Online Supplement

Original Research
Lipids, Lipid-Lowering Drug Target Genes, and COPD Risk: A Mendelian Randomization Study

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Figure S5 Scatter plot (A) and leave-one-out plot (B) of MR analysis between *LPL* and chronic obstructive pulmonary disease.

Table S1 Sources and characteristics of GWAS data included in this study.

Phenotypes		Consortium	Population	Sample Size	Total SNPs	PMID	GWAS ID[1]
exposures							
Primary analysis	HDL-C	GLGC	96% European ancestry	187,167	2,447,442	24097068	ieu-a-299
	LDL-C	GLGC	96% European ancestry	173,082	2,437,752	24097068	ieu-a-300
	Triglyceride	GLGC	96% European ancestry	177,861	2,439,433	24097068	ieu-a-302
Repeated analysis	HDL-C	UK Biobank	European ancestry	403,943	12,321,875	32203549	ieu-b-109
	LDL-C	UK Biobank	European ancestry	440,546	12,321,875	32203549	ieu-b-110
	Triglyceride	UK Biobank	European ancestry	441,016	12,321,875	32203549	ieu-b-111
Positive control							
Coronary heart disease		CARDIoGRAMplusC4D	77% European ancestry	184,305	9,455,779	26343387	ieu-a-7
Outcome							
Chronic obstructive pulmonary disease		FinnGen R11	European ancestry	394,244	21,305,758	NA	NA
Confounding factors							
Smoking initiation		GSCAN	European ancestry	632,802	11,802,365	30643251	ieu-b-4877
Cigarettes per day		GSCAN	European ancestry	337,334	11,913,712	30643251	ieu-b-25
Age of smoking initiation		GSCAN	European ancestry	341,427	11,894,779	30643251	ieu-b-24

Body mass index	GIANT	European ancestry	681,275	2,336,260	30124842	ieu-b-40
Asthma	UK Biobank	European ancestry	462,933	9,851,867	NA	ukb-b-18113
Gastroesophageal reflux disease	UKB, QSKIN	European ancestry	602,604	2,320,781	34187846	ebi-a-GCST90000514

Abbreviations: GLGC, Global Lipids Genetics Consortium; GSCAN, GWAS & Sequencing Consortium of Alcohol and Nicotine use; GIANT, Genetic Investigation of ANthropometric Traits; QSKIN, Queensland Sun and Health Study; CARDIoGRAMplusC4D, Coronary ARtery DIsease Genome wide Replication and Meta-analysis (CARDIoGRAM) plus The Coronary Artery Disease (C4D) Genetics; LDL-C, Low density lipoprotein cholesterol; HDL-C, high density lipoprotein cholesterol.

[1]All GWAS summary data is available in IEU Open GWAS by GWAS ID. (https://gwas.mrcieu.ac.uk/)

Table S2. Details of 11 lipid-lowering drug target genes.

Primary pharmacological action	Drug targets	Target genes	Chromosome	Location	Genetic instruments
Decrease LDL-C	LDL Receptor	*LDLR*	19	11200139..11244496	14
	HMG-CoA reductase	*HMGCR*	5	74632993..74657941	7
	Niemann-Pick C1-like protein 1	*NPC1L1*	7	44552134..44580929	3
	Proprotein convertase subtilisin/kexin type 9	*PCSK9*	1	55505221..55530525	12
	Apolipoprotein B-100	*APOB*	2	21224301..21266945	20
	ATP Binding Cassette Subfamily G Member 5	*ABCG5*	2	44039611..44065978	7
	ATP Binding Cassette Subfamily G Member 8	*ABCG8*	2	44066110..44110127	7
Decrease triglyceride	Angiopoietin-related protein 3	*ANGPTL3*	1	63063191..63071984	4
	Apolipoprotein C-III	*APOC3*	11	116700623..116703788	10
	Lipoprotein Lipase	*LPL*	8	19796764..19824770	24
Increase HDL-C	CETP protein	*CETP*	16	56995862..57017757	36

Abbreviations: LDL-C, low density lipoprotein cholesterol; HDL-C, high density lipoprotein cholesterol.

