

## *Supplementary Material*

### **Brief Research Report**

# **Effects of Platelet Count on Blood Pressure: Evidence from Observational and Genetic Investigations**

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**Figure S1.** Flowchart of observational and two-sample Mendelian randomization analyses

**Figure S2.** Directed acyclic graph

**Figure S3.** Mendelian randomization sensitivity analysis plots (effect of platelet count on systolic blood pressure)

**Figure S4.** Mendelian randomization sensitivity analysis plots (effect of systolic blood pressure on platelet count)

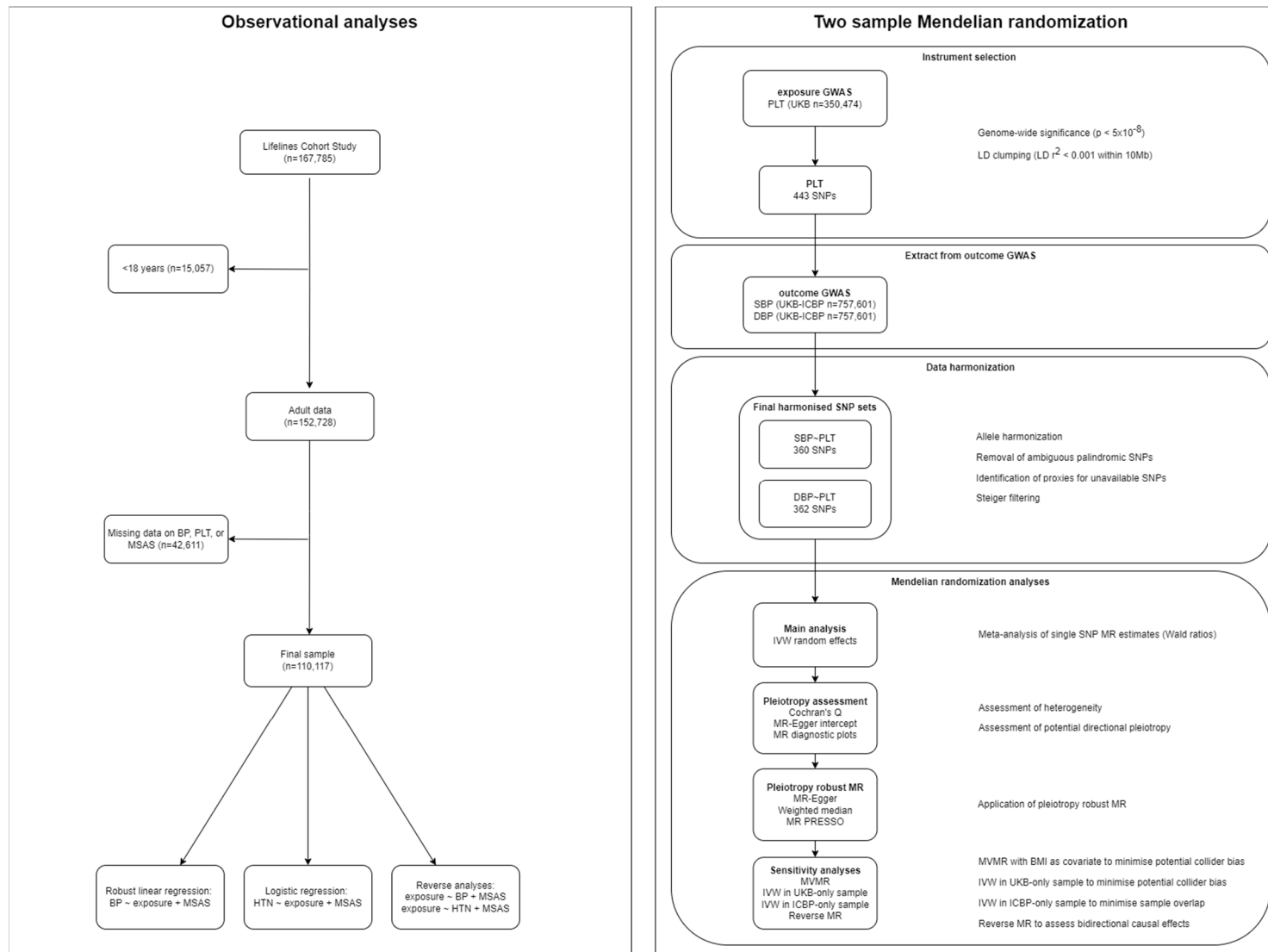
**Figure S5.** Mendelian randomization sensitivity analysis plots (effect of platelet count on diastolic blood pressure)

