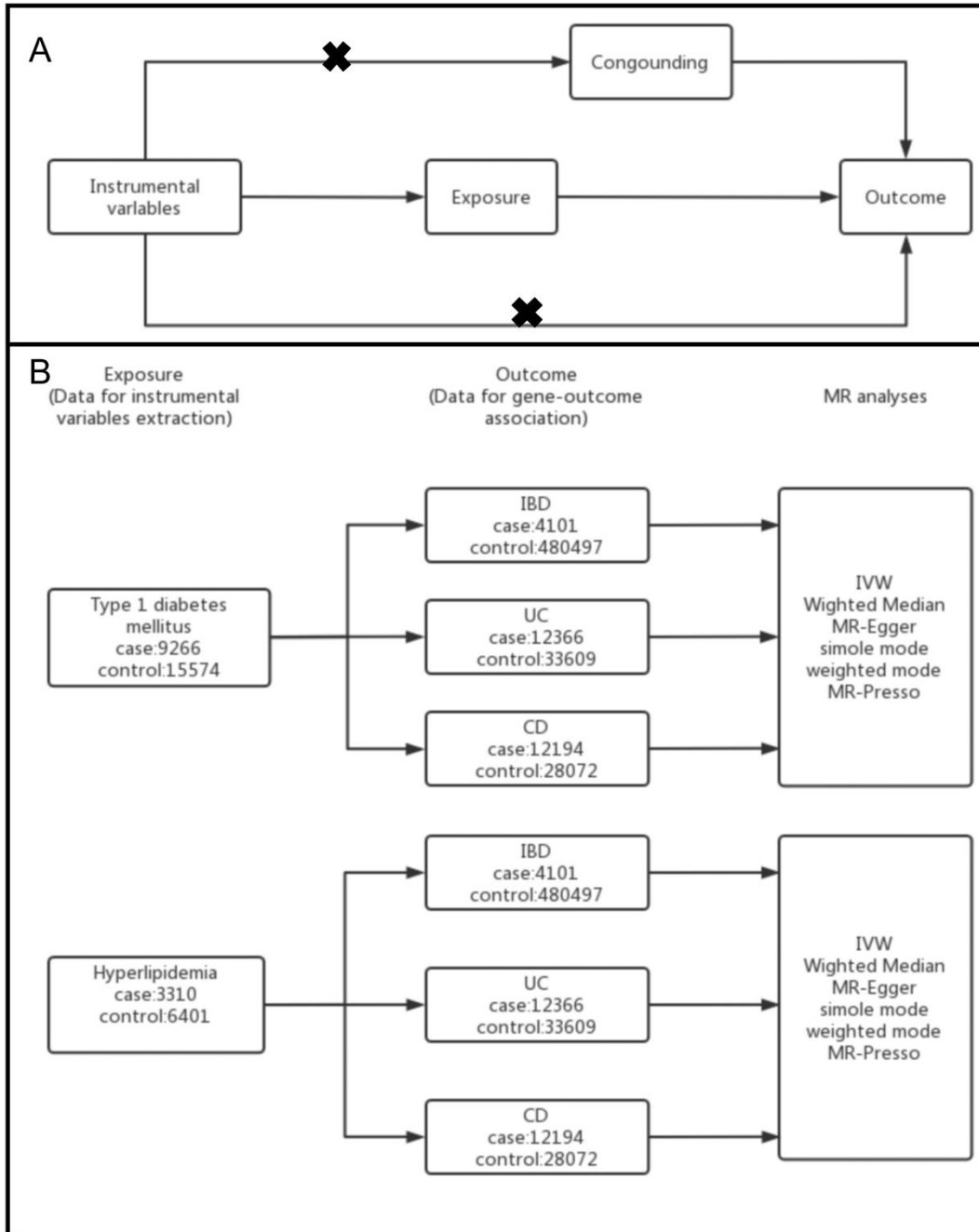**Figure S1. Schematic overview of the study design.**


(A) Mendelian randomization [MR] illustration. There are three principal assumptions in MR design, namely the genetic instrumental variables should [1] be associated with exposure, [2] be associated with outcome only via exposure and [3] not be associated with any measured or unmeasured confounding factors. **(B)** MR study from T1D, Hyperlipidemia to IBD: independent SNPs for T1D and Hyperlipidemia were identified as instrumental variables, whereas summary statistics of gene-IBD associations were retrieved separately from the GWAS performed by ieu. MR Analysis was performed on each result database.