Table S3. Genetic variants that were used as instruments variables for high-density lipoprotein cholesterol.

SNP	Chr	Pos	Alt	Ref	Beta	Se	Eaf	Pval	Samplesize	R^2	F-statistic
rs10019888	4	26062990	G	A	-0.027	0.0046	0.1636	4.90E-08	187077	0.000199505	37
rs10087900	8	144303418	A	G	-0.0231	0.0036	0.4393	2.17E-09	183672	0.000262873	48
rs102275	11	61557803	C	T	-0.0391	0.0035	0.372	6.40E-28	187085	0.000714309	134
rs103294	19	54797848	T	C	0.0523	0.0044	0.186	3.99E-30	175917	0.000828268	146
rs10468017	15	58678512	T	C	0.1179	0.0038	0.2757	1.21E-188	181223	0.005551532	1012
rs1047891	2	211540507	A	C	-0.0269	0.0039	0.3021	8.73E-10	182043	0.000305125	56
rs10761771	10	65230164	C	T	0.0198	0.0034	0.467	4.12E-09	182895	0.000195166	36
rs10808546	8	126495818	T	C	0.0409	0.0034	0.4459	4.11E-30	185835	0.000826613	154
rs11045163	12	20463526	G	A	0.0217	0.0035	0.4063	3.20E-09	187075	0.000227176	43
rs11065987	12	112072424	G	A	-0.0222	0.0035	0.4222	1.23E-09	187119	0.000240454	45
rs11765979	7	130445877	C	A	0.0412	0.0048	0.4578	3.11E-17	94311	0.000842674	80
rs11789603	9	107647019	T	C	0.06	0.006	0.08971	3.69E-21	184432	0.000587967	109
rs12133576	1	93816400	G	A	-0.0243	0.0035	0.6451	6.15E-11	187123	0.000270381	51
rs12145743	1	156700651	G	T	0.0203	0.0036	0.3311	1.80E-08	181336	0.000182533	33
rs12412743	10	114045333	T	C	-0.0291	0.0045	0.153	1.31E-09	187095	0.000219478	41
rs12740374	1	109817590	T	G	0.0343	0.0041	0.2124	1.69E-15	186888	0.000393621	74
rs12748152	1	27138393	T	C	-0.0506	0.0062	0.07124	9.74E-16	187057	0.000338812	63
rs12801636	11	65391317	A	G	0.0235	0.0042	0.2243	3.15E-08	187099	0.000192171	36
rs13076253	3	131751775	C	A	-0.0283	0.0048	0.1478	4.96E-09	186809	0.000201752	38
rs13099479	3	52677478	A	G	0.036	0.0062	0.08971	1.82E-08	187132	0.000211668	40
rs13107325	4	103188709	T	C	-0.0708	0.0078	0.07784	1.06E-15	179316	0.000719624	129
rs13702	8	19824492	C	T	0.1058	0.0038	0.3127	1.28E-160	187044	0.004811445	904