**Figure S6.** Mendelian randomization sensitivity analysis plots (effect of diastolic blood pressure on platelet count)

**Figure S7.** Comparison of effect estimates between observational, Mendelian randomization, and Mendelian randomization sensitivity analyses for platelet count

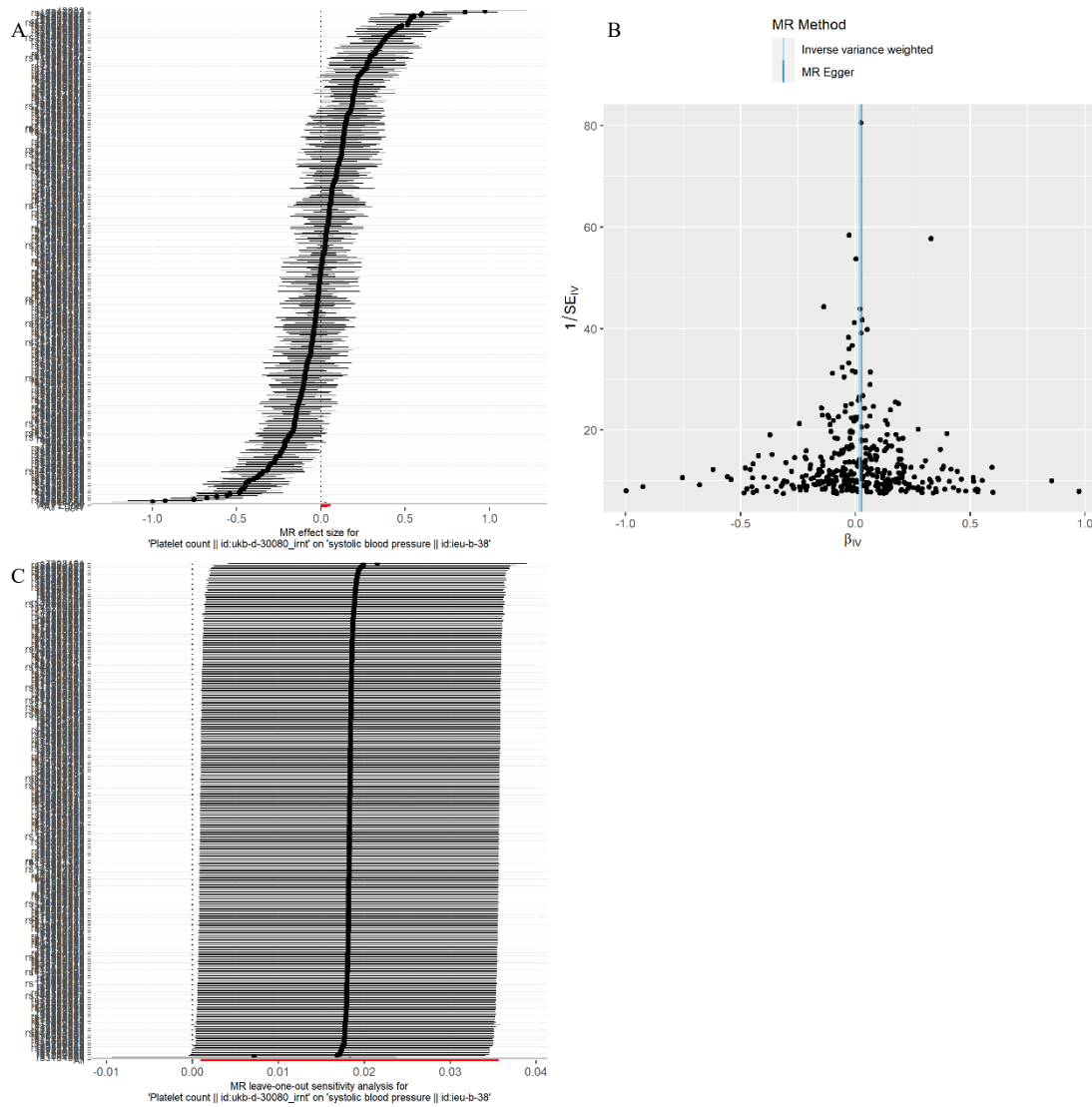
**Supplementary Document.** Consortia information of ICBP (International Consortium of Blood Pressure)

