299413	0.554455224	0.005920437
3 Weighted_mode	beta	0.311258179	0.129426222	0.05758745	0.564928912	0.018610428
4 MR-Egger	beta	0.375935570	0.209803912	-0.04201525	0.793886395	0.077191677
	parameter	estimate	se	lower_CI	upper_CI	p_value
5 MR-Egger	alpha	-0.002791481	0.006041587	-0.01482694	0.009243978	0.645387108

- Results look very consistent!
- MR Egger lacks power- so look at coefficient rather than p value!
- MR Egger intercept is a test for directional horizontal pleiotropy