rs1515110	2	227122216	T	G	-0.0323	0.0035	0.6187	8.04E-18	187081	0.000492246	92
rs1689797	1	182150978	A	C	-0.0358	0.0036	0.3021	2.85E-21	187126	0.000540431	101
rs16942887	16	67928042	A	G	0.0831	0.0051	0.1332	8.28E-54	185604	0.001594613	296
rs16965220	16	57065121	A	C	0.0219	0.0037	0.2982	7.91E-09	185512	0.000200742	37
rs17145738	7	72982874	T	C	0.0408	0.0053	0.1174	4.95E-13	184971	0.000344971	64
rs17173637	7	150529449	C	T	-0.0363	0.0057	0.09763	1.90E-08	183901	0.000232173	43
rs181360	22	21928916	G	T	-0.0376	0.0042	0.1992	9.24E-18	178216	0.000451044	80
rs1866956	8	19748921	T	C	0.0217	0.0037	0.6755	7.96E-10	187031	0.000206438	39
rs1883025	9	107664301	T	C	-0.0698	0.0041	0.2427	1.50E-65	186365	0.00179093	334
rs1936800	6	127436064	T	C	-0.02	0.0034	0.4723	3.05E-10	187111	0.000199386	37
rs1980493	6	32363215	C	T	-0.0318	0.0048	0.1227	3.76E-10	183275	0.000217709	40
rs2013208	3	50129399	T	C	0.0254	0.0036	0.5053	8.92E-12	169708	0.000322544	55
rs205262	6	34563164	G	A	-0.0283	0.0039	0.2665	3.88E-13	181707	0.000313112	57
rs2066714	9	107586753	C	T	0.0453	0.0071	0.1201	7.26E-10	93528	0.000433713	41
rs2241210	12	109950144	G	A	0.0332	0.0035	0.5528	2.49E-20	174782	0.000544974	95
rs2241770	16	56866196	C	T	-0.0989	0.0057	0.1029	6.78E-60	185537	0.001805838	336
rs2250802	10	113921354	A	G	-0.034	0.0038	0.6807	2.02E-17	184088	0.000502507	93
rs2278236	19	8431581	A	G	0.0331	0.0035	0.5435	3.18E-18	185450	0.000543659	101
rs2290547	3	47061183	A	G	-0.0297	0.0046	0.2111	3.69E-09	187142	0.000293801	55
rs2454722	12	123171218	G	A	0.0351	0.0044	0.1451	3.31E-14	186355	0.000305652	57
rs2602836	4	100014805	G	A	-0.0192	0.0034	0.5726	4.96E-08	187102	0.000180434	34
rs2606736	3	11400249	T	C	-0.0246	0.0043	0.6055	4.80E-08	129328	0.000289109	37
rs2642438	1	220970028	G	A	0.0303	0.0039	0.7454	7.78E-14	179439	0.000348468	63
rs2925979	16	81534790	C	T	0.0351	0.0037	0.7045	1.32E-19	185553	0.000512959	95
rs3741414	12	57844049	T	C	0.0296	0.004	0.1913	6.10E-14	187090	0.000271091	51
rs3822072	4	89741269	A	G	-0.0251	0.0034	0.4881	4.06E-12	187115	0.000314827	59