Figure S2. Leave-one-out plot and forest plot of MR analyses from T1DM on IBD
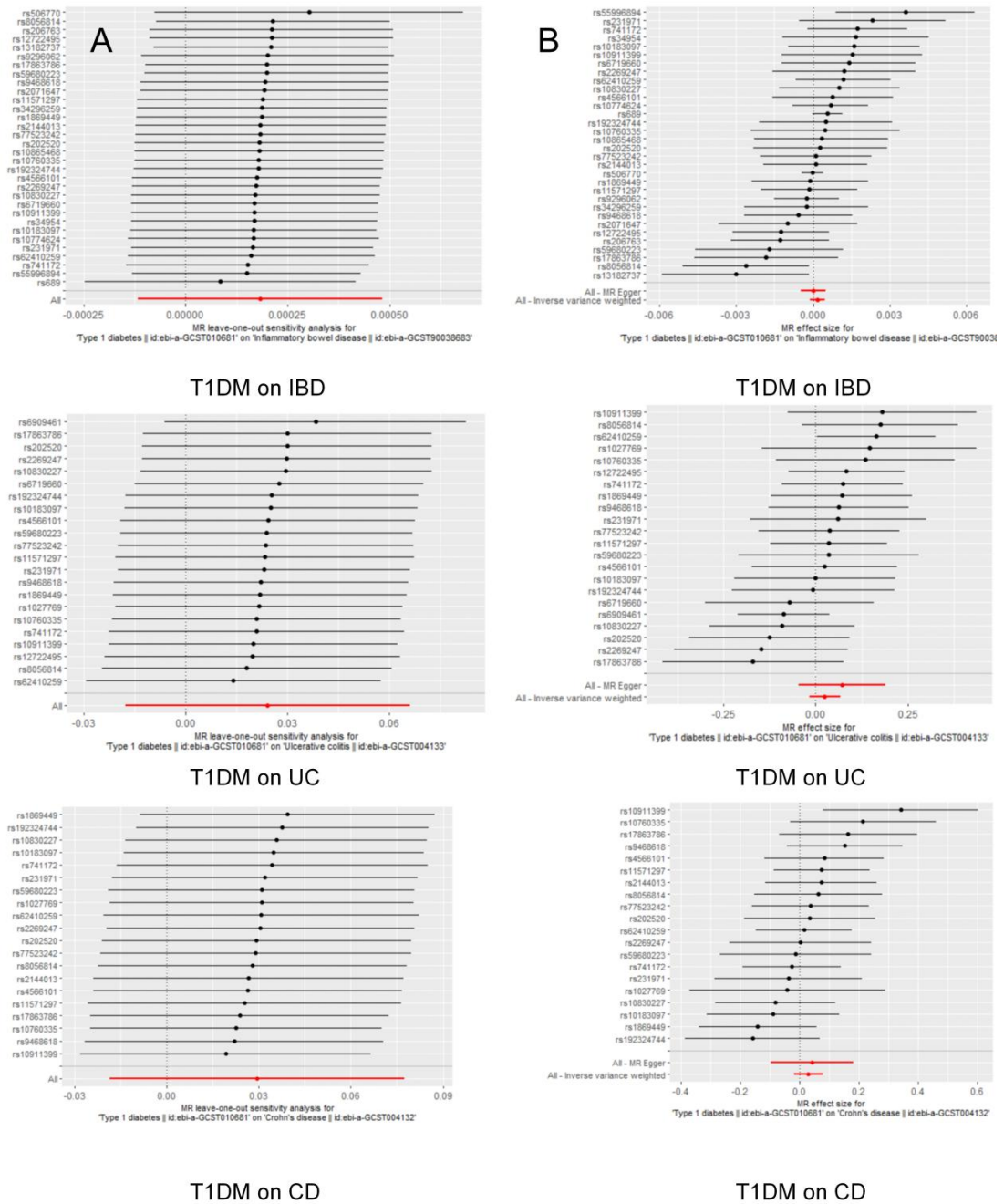

T1DM on IBD

T1DM on UC

T1DM on CD

(A) The leave-one-out sensitivity analysis plot of the causal effect of T1DM on IBD and its subtypes risk. After removing each SNP, the overall error lines did not change much, indicating that the results were reliable. All: the overall effect without removing SNPs. **(B)** The forest plot of the causal effect of T1DM on IBD and its subtypes risk. The effect of each SNP was calculated separately, and the overall effect was calculated using MR Egger and IVW methods.