**Supplementary references**



**Figure S1. Flowchart of observational and two-sample Mendelian randomization analyses.** Abbreviations: BP, blood pressure; HTN, hypertension; PLT, platelet count; MSAS, minimal sufficient adjustment sets; MSAS included age, glycated hemoglobin, gender, moderate-vigorous physical activity and smoking; LD, linkage disequilibrium; SBP, systolic blood pressure; DBP, diastolic blood pressure; SNPs, single nucleotide polymorphisms; IVW, inverse-variance weighted; MR, Mendelian randomization; MVMR, Multivariable Mendelian randomization.



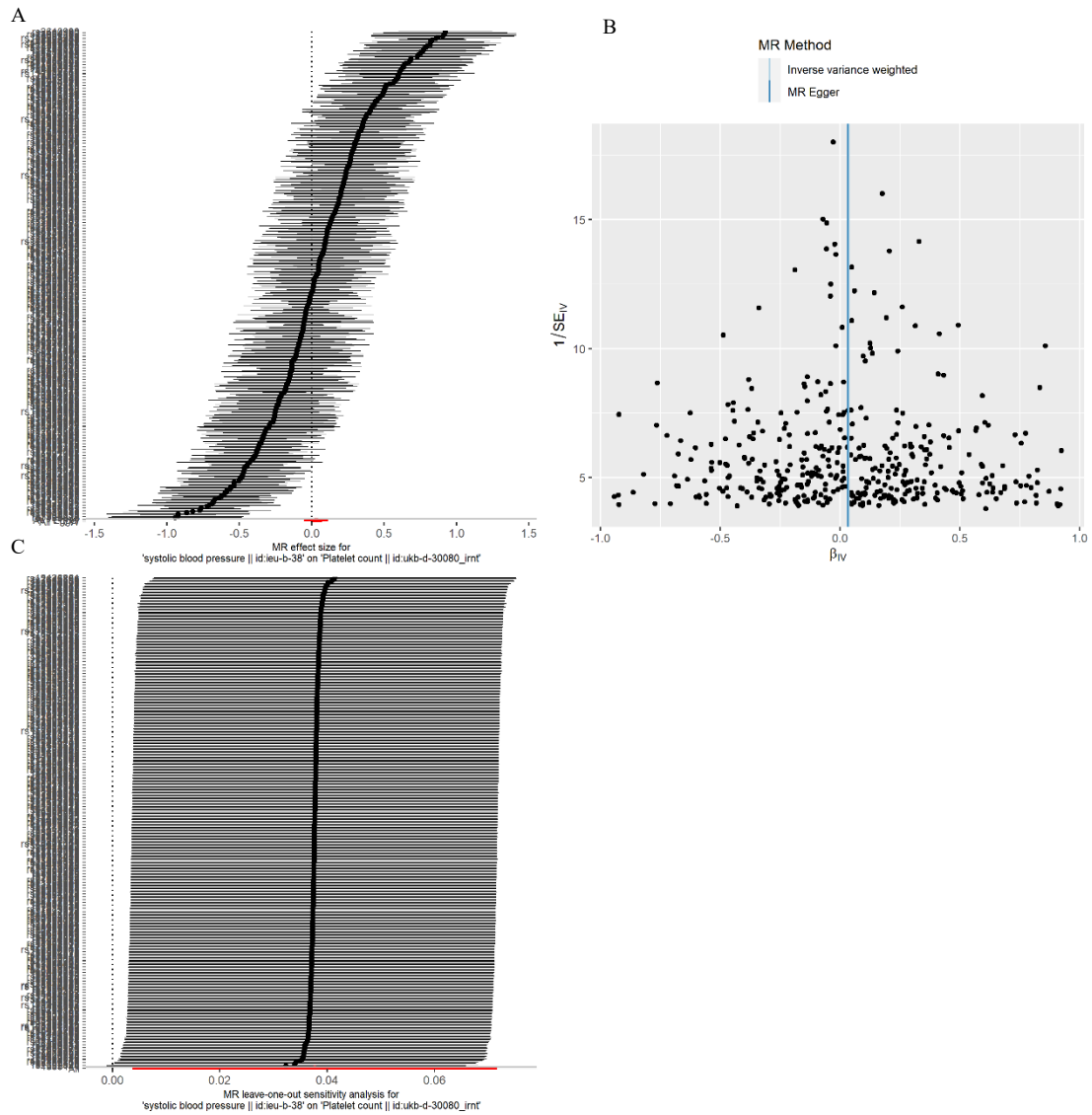


**Figure S3. Mendelian randomization sensitivity analysis plots (effect of platelet count on systolic blood pressure)**

A) Forest plot of single SNP MR estimates with 95%CI, red points indicate the pooled effect size from MR-Egger and inverse-variance weighted (IVW) random effects analyses.

B) MR funnel plot showing single SNP MR estimates against the reciprocal of the standard error of the causal estimate. Vertical lines show the pooled estimates from MR-Egger and IVW analyses.

C) MR leave-one-out plot. Each black point denotes the pooled IVW estimate effect after excluding one particular SNP from the analysis. The red point shows the pooled IVW estimate when including all SNPs.