rs3847502	11	47333685	A	C	0.048	0.0036	0.314	3.31E-38	187050	0.000992582	186
rs3861397	6	139828916	G	A	-0.024	0.0036	0.3417	8.40E-11	187084	0.000259132	48
rs4142995	7	17919258	T	G	-0.0263	0.0037	0.3839	9.36E-12	165161	0.000327198	54
rs4148005	17	66882466	G	T	-0.0283	0.0036	0.2995	5.74E-14	184431	0.000336053	62
rs4240624	8	9184231	A	G	0.0818	0.0058	0.9248	1.32E-45	185696	0.000930684	173
rs424346	15	59010962	T	C	0.0679	0.0113	0.04881	4.84E-08	128346	0.0004281	55
rs4379922	12	125351116	C	T	0.0247	0.0036	0.3496	9.56E-12	186203	0.000277444	52
rs4465830	20	44585420	G	A	-0.0597	0.0044	0.2018	5.17E-40	185505	0.001148184	213
rs4650994	1	178515312	A	G	-0.021	0.0034	0.4828	6.70E-09	186927	0.000220239	41
rs4660293	1	40028180	G	A	-0.0353	0.004	0.2361	2.86E-18	187027	0.000449482	84
rs4846914	1	230295691	A	G	0.0479	0.0034	0.5844	3.51E-41	186995	0.001114517	209
rs4917014	7	50305863	G	T	0.0222	0.0036	0.3404	1.03E-08	186868	0.000221313	41
rs492571	15	44211273	C	T	-0.0663	0.009	0.04222	1.27E-12	177352	0.000355501	63
rs4939883	18	47167214	C	T	0.0799	0.0045	0.8193	1.80E-66	185576	0.001890274	351
rs4969178	17	76388202	G	A	0.0263	0.0035	0.6266	1.53E-12	185426	0.000323673	60
rs4983559	14	105277209	A	G	-0.0197	0.0036	0.6227	9.57E-09	183672	0.000182359	34
rs499974	11	75455021	A	C	-0.0263	0.0044	0.1755	1.12E-08	186749	0.000200175	37
rs6031587	20	43038249	T	C	-0.0488	0.0074	0.0686	1.92E-09	163095	0.00030432	50
rs633695	15	58725839	G	A	0.0885	0.0054	0.285	7.82E-58	92820	0.003192033	297
rs6450176	5	53298025	A	G	-0.0254	0.0039	0.2784	6.87E-10	187132	0.000259217	49
rs6567160	18	57829135	C	T	-0.0257	0.0041	0.2309	2.92E-09	185608	0.000234586	44
rs676210	2	21231524	A	G	0.066	0.004	0.2309	2.34E-54	187081	0.001547122	290
rs6805251	3	119560606	C	T	-0.02	0.0035	0.6187	1.33E-08	186301	0.000188728	35
rs686030	9	15304782	A	C	0.055	0.0049	0.8588	4.29E-27	187035	0.000733638	137
rs687339	3	135932359	T	C	-0.0316	0.0042	0.7665	7.11E-13	187105	0.00035744	67
rs702485	7	6449272	G	A	0.0243	0.0034	0.4499	6.45E-12	186974	0.000292281	55

rs7306660	12	125327384	A	G	-0.0345	0.0036	0.3694	3.34E-19	186939	0.000554522	104
rs731839	19	33899065	A	G	0.022	0.0037	0.6583	3.44E-09	185498	0.000217743	40
rs737337	19	11347493	C	T	-0.0565	0.0061	0.0686	4.56E-17	185432	0.000407931	76
rs7607980	2	165551201	C	T	0.0447	0.0052	0.1491	1.81E-15	187036	0.000506992	95
rs838876	12	125259888	G	A	-0.0493	0.0039	0.6741	7.32E-33	173066	0.001067905	185
rs9457931	6	160929904	G	A	-0.0552	0.0073	0.0686	7.30E-13	171669	0.000389375	67
rs970548	10	46013277	C	A	0.0258	0.0039	0.277	1.71E-10	186596	0.000266617	50
rs998584	6	43757896	A	C	-0.026	0.0038	0.5145	2.27E-11	183791	0.000337716	62
rs9989419	16	56985139	G	A	0.1473	0.0036	0.595	1.00E-200	177532	0.010457009	1876

Table S4. Genetic variants that were used as instruments variables for low-density lipoprotein cholesterol.