Figure S3. Leave-one-out plot and forest plot of MR analyses from Hyperlipidemia on IBD
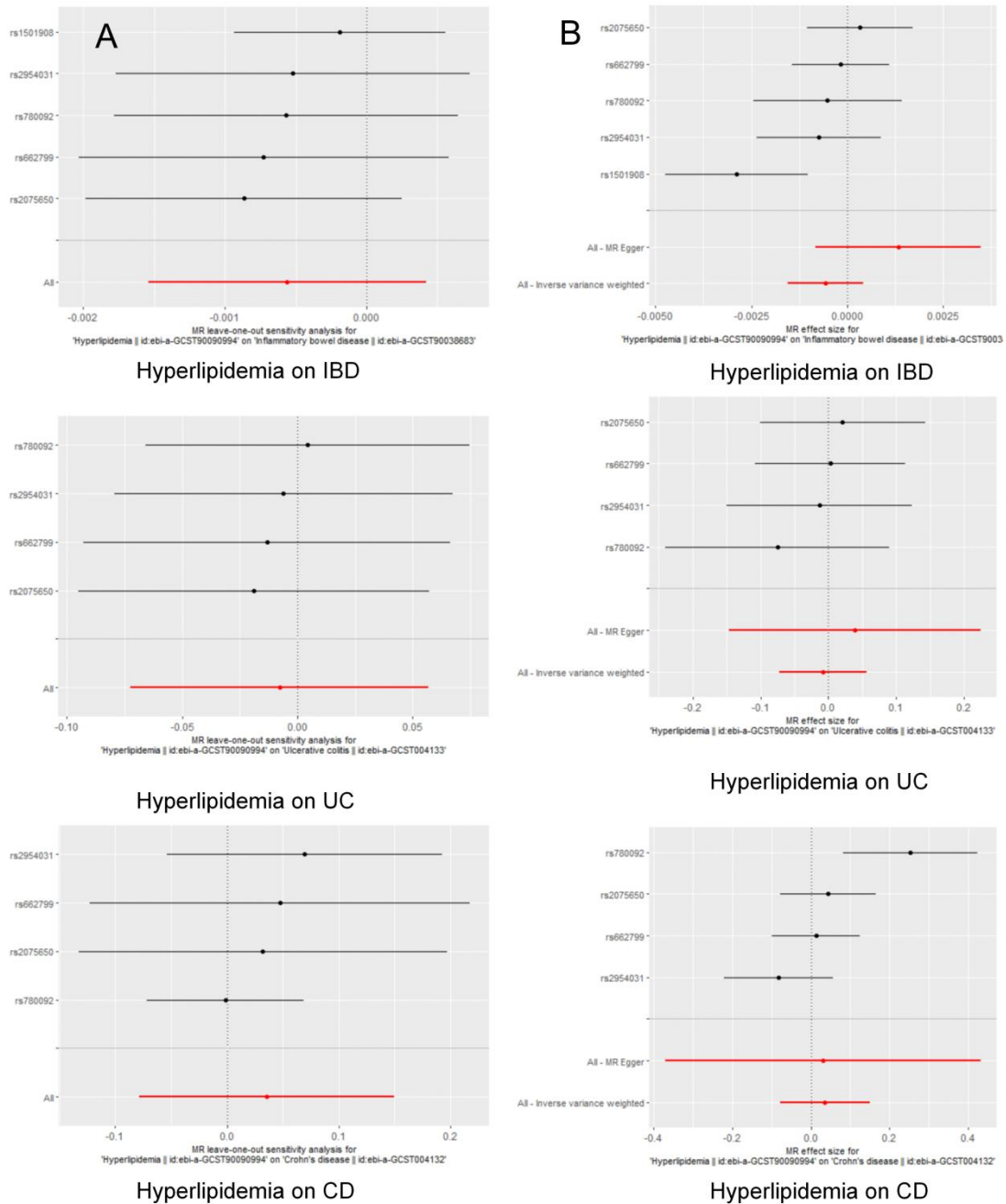
Hyperlipidemia on IBD

Hyperlipidemia on IBD

Hyperlipidemia on UC

Hyperlipidemia on UC
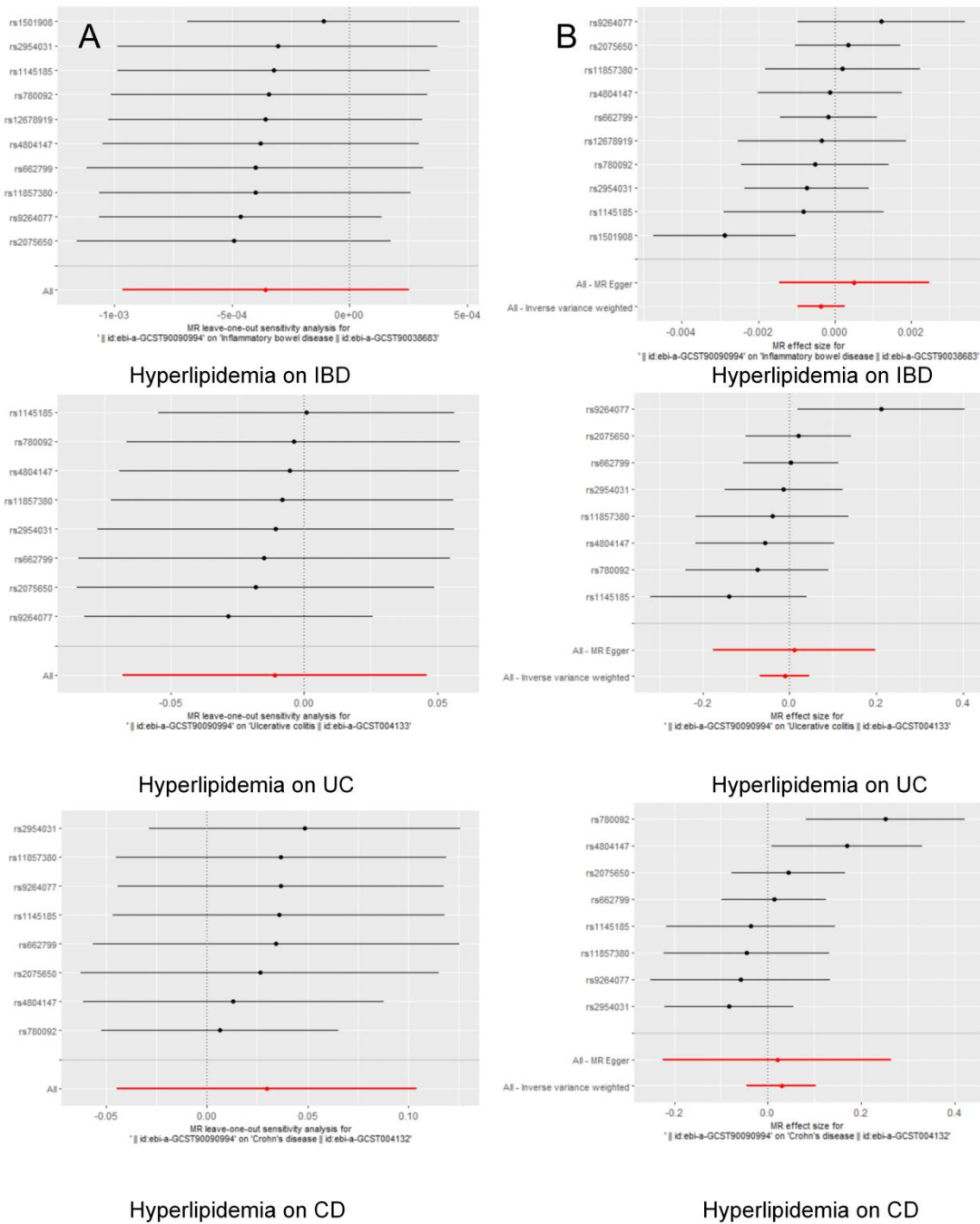
Hyperlipidemia on CD

