Disease	Gene	nsnp	method	pval		OR(95% CI)
Coronary heart disease	ANGPTL3	4	Weighted median	0.078	<b>•</b>	0.840 (0.691 to 1.020)
		4	Inverse variance weighted	0.031	ю.	0.826 (0.693 to 0.983)
	APOB	20	Weighted median	<0.001	•	0.729 (0.641 to 0.829)
		20	Inverse variance weighted	<0.001		0.761 (0.680 to 0.852)
	APOC3	10	Weighted median	<0.001		0.760 (0.665 to 0.869)
		10	Inverse variance weighted	<0.001	•	0.805 (0.722 to 0.897)
	HMGCR	7	Weighted median	<0.001	101	0.668 (0.548 to 0.815)
		7	Inverse variance weighted	<0.001		0.692 (0.595 to 0.806)
	LPL	23	Weighted median	<0.001		0.672 (0.597 to 0.757)
		23	Inverse variance weighted	<0.001	•	0.643 (0.588 to 0.702)
	NPC1L1	3	Weighted median	0.008	н	0.606 (0.418 to 0.877)
		3	Inverse variance weighted	0.002	₩-	0.604 (0.438 to 0.833)
	PCSK9	12	Weighted median	<0.001	101	0.600 (0.505 to 0.712)
		12	Inverse variance weighted	<0.001		0.600 (0.520 to 0.693)

Disease	Gene	nsnp	method	pval		OR(95% CI)
Coronary heart disease	ANGPTL3	3	Weighted median	0.094	ю.	0.755 (0.543 to 1.049)
		3	Inverse variance weighted	0.037	H <del></del>	0.737 (0.553 to 0.982)
	APOB	15	Weighted median	0.001	101	0.774 (0.662 to 0.906)
		15	Inverse variance weighted	<0.001	101	0.734 (0.627 to 0.859)
	APOC3	5	Weighted median	<0.001	₩.	0.527 (0.401 to 0.694)
		5	Inverse variance weighted	<0.001	101	0.512 (0.408 to 0.641)
	HMGCR	7	Weighted median	<0.001	ю	0.603 (0.468 to 0.776)
		7	Inverse variance weighted	<0.001		0.628 (0.520 to 0.759)
	LPL	2	Inverse variance weighted	< 0.001	•	0.235 (0.136 to 0.406)
	PCSK9	9	Weighted median	< 0.001	104	0.446 (0.343 to 0.581)
		9	Inverse variance weighted	< 0.001		0.455 (0.378 to 0.548)

Figure S1. Association of genetically-proxied drug targets with risk of coronary heart disease.

Forest plot A is the association of genetically proxied lipid-lowering drug targets with risk of CHD using primary lipid modifying effect. Forest plot B is the association of genetically proxied lipid-lowering drug targets with risk of CHD using alternative lipid modifying effect. Data are represented as odds ratios (ORs) with 95% confidence intervals (error bars). An OR of <1.00 suggests a decreased risk of disease associated with lipid-lowering drug treatment. Abbreviations: CHD, Coronary heart disease; OR, odds ratio; Apo-B, Apolipoprotein-B; SNP, single-nucleotide polymorphisms; HMGCR, HMG-CoA reductase; NPC1L1, Niemann-Pick C1-like protein 1; PCSK9, proprotein convertase subtilisin/kexin type 9; APOB, Apolipoprotein B-100; ANGPTL3, angiopoietin-like 3; APOC3, Apolipoprotein C-III; LPL, lipoprotein lipase.