SNP	Chr	Pos	Alt	Ref	Beta	Se	Eaf	Pval	Samplesize	R^2	F-statistic
rs10195252	2	165513091	C	T	-0.0238	0.0039	0.4182	3.81E-08	157208	0.00027564	43
rs10490626	2	118835841	A	G	-0.0508	0.0069	0.07916	1.70E-12	173044	0.000376225	65
rs10832962	11	18656271	T	C	0.032	0.004	0.719	6.62E-14	172920	0.000413776	72
rs10893499	11	126241979	A	G	0.0521	0.0053	0.1438	3.86E-21	172980	0.000668405	116
rs10903129	1	25768937	G	A	0.0328	0.0037	0.5369	3.03E-17	169920	0.00053499	91
rs10947332	6	32677440	A	G	0.0504	0.0056	0.1319	6.97E-18	169263	0.000581709	99
rs112201728	6	160551486	T	C	0.0675	0.0104	0.05805	8.51E-10	83123	0.000498273	41
rs11563251	2	234679384	T	C	0.0345	0.0062	0.1253	4.50E-08	172855	0.000260903	45
rs11591147	1	55505647	T	G	-0.497	0.018	0.01715	8.57E-143	77417	0.008327107	650
rs1169288	12	121416650	C	A	0.0375	0.004	0.3338	6.45E-21	163086	0.000625437	102
rs12066643	1	56240278	T	C	-0.0389	0.0064	0.1187	1.06E-08	171295	0.000316595	54
rs1250229	2	216304384	C	T	0.0243	0.0042	0.7889	3.13E-08	173032	0.000196677	34
rs12721109	19	45447221	A	G	-0.4462	0.0183	0.01715	2.99E-122	99409	0.006711823	672
rs12748152	1	27138393	T	C	0.0499	0.0066	0.07124	3.21E-12	172988	0.000329502	57
rs12916	5	74656539	C	T	0.0733	0.0038	0.4314	7.79E-78	168357	0.002635876	445
rs13206249	6	16175022	A	G	-0.0378	0.0062	0.2164	4.53E-08	87149	0.00048458	42
rs13277801	8	59353534	T	C	-0.0338	0.0038	0.653	3.99E-17	173010	0.000517733	90
rs1367117	2	21263900	A	G	0.1186	0.004	0.2876	9.48E-183	173007	0.005763843	1003
rs1408272	6	25842951	G	T	-0.052	0.0083	0.05277	3.68E-09	167888	0.000270321	45
rs1564348	6	160578860	C	T	0.0481	0.005	0.1451	2.76E-21	172989	0.000573988	99
rs16831243	2	135762344	T	C	0.0378	0.0055	0.1807	9.06E-12	162945	0.000423072	69
rs16891156	6	160608804	C	A	0.0965	0.0171	0.01847	8.23E-09	90465	0.000337641	31
rs17404153	3	132163200	T	G	-0.0336	0.0054	0.1438	1.83E-09	172898	0.000277999	48

rs174583	11	61609750	T	C	-0.0522	0.0038	0.3747	7.00E-41	172982	0.00127686	221
rs1800961	20	43042364	T	C	-0.0685	0.0106	0.0343	6.03E-10	142698	0.000310848	44
rs1801689	17	64210580	C	A	0.1028	0.0139	0.03694	9.81E-12	111143	0.000751911	84
rs1883025	9	107664301	T	C	-0.0296	0.0044	0.2427	6.14E-11	172330	0.000322071	56
rs2000999	16	72108093	A	G	0.065	0.0046	0.1847	4.22E-41	171510	0.001272451	219
rs2030746	2	121309488	T	C	0.0214	0.0038	0.3984	8.60E-09	173024	0.000219525	38
rs2073547	7	44582331	G	A	0.0485	0.0049	0.1939	1.92E-21	169889	0.000735326	125
rs2228603	19	19329924	T	C	-0.104	0.0072	0.07124	4.43E-44	158643	0.001431278	227
rs2315065	6	161108144	A	C	0.1102	0.0158	0.08707	5.23E-12	67446	0.001930631	130
rs2328223	20	17845921	C	A	0.0299	0.005	0.2493	5.63E-09	170762	0.000334627	57
rs2390536	7	21485397	A	G	0.0223	0.0038	0.3681	2.04E-08	172981	0.000231342	40
rs2419604	10	113944271	G	A	-0.0302	0.004	0.6821	7.49E-14	172807	0.000395533	68
rs247616	16	56989590	T	C	-0.0547	0.0041	0.2929	2.57E-37	171458	0.001239381	213
rs2495495	1	55496556	C	T	-0.0342	0.0059	0.8654	3.52E-08	162403	0.000272486	44
rs2587534	1	234849339	A	G	0.0391	0.0037	0.5277	8.06E-25	172966	0.000762059	132
rs2642438	1	220970028	G	A	0.0352	0.0042	0.7454	7.32E-16	165470	0.000470287	78
rs267733	1	150958836	G	A	-0.0331	0.0053	0.1372	5.29E-09	164562	0.000259388	43
rs2710642	2	63149557	A	G	0.0239	0.0038	0.6187	6.09E-09	172994	0.000269509	47
rs2737252	8	116663898	A	G	-0.0314	0.0041	0.2559	7.04E-14	172950	0.000375484	65
rs2738459	19	11238473	C	A	-0.0532	0.0058	0.4446	2.26E-19	88433	0.001397747	124
rs2886232	17	67150176	C	T	-0.0451	0.0064	0.8799	3.88E-11	162498	0.000429892	70
rs2965157	19	45176340	C	T	-0.1886	0.0112	0.02111	7.29E-62	170260	0.001470061	251
rs314253	17	7091650	C	T	-0.0242	0.0038	0.3351	3.44E-10	169706	0.000260971	44
rs3184504	12	111884608	C	T	0.0268	0.0038	0.5343	4.20E-12	164996	0.00035743	59
rs364585	20	12962718	G	A	0.0249	0.0038	0.6332	4.28E-10	171526	0.000288004	49
rs3757354	6	16127407	T	C	-0.0382	0.0044	0.2098	2.09E-17	172987	0.000483837	84