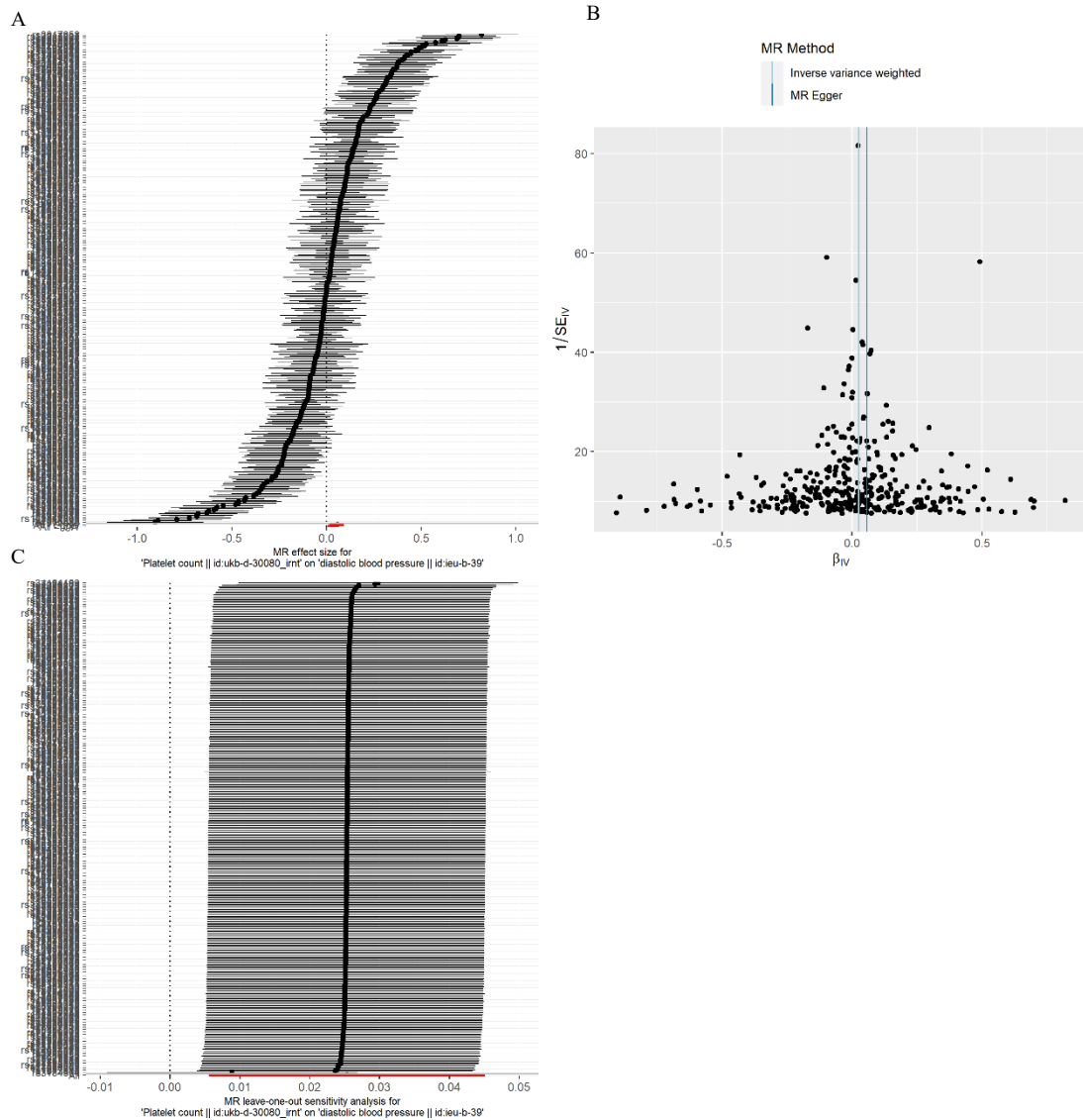


**Figure S4. Mendelian randomization sensitivity analysis plots (effect of systolic blood pressure on platelet count)**

A) Forest plot of single SNP MR estimates with 95%CI, red points indicate the pooled effect size from MR-Egger and inverse-variance weighted (IVW) random effects analyses.

B) MR funnel plot showing single SNP MR estimates against the reciprocal of the standard error of the causal estimate. Vertical lines show the pooled estimates from MR-Egger and IVW analyses.

C) MR leave-one-out plot. Each black point denotes the pooled IVW estimate effect after excluding one particular SNP from the analysis. The red point shows the pooled IVW estimate when including all SNPs.