Hyperlipidemia on CD

(A) The leave-one-out sensitivity analysis plot of the causal effect of Hyperlipidemia on IBD and its subtypes risk. After removing each SNP, the overall error lines did not change much, indicating that the results were reliable. All: the overall effect without removing SNPs. **(B)** The forest plot of the causal effect of Hyperlipidemia on IBD and its subtypes risk. The effect of each SNP was calculated separately, and the overall effect was calculated using MR Egger and IVW methods.

Figure S4. Scatter plot and funnel plot from Hyperlipidemia on IBD

Hyperlipidemia on IBD

Hyperlipidemia on UC

Hyperlipidemia on CD
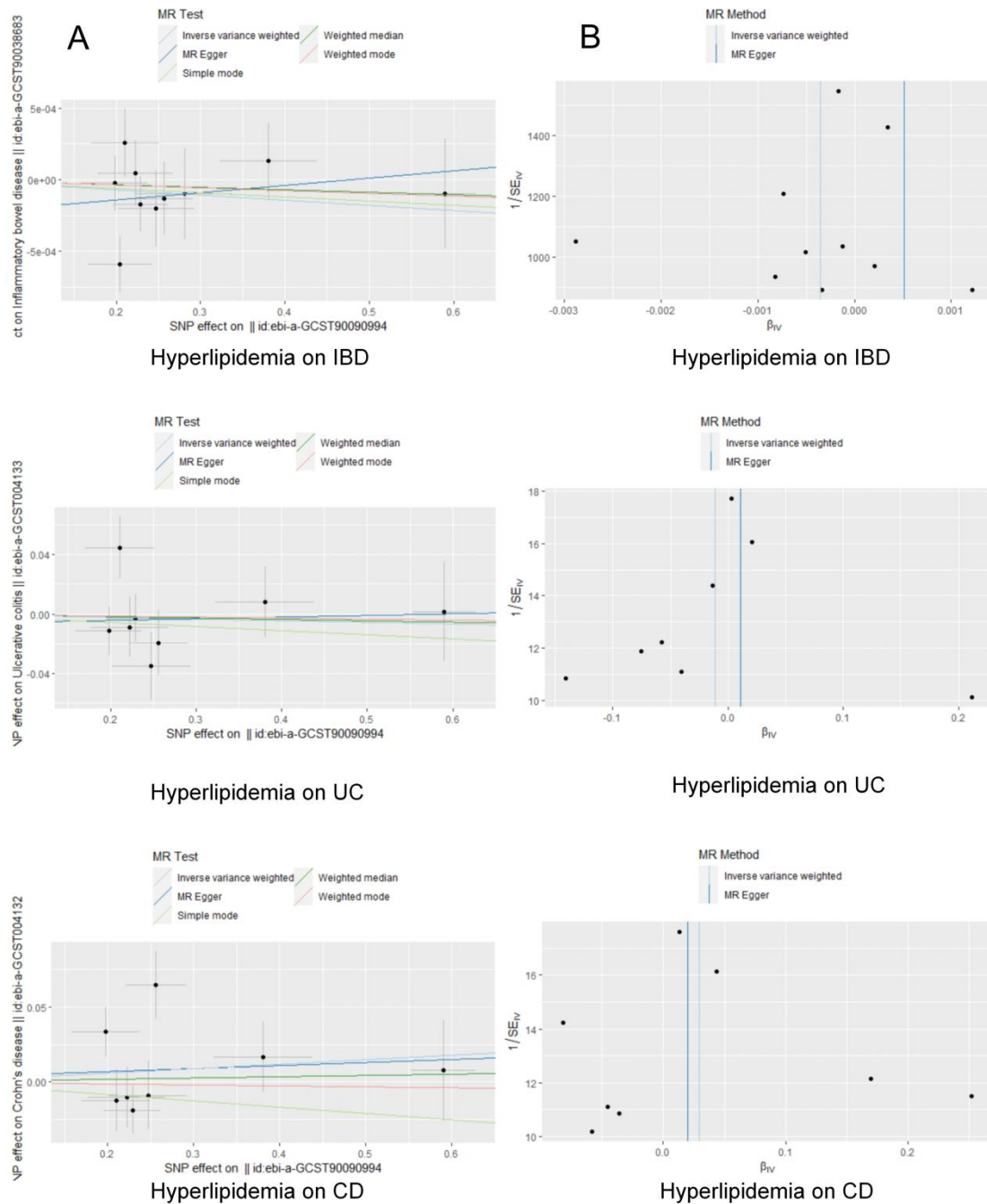
(A) Scatter plots of risk causality of hyperlipidemia for IBD and its subtypes after repeated screening of instrumental variables.. Analyses were conducted using the inverse-variance weighted, MR-Egger, Weighted Median, Simple Mode, and Weighted Mode methods. The slope of each line corresponding to the causal estimates for each method. **(B)** The funnel plot of the causal effect of Hyperlipidemia on IBD and its subtypes risk. Individual SNP was delineated in the background.; IBD, inflammatory bowel disease; UC,.ulcerative colitis;CD,Crohn's disease; SNP, single nucleotide polymorphism.