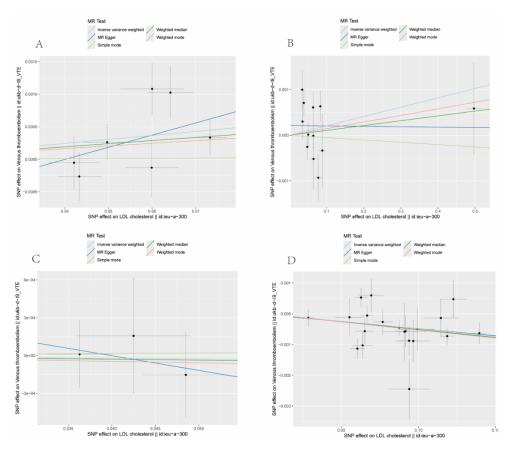


Figure S2. Scatter plot of the association between LDL and VTE using SNPs within or near the HMGCR, PCSK9, NPC1L1, and APOB locus.

A. HMGCR inhibitor on VTE risk; B. PCSK9 inhibitor on VTE risk; C. NPC1L1 inhibitor on VTE risk. D. APOB inhibitor on VTE risk.

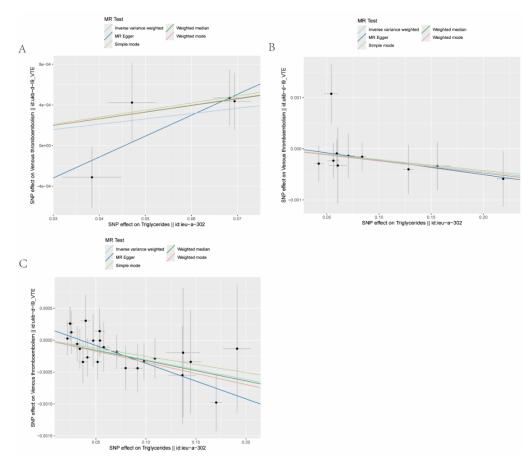


Figure S3. Scatter plot of the association between TG and VTE using SNPs within or near the ANGPTL3, APOC3 and LPL locus.

A. ANGPTL3 inhibitor on VTE risk; B. APOC3 inhibitor on VTE risk; C. LPL inhibitor on VTE risk.

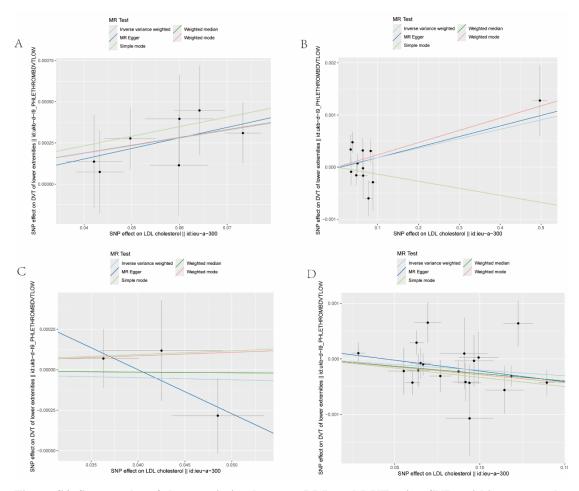


Figure S4. Scatter plot of the association between LDL and DVT using SNPs within or near the HMGCR, PCSK9, NPC1L1, and APOB locus.

A. HMGCR inhibitor on DVT risk; B. PCSK9 inhibitor on DVT risk; C. NPC1L1 inhibitor on DVT risk. D. APOB inhibitor on DVT risk.

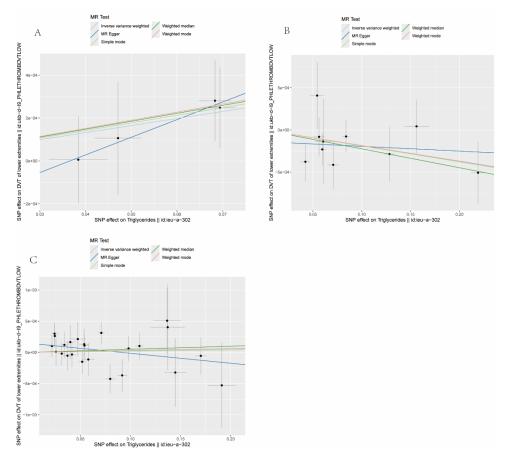


Figure S5. Scatter plot of the association between TG and DVT using SNPs within or near the ANGPTL3, APOC3 and LPL locus.