rs3780181	9	2640759	G	A	-0.0445	0.0074	0.05277	1.76E-09	171976	0.000197967	34
rs4253776	22	46629479	G	A	0.0311	0.0059	0.124	3.35E-08	171071	0.000210124	36
rs4530754	5	122855416	A	G	0.0275	0.0036	0.5818	3.58E-12	173003	0.000368004	64
rs4722551	7	25991826	C	T	0.0391	0.0049	0.1702	3.95E-14	172946	0.000431834	75
rs4942486	13	32953388	C	T	-0.0243	0.0037	0.5383	2.26E-11	171930	0.000293513	50
rs4970712	1	92993547	C	A	0.0339	0.0044	0.8061	2.46E-13	173036	0.000359249	62
rs4970834	1	109814880	T	C	-0.1503	0.0047	0.1873	1.00E-200	172825	0.006877269	1197
rs5763662	22	30378703	T	C	0.0767	0.0121	0.02507	1.19E-08	162777	0.000287573	47
rs579459	9	136154168	C	T	0.0665	0.0045	0.215	2.42E-44	172706	0.00149273	258
rs6016373	20	39154095	G	A	-0.0349	0.0037	0.3734	7.95E-19	171559	0.000569962	98
rs6065311	20	39724338	C	T	0.0417	0.0036	0.4604	1.66E-30	171333	0.000863991	148
rs6504872	17	45438952	T	C	0.0274	0.0037	0.4723	3.48E-13	171519	0.000374228	64
rs6511720	19	11202306	T	G	-0.2209	0.0061	0.09763	1.00E-200	170608	0.00859784	1480
rs6544713	2	44073881	C	T	-0.0806	0.0041	0.7058	4.84E-83	172940	0.002697891	468
rs6693893	1	109797763	C	T	-0.0767	0.0132	0.03562	2.88E-08	83065	0.000404169	34
rs6709904	2	44080324	G	A	-0.055	0.0085	0.1135	4.58E-10	89852	0.000608737	55
rs676388	19	49211969	C	T	0.0265	0.0039	0.4631	1.31E-11	166830	0.000349213	58
rs6818397	4	3434885	G	T	-0.0224	0.004	0.5871	1.68E-08	172685	0.000243267	42
rs6882076	5	156390297	C	T	0.0456	0.0038	0.6662	3.31E-31	173006	0.000924806	160
rs6909746	6	116352750	T	C	-0.0263	0.0037	0.3918	7.86E-11	170097	0.000329649	56
rs7254892	19	45389596	A	G	-0.4853	0.0119	0.03166	1.00E-200	139198	0.014440737	2040
rs72902576	2	21275480	G	T	-0.0933	0.0133	0.03694	9.58E-12	82068	0.000619361	51
rs7534572	1	62999675	G	C	0.0407	0.0058	0.69	1.29E-11	75145	0.000708646	53
rs7551981	1	55719166	T	G	0.0472	0.0038	0.595	1.36E-33	173021	0.001073707	186
rs75687619	19	45399344	T	G	0.1735	0.0161	0.02375	8.05E-24	82003	0.001395898	115
rs7640978	3	32533010	T	C	-0.0392	0.0069	0.1055	9.84E-09	172228	0.000290025	50

