Two-Sample Mendelian Randomization: Practical 2

Does BMI causally affect Coronary Heart Disease?

Chris Flatley

Two-Sample Mendelian Randomization: Practical 2

- File access
- 1. Website
  - https://cnsgenomics.com/data/teaching/GNGWS24/module4/Practice_2_TSMR
- 2. Server
  - ~/data/module4/Practice_2_TSMR
- Files
  - TSMR_prac.html
  - ./Data/Giant_snps_all.csv
  - ./Data/Giant_snps_euro.csv
  - ./Data/CARDIOGRAM_CLEANED.txt

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- Run this session in pairs
- R packages: metafor, plyr, meta, rmeta
- Open ‘TSMR_prac.html’ and run the blocks of code in R/ R studio
- Remember to set your working directory to the same directory where you downloaded the course material at the beginning of the prac in R/ R studio
- e.g. setwd("/home/**YOURNAMEHERE**/MR/PRACTICAL3/")
- Run the code in 5 blocks (labelled PART 1 through PART 5)
- Answer the questions as you go

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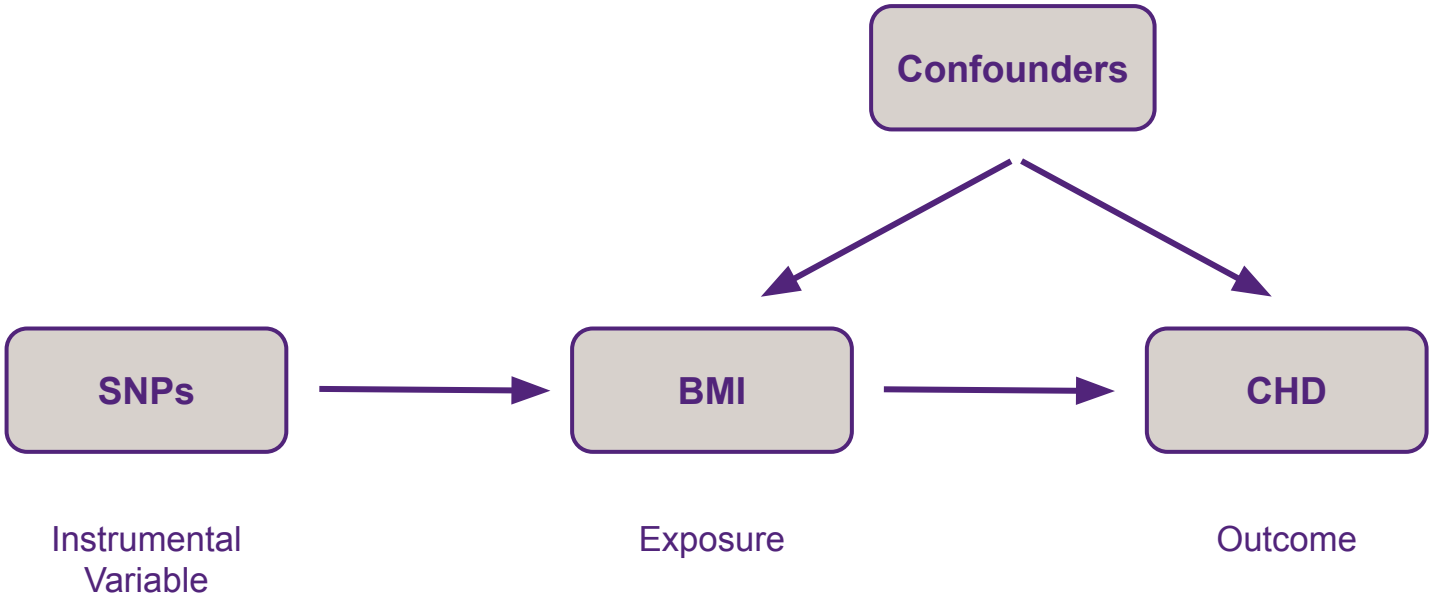

Does BMI causally affect Coronary Heart Disease?

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Objectives

- Identify independent SNPs from BMI GWAS for use as the instrument variable of MR.
  - Data is preprocessed - threshold cut-off (p<5-08) and clumping (LD independence, 10,000 kb, r2=0.001)
- Merge and harmonize with SNPs from the CHD GWAS.
- Check for palindromic SNPs and for SNPs in opposing directions.
- Estimate Wald Ratio and meta analyze results.
- Calculate heterogeneity statistics.
- Run sensitivity analyses.

Sensitivity Analyses

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Interpret the results

Parameter		estimate	se	lower_CI	upper_CI	p_value
IVW	**beta**	0.288	0.086	0.116	0.460	0.001
MR-Egger	**beta**	0.376	0.210	-0.042	0.794	0.077
MR-Egger-Intercept	**alpha**	-0.003	0.006	-0.015	0.009	0.645
Weighted_median	**beta**	0.380	0.118	0.083	0.554	0.006
Weighted_mode	**beta**	0.311	0.129	0.058	0.565	0.019

- How consistent do the estimates of the causal effect look across the different approaches?

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- How consistent do the estimates of the causal effect look across the different approaches?
  - The coefficients are reasonably consistent across the different sensitivity analyses

Sensitivity Analyses

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- Does a p value of p=0.64 for the MR Egger intercept indicate the pleiotropy is not present in the data?

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- Does a p value of p=0.64 for the MR Egger intercept indicate the pleiotropy is not present in the data?
    - This result suggests that directional pleiotropy is not present in the data (balanced pleiotropy may still be present - i.e. when the pleiotropic effects of SNPs tend to balance out).

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- Should we be concerned that the p value for the slope of MR Egger is > 0.05?

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- Should we be concerned that the p value for the slope of MR Egger is > 0.05?
  - No MR Egger has low power in general - more important is whether the coefficient is similar to that obtained using the other approaches.