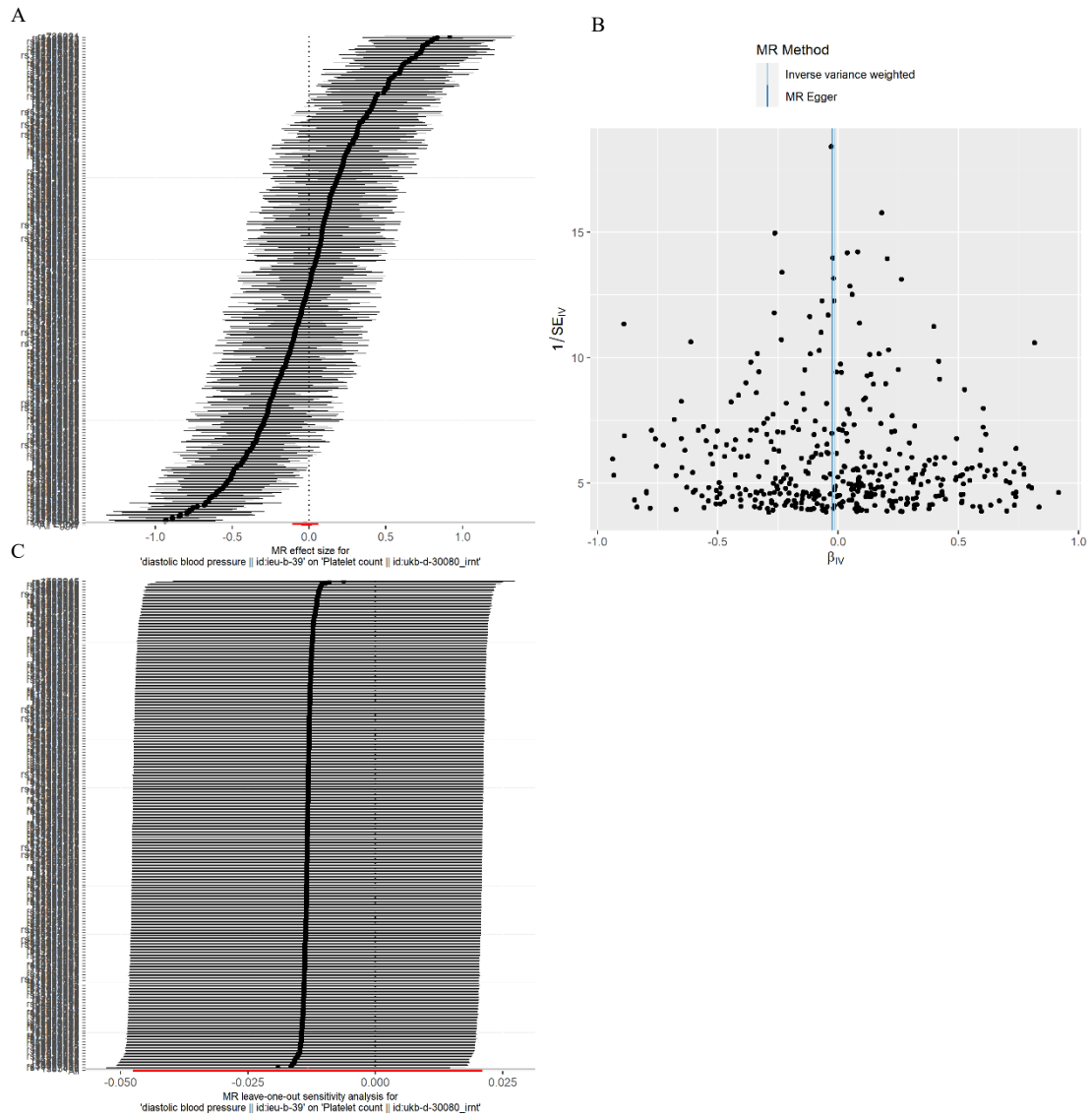
**Figure S5. Mendelian randomization sensitivity analysis plots (effect of platelet count on diastolic blood pressure)**

A) Forest plot of single SNP MR estimates with 95%CI, red points indicate the pooled effect size from MR-Egger and inverse-variance weighted (IVW) random effects analyses.

B) MR funnel plot showing single SNP MR estimates against the reciprocal of the standard error of the causal estimate. Vertical lines show the pooled estimates from MR-Egger and IVW analyses.

C) MR leave-one-out plot. Each black point denotes the pooled IVW estimate effect after excluding one particular SNP from the analysis. The red point shows the pooled IVW estimate when including all SNPs.