Figure S5. Leave-one-out plot and forest plot of MR analyses from Hyperlipidemia on IBD

Hyperlipidemia on IBD

Hyperlipidemia on UC

Hyperlipidemia on CD

(A) Residual sensitivity analysis of causality between hyperlipidemia and IBD and its subtypes after re-screening of instrumental variables. After removing each SNP, the overall error lines did not change much, indicating that the results were reliable. All: the overall effect without removing SNPs. (B) The forest plot of the causal effect of Hyperlipidemia on IBD and its subtypes risk. The effect of each SNP was calculated separately, and the overall effect was calculated using MR Egger and IVW methods.

Table S1. Instrumental variables for T1DM on IBD (significant level of $p < 5*10^{-6}$).

SNP	EAF	P-value	Bate	Se	R²	F statistics
rs10911399	0.0455	6.75E-09	-0.3707	0.064	0.011936101	300.0503159
rs2269247	0.1804	7.28E-09	0.1709	0.0295	0.008636795	216.3896233
rs1869449	0.2967	4.55E-11	0.1769	0.0269	0.013060019	328.6772961
rs10865468	0.2527	4.66E-09	-0.1624	0.0277	0.009960985	249.900188
rs11571297	0.4844	1.11E-16	-0.1964	0.0237	0.019267706	487.9734039
rs10183097	0.1362	1.82E-10	0.2053	0.0322	0.009917408	248.7960036
rs192324744	0.0131	1.36E-10	0.562	0.0875	0.008166709	204.5149276
rs6719660	0.9354	2.52E-08	0.2918	0.0524	0.010290357	258.2493728
rs17863786	0.0293	4.26E-11	0.4144	0.0628	0.009768371	245.0202439
rs1027769	0.9966	3.52E-10	-0.9962	0.1588	0.006725474	168.1783919
rs62410259	0.077	1.02E-12	-0.3796	0.0533	0.020482116	519.3726577
rs17125653	0.077	4.75E-09	0.2355	0.0402	0.007883231	197.3595186
rs13182737	0.2553	1.49E-08	0.1465	0.0259	0.008160888	204.3679583
rs9296062	0.0509	1.37E-37	0.6913	0.054	0.046173507	1202.375469
rs6909461	0.2529	3.06E-21	-0.314	0.0332	0.03725777	961.2214597
rs506770	0.768	3.33E-123	1.0048	0.0426	0.35978119	13958.11095

rs185774696	0.1772	2.66E-54	0.6489	0.0418	0.1227845	3476.593151
rs9468618	0.0975	7.53E-10	-0.3009	0.0489	0.015934051	402.178283
rs206763	0.0202	2.93E-18	0.6792	0.0779	0.018260563	461.9920903
rs2144013	0.2093	1.76E-12	0.2234	0.0317	0.016518755	417.184189
rs34296259	0.0082	1.43E-08	0.6637	0.1171	0.007164924	179.2466708
rs10760335	0.3205	2.43E-08	0.1357	0.0243	0.008020606	200.826564
rs77523242	0.0623	5.42E-09	-0.3705	0.0635	0.016038302	404.8524878
rs12722495	0.1122	1.27E-14	-0.3145	0.0408	0.019705129	499.2742701
rs689	0.7109	2.30E-87	0.7004	0.0354	0.201641016	6273.317701
rs10830227	0.5741	1.02E-11	0.1582	0.0233	0.01223878	307.7533523
rs79075295	0.0921	1.46E-11	-0.4192	0.0621	0.029388011	752.0403816
rs202520	0.7222	7.97E-10	-0.1573	0.0256	0.009928352	249.0732944
rs59680223	0.0081	5.00E-10	0.6421	0.1032	0.006625036	165.6500827
rs10774624	0.5037	1.34E-25	-0.2556	0.0244	0.032663891	838.7009675
rs2071647	0.2755	3.30E-09	0.1526	0.0258	0.009296063	233.0621721
rs201417739	0.075	3.41E-10	-0.416	0.0663	0.02401152	611.0708743
rs55996894	0.204	3.13E-08	-0.1785	0.0323	0.010347839	259.7070369
rs4566101	0.2697	6.23E-12	0.1755	0.0255	0.012132952	305.059538
rs741172	0.3205	3.11E-15	-0.2034	0.0258	0.018019776	455.7884009

SNP	EAF	P-value	Bate	Se	R²	F statistics
rs231971	0.1026	1.55E-09	0.2411	0.0399	0.010704289	268.7499172
rs8056814	0.0793	1.99E-10	0.2641	0.0415	0.010184932	255.5763659

Table S2. Instrumental variables for T1DM on CD(significant level of $p < 5*10^{-8}$).

