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 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

		Exposu	ire GWAS		Outcome GWAS			
		Effect	Other	Effect allele		Effect	Other	Effect allele
SNP	Effect	allele	allele	frequency	Effect	allele	allele	frequency
rs12345	0.132	А	G	0.28	0.022	А	G	0.26
rs23456	-0.485	G	Т	0.41	0.056	Т	G	0.61
rs34567	0.203	G	С	0.11	-0.046	G	С	0.88
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1		Expos	ure GWAS			Outco	me GWAS	
		Expos Effect	ure GWAS	Effect allele		Outco Effect	me GWAS Other	Effect allele
SNP	Effect	Expos Effect allele	ure GWAS Other allele	Effect allele frequency	Effect	Outco Effect allele	me GWAS Other allele	Effect allele frequency
SNP rs12345	<i>Effect</i> 0.132	Expos Effect allele A	ure GWAS Other allele G	Effect allele frequency 0.28	Effect 0.022	Outco Effect allele A	me GWAS Other allele G	Effect allele frequency 0.26
SNP rs12345 rs23456	<i>Effect</i> 0.132 -0.485	Expos Effect allele A G	ure GWAS Other allele G T	Effect allele frequency 0.28 0.41	<i>Effect</i> 0.022 -0.056	Outco Effect allele A G	me GWAS Other allele G T	Effect allele frequency 0.26 0.39

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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")

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	🖒 Answ	ers.docx				26 KB	

- 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_Cl	upper_Cl	p_value
1 IVW	beta 0.28765855	3 0.086237732	0.11590122 0	459415882	0.001318512
2 Weighted_median	beta 0.37965298	2 0.117839188	0.08299413 0	554455224	0.005920437
3 Weighted_mode	beta 0.31125817	9 0.129426222	0.05758745 0	564928912	0.018610428
4 MR-Egger	beta 0.37593557	0 0.209803912	-0.04201525 0	.793886395	0.077191677

parameter estimate se lower_Cl upper_Cl p_value alpha -0.002791481 0.006041587 -0.01482694 0.009243978 0.645387108

• Results look very consistent!

5 MR-Egger

- MR Egger lacks power- so look at coefficient rather than p value!
- MR Egger intercept is a test for <u>directional</u> horizontal pleiotropy