A. ANGPTL3 inhibitor on DVT risk; B. APOC3 inhibitor on DVT risk; C. LPL inhibitor on DVT risk.

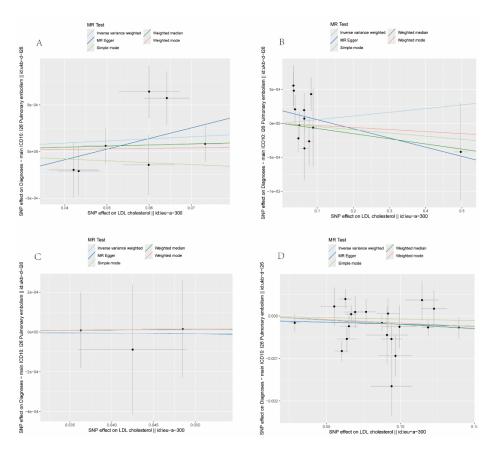


Figure S6. Scatter plot of the association between LDL and PE using SNPs within or near the HMGCR, PCSK9, NPC1L1, and APOB locus.

A. HMGCR inhibitor on PE risk; B. PCSK9 inhibitor on PE risk; C. NPC1L1 inhibitor on PE risk. D. APOB inhibitor on PE risk.

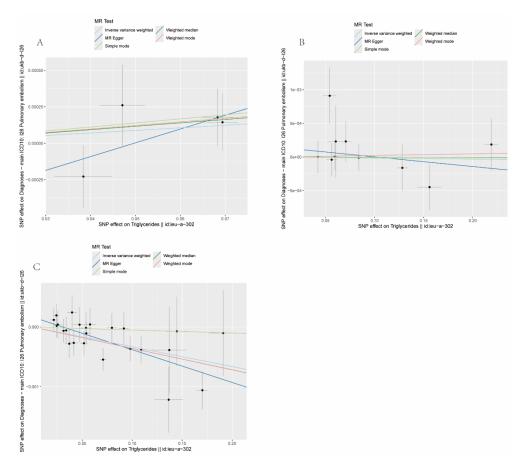
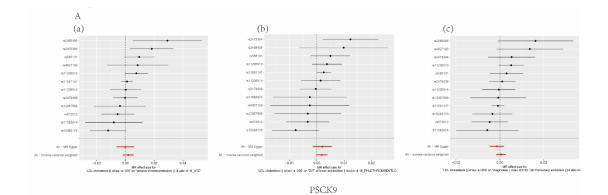
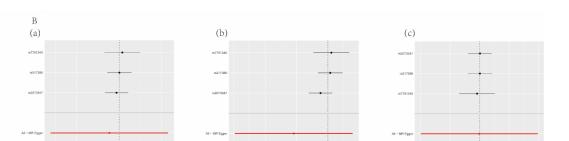


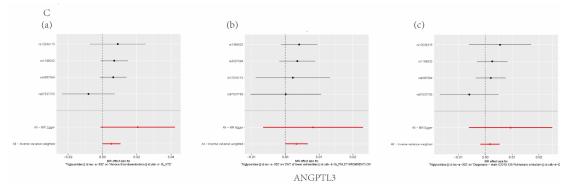
Figure S7. Scatter plot of the association between TG and PE using SNPs within or near the ANGPTL3, APOC3 and LPL locus.

