

CRP AND BLOOD PRESSURE

Q1. As you're running the commands below, fill in the graphical representation of the IV analysis with the appropriate variables and beta-coefficients.

Q2. What does the observational linear regression of SBP on CRP show?

A. Increased CRP predicts higher SBP. Every unit increase in CRP is associated with an increase in SBP of 19.1mmHg (0.45SE) $p < 2 \times 10^{-16}$

Q3. What does the OLS regression of CRP on the CRP SNP rs3091244 show?

A. The rs3091244 SNP is associated with higher CRP. Each copy of the effect allele is associated with an increase in CRP of 0.04 units (0.003 SE) $p < 2 \times 10^{-16}$

Q4. What do the OLS regressions of potential confounders (income, HDL) show?

A. That higher income is associated with lower BP and lower CRP, but income is not associated with the CRP-related *CRP* genotype. Same for HDL: that higher HDL associates with lower BP and lower CRP, but HDL is not associated with the *CRP* genotype.

Q5. What are the implications for these income and HDL associations for the observational CRP-SBP association?

A. The observational association between CRP and SBP could be due to confounding by HDL and Income

Q6. Compare the unadjusted and covariate-adjusted OLS observational regressions. What do they show?

A. The observational association for CRP and SBP reduces after covariate adjustment for HDL and Income in the regression model. However, an association still remains

Q7. What could explain this?

A. That there are other unmeasured confounding factors not being accounted for in the OLS regression model, OR that there is reverse causation of SBP effects on CRP, OR that CRP has some causal effects, over and above confounding. (Additionally, measurement error in the covariates can also lead to persisting associations after covariate adjustment has occurred).

Q8. Run the necessary OLS regressions to compute a Wald estimator

	Estimate	Std. Error	t value	Pr(> t)
CRP~rs3091244	0.041937	0.002838	14.78	<2e-16 ***
SBP~rs3091244	-0.1014	0.1396	-0.726	0.468

Q9. From the above output, compute the causal effect using the Wald estimator, as well as its SE and 95% CI. What do the results show and what do they mean?

A. Little evidence of causal effect of CRP on SBP

Wald estimator causal Beta = $-0.1014/0.0419 = -2.42$

SE = $0.1396/0.0419 = 3.33$

95% CI = -8.95 to 4.11

Q10. Rerun the observational OLS of CRP and SBP and compare with the results from the Wald estimator. What do you notice about the Beta and SEs?

A. The OLS estimator has a much larger beta and a much smaller SE than the Wald ratio estimate.

Q11. What do the TSLS results show and did it differ to the Wald estimator?

A. No strong evidence of causal effect of CRP on SBP. No difference in the beta coefficients between Wald and TSLS, but SE slightly different

Q12. Are they the same as 'ivreg' TSLS function?

A. Coefficient is the same but SE is slightly smaller than what it should be

	Estimate	Std. Error	t value	Pr(> t)
Pred_CRP	-2.418	3.329	-0.726	0.468

Q13. Looking at the F-statistic, determine if weak instruments may be an issue

A. Fstat in both is 218. This is well over the threshold of 10, so no issues with weak instruments

Q14. How would having weak instruments change the causal estimate of CRP on SBP, in this study (single sample)?

A. For single-sample MR, weak instruments biases causal IV estimates towards the confounded observational association. So the null IV estimate would increase towards the observational association beta (observational beta = 19.1)