SNP	EAF	P-value	Bate	Se	R²	F statistics
rs10911399	0.0455	6.75E-09	-0.3707	0.064	0.011936101	300.0503159
rs2269247	0.1804	7.28E-09	0.1709	0.0295	0.008636795	216.3896233
rs1869449	0.2967	4.55E-11	0.1769	0.0269	0.013060019	328.6772961
rs202520	0.7222	7.97E-10	-0.1573	0.0256	0.009928352	249.0732944
rs11571297	0.4844	1.11E-16	-0.1964	0.0237	0.019267706	487.9734039
rs10183097	0.1362	1.82E-10	0.2053	0.0322	0.009917408	248.7960036
rs192324744	0.0131	1.36E-10	0.562	0.0875	0.008166709	204.5149276
rs6719660	0.9354	2.52E-08	0.2918	0.0524	0.010290357	258.2493728
rs17863786	0.0293	4.26E-11	0.4144	0.0628	0.009768371	245.0202439
rs1027769	0.9966	3.52E-10	-0.9962	0.1588	0.006725474	168.1783919
rs62410259	0.077	1.02E-12	-0.3796	0.0533	0.020482116	519.3726577
rs34954	0.0443	1.25E-08	-0.4912	0.0863	0.020430172	518.028015
rs13182737	0.2553	1.49E-08	0.1465	0.0259	0.008160888	204.3679583

rs231971	0.1026	1.55E-09	0.2411	0.0399	0.010704289	268.7499172
rs6909461	0.2529	3.06E-21	-0.314	0.0332	0.03725777	961.2214597
rs201417739	0.075	3.41E-10	-0.416	0.0663	0.02401152	611.0708743
rs185774696	0.1772	2.66E-54	0.6489	0.0418	0.1227845	3476.593151
rs9468618	0.0975	7.53E-10	-0.3009	0.0489	0.015934051	402.178283
rs206763	0.0202	2.93E-18	0.6792	0.0779	0.018260563	461.9920903
rs2144013	0.2093	1.76E-12	0.2234	0.0317	0.016518755	417.184189
rs8056814	0.0793	1.99E-10	0.2641	0.0415	0.010184932	255.5763659
rs10760335	0.3205	2.43E-08	0.1357	0.0243	0.008020606	200.826564
rs77523242	0.0623	5.42E-09	-0.3705	0.0635	0.016038302	404.8524878
rs12722495	0.1122	1.27E-14	-0.3145	0.0408	0.019705129	499.2742701
rs741172	0.3205	3.11E-15	-0.2034	0.0258	0.018019776	455.7884009
rs10830227	0.5741	1.02E-11	0.1582	0.0233	0.01223878	307.7533523
rs79075295	0.0921	1.46E-11	-0.4192	0.0621	0.029388011	752.0403816
rs1131017	0.5803	4.24E-25	-0.2461	0.0238	0.029501545	755.0340495
rs59680223	0.0081	5.00E-10	0.6421	0.1032	0.006625036	165.6500827
rs10774624	0.5037	1.34E-25	-0.2556	0.0244	0.032663891	838.7009675
rs4566101	0.2697	6.23E-12	0.1755	0.0255	0.012132952	305.059538

Table S3. Instrumental variables for T1DM on UC(significant level of p <5*10⁻⁸).

SNP	EAF	P-value	Bate	Se	R²	F statistics
rs10911399	0.0455	6.75E-09	-0.3707	0.064	0.011936101	300.0503159
rs2269247	0.1804	7.28E-09	0.1709	0.0295	0.008636795	216.3896233
rs1869449	0.2967	4.55E-11	0.1769	0.0269	0.013060019	328.6772961
rs202520	0.7222	7.97E-10	-0.1573	0.0256	0.009928352	249.0732944
rs11571297	0.4844	1.11E-16	-0.1964	0.0237	0.019267706	487.9734039
rs10183097	0.1362	1.82E-10	0.2053	0.0322	0.009917408	248.7960036
rs192324744	0.0131	1.36E-10	0.562	0.0875	0.008166709	204.5149276
rs6719660	0.9354	2.52E-08	0.2918	0.0524	0.010290357	258.2493728
rs17863786	0.0293	4.26E-11	0.4144	0.0628	0.009768371	245.0202439
rs1027769	0.9966	3.52E-10	-0.9962	0.1588	0.006725474	168.1783919
rs62410259	0.077	1.02E-12	-0.3796	0.0533	0.020482116	519.3726577
rs34954	0.0443	1.25E-08	-0.4912	0.0863	0.020430172	518.028015
rs13182737	0.2553	1.49E-08	0.1465	0.0259	0.008160888	204.3679583
rs231971	0.1026	1.55E-09	0.2411	0.0399	0.010704289	268.7499172
rs6909461	0.2529	3.06E-21	-0.314	0.0332	0.03725777	961.2214597
rs201417739	0.075	3.41E-10	-0.416	0.0663	0.02401152	611.0708743
rs185774696	0.1772	2.66E-54	0.6489	0.0418	0.1227845	3476.593151