rs7832643	8	145022657	T	G	0.0339	0.0038	0.405	2.67E-17	164854	0.000553862	91
rs8017377	14	24883887	A	G	0.0303	0.0038	0.4591	2.52E-15	172866	0.000455973	79
rs9875338	3	12296469	A	G	-0.027	0.0037	0.3879	2.21E-11	172895	0.000346178	60
rs9987289	8	9183358	G	A	0.0714	0.0066	0.9248	8.53E-24	160102	0.000709075	114

Table S5. Genetic variants that were used as instruments variables for triglyceride.

SNP	Chr	Pos	Alt	Ref	Beta	Se	Eaf	Pval	Samplesize	R^2	F-statistic
rs10401969	19	19407718	C	T	-0.121	0.0065	0.07124	9.70E-70	176173	0.00193744	342
rs10440120	3	12486964	A	C	-0.0306	0.0044	0.1675	5.34E-11	174886	0.000261139	46
rs10501321	11	47294626	C	T	-0.0216	0.0035	0.314	1.41E-08	177680	0.000200998	36
rs10761762	10	65184717	C	T	-0.027	0.0033	0.467	1.06E-17	177823	0.000362912	65
rs11057408	12	124464836	T	G	-0.0258	0.0035	0.3628	2.05E-12	174454	0.00030776	54
rs11613352	12	57792580	T	C	-0.028	0.0039	0.1913	9.40E-14	177799	0.000242576	43
rs11974409	7	72989390	G	A	-0.0899	0.0042	0.1939	1.36E-100	177786	0.002526481	450
rs12280753	11	116613660	T	C	0.1931	0.0064	0.06728	1.22E-179	177747	0.004679849	836
rs1260326	2	27730940	C	T	-0.1148	0.0034	0.5871	1.00E-200	177765	0.006389557	1143
rs12676857	8	18266572	C	T	0.0332	0.0046	0.1544	7.29E-12	177732	0.000287818	51
rs12678919	8	19844222	G	A	-0.1702	0.0056	0.1214	1.82E-199	177750	0.00617958	1105
rs12748152	1	27138393	T	C	0.0372	0.0059	0.07124	1.10E-09	177762	0.000183123	33
rs1321257	1	230305312	A	G	-0.0402	0.0034	0.5937	5.99E-31	177758	0.000779643	139
rs13389219	2	165528876	T	C	-0.0271	0.0034	0.409	2.60E-15	177783	0.000355042	63
rs16948098	15	44219607	A	G	0.08	0.0089	0.0409	4.84E-17	163328	0.000502108	82
rs174535	11	61551356	C	T	0.047	0.0034	0.3628	1.73E-41	177773	0.001021336	182
rs17513135	1	40035686	T	C	0.022	0.0039	0.2322	1.63E-08	174742	0.000172578	30
rs1832007	10	5254847	G	A	-0.0327	0.0047	0.1319	1.72E-12	177504	0.000244873	43
rs2043085	15	58680954	C	T	-0.0327	0.0034	0.6319	7.81E-20	176147	0.000497439	88
rs2068888	10	94839642	A	G	-0.0241	0.0034	0.4908	1.68E-11	177712	0.000290307	52
rs2239520	6	31088922	A	G	-0.0236	0.0037	0.3734	4.14E-10	151047	0.000260627	39
rs2247056	6	31265490	C	T	0.0378	0.0039	0.7823	3.86E-21	174062	0.000486682	85
rs2250802	10	113921354	A	G	0.023	0.0037	0.6807	1.21E-10	174734	0.000229954	40