A. ANGPTL3 inhibitor on PE risk; B. APOC3 inhibitor on PE risk; C. LPL inhibitor on PE risk.









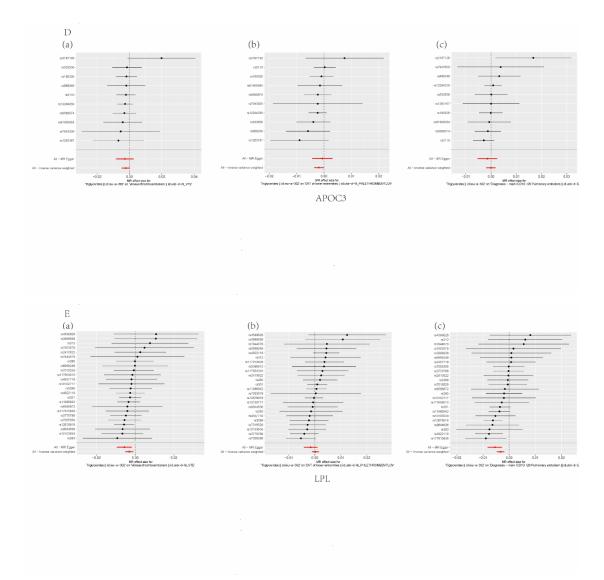
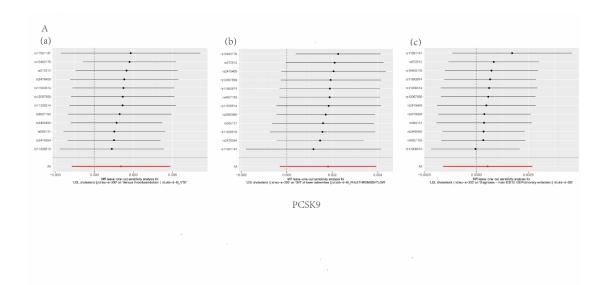
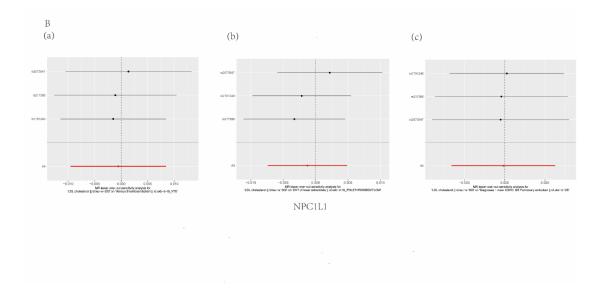
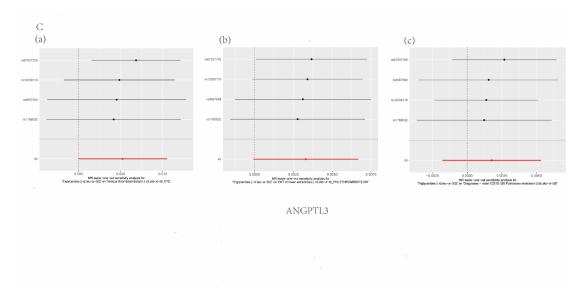


Figure S8. Forest plots showed the casual effect estimates of each SNP in PCSK9, NPC1L1, ANGPTL3, APOC3 inhibition and LPL activation instruments on VTE, DVT and PE.

A. (a) PCSK9 inhibitor on VTE risk; (b) PCSK9 inhibitor on DVT risk; (c) PCSK9 inhibitor on PE risk. B. (a) NPC1L1 inhibitor on VTE risk; (b) NPC1L1 inhibitor on DVT risk; (c) NPC1L1 inhibitor on PE risk. C. (a) ANGPTL3 inhibitor on VTE risk; (b) ANGPTL3 inhibitor on DVT risk; (c) ANGPTL3 inhibitor on PE risk. D. (a) APOC3 inhibitor on VTE risk; (b) APOC3 inhibitor on DVT risk; (c) APOC3 inhibitor on PE risk. E. (a) LPL activation on VTE risk; (b) LPL activation on DVT risk; (c) LPL activation on PE risk.