rs9468618	0.0975	7.53E-10	-0.3009	0.0489	0.015934051	402.178283
rs206763	0.0202	2.93E-18	0.6792	0.0779	0.018260563	461.9920903
rs2144013	0.2093	1.76E-12	0.2234	0.0317	0.016518755	417.184189
rs8056814	0.0793	1.99E-10	0.2641	0.0415	0.010184932	255.5763659
rs10760335	0.3205	2.43E-08	0.1357	0.0243	0.008020606	200.826564
rs77523242	0.0623	5.42E-09	-0.3705	0.0635	0.016038302	404.8524878
rs12722495	0.1122	1.27E-14	-0.3145	0.0408	0.019705129	499.2742701
rs741172	0.3205	3.11E-15	-0.2034	0.0258	0.018019776	455.7884009
rs10830227	0.5741	1.02E-11	0.1582	0.0233	0.01223878	307.7533523
rs79075295	0.0921	1.46E-11	-0.4192	0.0621	0.029388011	752.0403816
rs1131017	0.5803	4.24E-25	-0.2461	0.0238	0.029501545	755.0340495
rs59680223	0.0081	5.00E-10	0.6421	0.1032	0.006625036	165.6500827
rs10774624	0.5037	1.34E-25	-0.2556	0.0244	0.032663891	838.7009675
rs4566101	0.2697	6.23E-12	0.1755	0.0255	0.012132952	305.059538

Table S4. Instrumental variables for Hyperlipidemia on IBD(significant level of $p < 5*10^{-8}$)

SNP	EAF	P-value	Bate	Se	R²	F statistics
rs780092	0.364	1.09E-13	-0.2564	0.03451	0.03043859	304.9003262
rs1501908	0.7302	4.80E-08	0.2047	0.03751	0.016510091	163.0377676
rs2954031	0.5309	1.87E-12	-0.2289	0.0325	0.02609755	260.2513282
rs662799	0.7244	8.11E-58	-0.5901	0.03682	0.139039718	1568.427458
rs2075650	0.08196	3.25E-11	0.3808	0.05739	0.021821642	216.6596579

Table S5. Instrumental variables for Hyperlipidemia on CD(significant level of $p < 5*10^{-8}$)

SNP	EAF	P-value	Bate	Se	R²	F statistics
rs780092	0.364	1.09E-13	-0.2564	0.03451	0.03043859	304.9003262
rs2954031	0.5309	1.87E-12	-0.2289	0.0325	0.02609755	260.2513282
rs662799	0.7244	8.11E-58	-0.5901	0.03682	0.139039718	1568.427458
rs2075650	0.08196	3.25E-11	0.3808	0.05739	0.021821642	216.6596579

Table S6. Instrumental variables for Hyperlipidemia on UC(significant level of $p < 5*10^{-8}$)

SNP	EAF	P-value	Bate	Se	R²	F statistics
rs780092	0.364	1.09E-13	-0.2564	0.03451	0.03043859	304.9003262
rs2954031	0.5309	1.87E-12	-0.2289	0.0325	0.02609755	260.2513282
rs662799	0.7244	8.11E-58	-0.5901	0.03682	0.139039718	1568.427458
rs2075650	0.08196	3.25E-11	0.3808	0.05739	0.021821642	216.6596579

Table S7. MR analysis of the causality of Hyperlipidemia on IBD (significant level of $p < 1*10^{-6}$)

Exposure	Outcome	Number of SNPs	F statistic	Methods	OR (95%CI)	SE	P
Hyperlipidemia	IBD	10	319.324	MR-Egger	1.000（0.998-1.002）	0.0010	0.625
				Weighted median	0.999（0.999-1.000）	0.0010	0.630
				IVW	0.999（0.999-1.000）	0.0003	0.252
				Simple mode	0.999（0.998-1.000）	0.0005	0.604
				Weighted mode	0.999（0.998-1.000）	0.0004	0.709
Hyperlipidemia	CD	8	366.575	MR-Egger	1.020（0.798-1.303）	0.124	0.877
				Weighted median	1.008（0.937-1.085）	0.037	0.8184
				IVW	1.030（0.956-1.109）	0.037	0.435

				Simple mode	0.958（0.864-1.063）	0.053	0.453
				Weighted mode	0.993 （0.903-1.092）	0.048	0.8956
Hyperlipidemia	UC	9	361.2537491	MR-Egger	1.011(0.838-1.219)	0.095	0.911
				Weighted median	0.990(0.927-1.058)	0.033	0.787
				IVW	0.989(0.934-1.047)	0.029	0.704
				Simple mode	0.972(0.887-1.066)	0.046	0.575
				Weighted mode	0.993(0.917-1.074)	0.040	0.870

IBD, inflammatory bowel disease; UC,.ulcerative colitis;CD,Crohn's disease; IVW, inverse variance weighted; OR，odds ratio; CI, confidence interval; SE, standard error