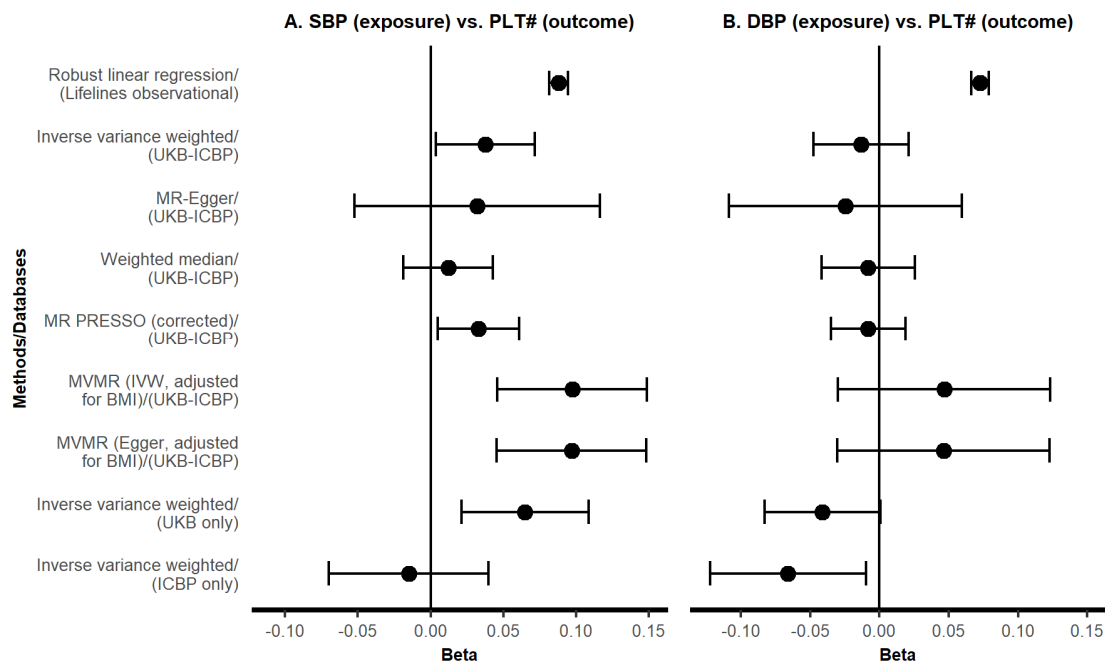


**Figure S6. Mendelian randomization sensitivity analysis plots (effect of diastolic blood pressure on platelet count)**

A) Forest plot of single SNP MR estimates with 95%CI, red points indicate the pooled effect size from MR-Egger and inverse-variance weighted (IVW) random effects analyses.

B) MR funnel plot showing single SNP MR estimates against the reciprocal of the standard error of the causal estimate. Vertical lines show the pooled estimates from MR-Egger and IVW analyses.

C) MR leave-one-out plot. Each black point denotes the pooled IVW estimate effect after excluding one particular SNP from the analysis. The red point shows the pooled IVW estimate when including all SNPs.



**Figure S7. Comparison of effect estimates between observational, Mendelian randomization, and Mendelian randomization sensitivity analyses for platelet count.** Panels A and B show the results of reverse analyses with SBP and DBP as the exposures and platelet count as the outcome. The X-axis indicates effect size as standard deviations difference in outcome per one standard deviation higher value of exposure. The Y-axis indicates analysis method (with their respective data source). Error bars indicate 95% confidence interval (CI). Lifelines observational regression estimates were adjusted for age, sex, glycated hemoglobin, non-occupational physical activity and smoking. Abbreviations: MR PRESSO: Mendelian Randomization Pleiotropy RESidual Sum and Outlier; MVMR: multivariable Mendelian randomization; IVW: inverse variance weighted; UKB: UK Biobank; ICBP: International Consortium of Blood Pressure; PLT#, platelet count; SBP: systolic blood pressure; DBP: diastolic blood pressure.

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