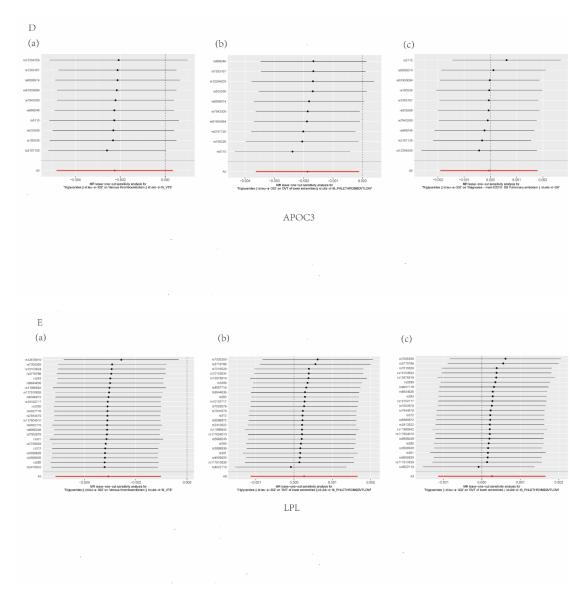


Figure S9. Leave-one-out analysis of genetically PCSK9, NPC1L1, ANGPTL3, APOC3 inhibition and LPL activation instruments on VTE, DVT and PE.

A. (a) PCSK9 inhibitor on VTE risk; (b) PCSK9 inhibitor on DVT risk; (c) PCSK9 inhibitor on PE risk. B. (a) NPC1L1 inhibitor on VTE risk; (b) NPC1L1 inhibitor on DVT risk; (c) NPC1L1 inhibitor on PE risk. C. (a) ANGPTL3 inhibitor on VTE risk; (b) ANGPTL3 inhibitor on DVT risk; (c) ANGPTL3 inhibitor on PE risk. D. (a) APOC3 inhibitor on VTE risk; (b) APOC3 inhibitor on DVT risk; (c) APOC3 inhibitor on PE risk. E. (a) LPL activation on VTE risk; (b) LPL activation on DVT risk; (c) LPL activation on PE risk.

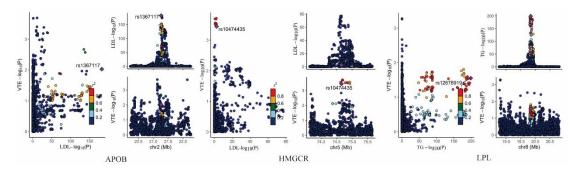


Figure S10. The colocalization visualization result for VTE within the APOB, HMGCR and LPL gene.

A. The colocalization visualization result for LDL-C and VTE within the APOB gene. B. The colocalization visualization result for LDL-C and VTE within the HMGCR gene. C. The colocalization visualization result for TG and VTE within the LPL gene.

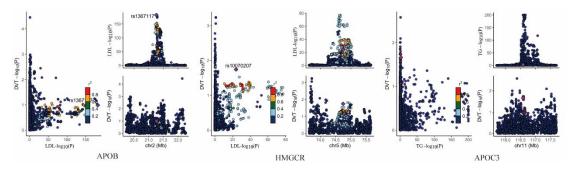
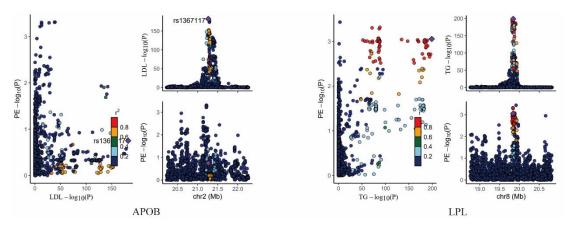


Figure S11. The colocalization visualization result for DVT within the APOB, HMGCR and APOC3 gene.

A. The colocalization visualization result for LDL-C and DVT within the APOB gene. B. The colocalization visualization result for LDL-C and DVT within the HMGCR gene. C. The colocalization visualization result for TG and VTE within the APOC3 gene.



**Figure S12.** The colocalization visualization result for PE within the APOB and LPL gene.

A. The colocalization visualization result for LDL-C and PE within the APOB gene. B. The colocalization visualization result for TG and PE within the LPL gene.