Table S8. Sensitivity analyses of MR.(significant level of $p < 1*10^{-6}$)

Exposure	outcome	Horizontal pleiotropy						Heterogeneity					
		MR-PRESSO global outlier test				MR-Egger regression		MR-Egger			IVW		
		P	Outlier	OR(95% CI)[*]	P[*]	Intercept	P	Q statistic	P	P[#]	Q statistic	P	P[#]
Hyperlipidemia	IBD	0.3136	NA	NA	NA	-0.0002	0.390	9.884	0.273	NA	10.902	0.282	NA

| | CD | 0.0729 | NA | NA | NA | 0.0027 | 0.938 | 14.098 | 0.028 | NA | 14.113 | 0.049 | NA |
| | UC | 0.3773 | NA | NA | NA | -0.0063 | 0.814 | 8.332 | 0.214 | NA | 8.416 | 0.297 | NA |

[*]MR analysis using IVW method after removing outliers identified by MR-PRESSO method.

[#]Heterogeneity test after removing outliers.

IBD, inflammatory bowel disease; CD, Crohn's disease; UC, ulcerative colitis; ; IVW, inverse variance weighted; OR, odds ratio; CI, confidence interval; SE, standard error.

Table S9. Instrumental variables for Hyperlipidemia on IBD(significant level of $p < 1*10^{-6}$)

SNP	EAF	P-value	Bate	Se	R²	F statistics
rs1145185	0.1403	5.16E-08	0.2475	0.1403	0.014776957	145.6663079
rs11857380	0.1442	7.46E-07	0.2228	0.1442	0.012251744	120.4648414
rs12678919	0.1002	7.56E-07	-0.2809	0.1002	0.014228109	140.1778608
rs1501908	0.7302	4.80E-08	0.2047	0.7302	0.016510091	163.0377676
rs2075650	0.08196	3.25E-11	0.3808	0.08196	0.021821642	216.6596579
rs2954031	0.5309	1.87E-12	-0.2289	0.0325	0.02609755	260.2513282
rs4804147	0.2208	4.55E-07	0.198	0.03925	0.013489889	132.8053352
rs662799	0.7244	8.11E-58	-0.5901	0.03682	0.139039718	1568.427458
rs780092	0.364	1.09E-13	-0.2564	0.03451	0.03043859	304.9003262
rs9264077	0.2022	1.63E-07	0.2105	0.04019	0.01429583	140.8547377

Table S10. Instrumental variables for Hyperlipidemia on CD (significant level of $p < 1*10^{-6}$)

SNP	EAF	P-value	Bate	Se	R²	F statistics
rs1145185	0.1403	5.16E-08	0.2475	0.1403	0.014776957	145.6663079
rs2075650	0.08196	3.25E-11	0.3808	0.08196	0.021821642	216.6596579
rs9264077	0.2022	1.63E-07	0.2105	0.04019	0.01429583	140.8547377
rs1501908	0.7302	4.80E-08	0.2047	0.7302	0.016510091	163.0377676
rs2954031	0.5309	1.87E-12	-0.2289	0.0325	0.02609755	260.2513282
rs4804147	0.2208	4.55E-07	0.198	0.03925	0.013489889	132.8053352
rs662799	0.7244	8.11E-58	-0.5901	0.03682	0.139039718	1568.427458
rs780092	0.364	1.09E-13	-0.2564	0.03451	0.03043859	304.9003262

Table S11. Instrumental variables for Hyperlipidemia on UC (significant level of $p < 1*10^{-6}$)

SNP	EAF	P-value	Bate	Se	R²	F statistics
rs1145185	0.1403	5.16E-08	0.2475	0.1403	0.014776957	145.6663079
rs11857380	0.1442	7.46E-07	0.2228	0.1442	0.012251744	120.4648414
rs2075650	0.08196	3.25E-11	0.3808	0.08196	0.021821642	216.6596579
rs9264077	0.2022	1.63E-07	0.2105	0.04019	0.01429583	140.8547377
rs2954031	0.5309	1.87E-12	-0.2289	0.0325	0.02609755	260.2513282
rs4804147	0.2208	4.55E-07	0.198	0.03925	0.013489889	132.8053352

rs662799	0.7244	8.11E-58	-0.5901	0.03682	0.139039718	1568.427458
rs780092	0.364	1.09E-13	-0.2564	0.03451	0.03043859	304.9003262

Table S12.Detailed data sources for Instrumental variables

Disease	Study	Journal	PMID	Sample size	GWAS ID
IBD	Handan Melike Dönertaş et al.	Nat Aging	33959723	484,598	ebi-a-GCST90038683
CD	de Lange KM et al.	Nat Genet.	28067908	40,266	ebi-a-GCST004132
UC	de Lange KM et al.	Nat Genet.	28067908	45,975	ebi-a-GCST004133
T1DM	Forgetta V et al.	Diabetes	32005708	24840	ebi-a-GCST010681
Hyperlipidemia	Chou WC et al.	NPJ Genom Med	35046404	9,714	ebi-a-GCST90090994

IBD, inflammatory bowel disease; CD, Crohn's disease; UC, ulcerative colitis;T1DM,Type 1 Diabetes Mellitus