rs247616	16	56989590	T	C	-0.0393	0.0037	0.2929	1.12E-25	176146	0.000639757	113
rs2665357	6	160848167	C	A	0.0212	0.0033	0.5092	8.33E-10	172850	0.000224644	39
rs287621	7	130435181	C	T	-0.0222	0.0037	0.7296	7.67E-09	177813	0.000194459	35
rs2954022	8	126482621	A	C	-0.078	0.0033	0.4697	2.23E-113	177750	0.003030829	540
rs2972146	2	227100698	T	G	0.0281	0.0034	0.6227	2.97E-15	174704	0.000371029	65
rs3198697	16	15129940	T	C	-0.0198	0.0034	0.3826	2.21E-08	175934	0.000185213	33
rs3760627	19	45457180	C	T	0.0189	0.0034	0.4683	5.29E-09	176201	0.000177887	31
rs3761445	22	38595411	A	G	0.0232	0.0034	0.6148	8.06E-12	175846	0.000254933	45
rs38855	7	116358044	G	A	-0.0187	0.0033	0.4736	2.11E-08	177825	0.000174358	31
rs439401	19	45414451	C	T	0.0659	0.0038	0.6201	1.42E-66	152584	0.002046124	313
rs442177	4	88030261	T	G	0.0309	0.0033	0.5528	1.32E-18	177798	0.000472081	84
rs4587594	1	63133930	A	G	-0.0694	0.0035	0.31	3.50E-82	177772	0.002060439	367
rs4719841	7	25997536	G	A	0.0232	0.0034	0.3826	8.86E-11	177775	0.000254283	45
rs4810479	20	44545048	T	C	-0.0474	0.0038	0.7124	2.07E-34	176192	0.00092066	162
rs588136	15	58730498	T	C	-0.0495	0.0041	0.7942	3.37E-30	176173	0.000800969	141
rs6029143	20	39118662	T	C	-0.0388	0.0071	0.05805	4.93E-08	176257	0.000164636	29
rs634869	6	139831757	C	T	-0.0272	0.0033	0.562	1.78E-14	177755	0.000364232	65
rs645040	3	135926622	T	G	0.0293	0.004	0.7691	1.83E-12	177779	0.00030491	54
rs676210	2	21231524	A	G	-0.0733	0.0039	0.2309	3.28E-71	177782	0.001908291	340
rs6831256	4	3473139	G	A	0.0258	0.0035	0.409	1.60E-12	177495	0.000321796	57
rs6882076	5	156390297	C	T	0.0286	0.0035	0.6662	1.51E-15	177778	0.000363792	65
rs6995541	8	10671260	G	A	0.0265	0.0037	0.3219	1.34E-12	177486	0.000306575	54
rs719726	6	127414801	T	C	0.0199	0.0035	0.529	2.49E-08	168319	0.000197339	33
rs7248104	19	7224431	A	G	-0.0222	0.0034	0.4169	5.04E-10	176083	0.000239613	42
rs731839	19	33899065	A	G	-0.0224	0.0036	0.6583	2.65E-09	176161	0.000225733	40
rs7350481	11	116586283	C	T	-0.2254	0.0066	0.90237	1.00E-200	177677	0.008951705	1605

rs749671	16	31088347	A	G	-0.0211	0.0034	0.3945	6.11E-10	176205	0.000212694	37
rs8077889	17	41878166	C	A	0.0252	0.0042	0.2441	9.88E-09	176194	0.000234349	41
rs948690	11	116529468	C	T	-0.0306	0.0052	0.3047	6.57E-09	91013	0.000396751	36
rs9686661	5	55861786	T	C	0.0379	0.0044	0.1768	2.54E-16	177050	0.000418115	74
rs998584	6	43757896	A	C	0.0293	0.0037	0.5145	3.42E-15	174573	0.000428884	75

Table S6. Mendelian randomization analysis of 3 lipid traits and coronary heart disease.

Exposures	MR analysis							Sensitivity analysis			
	IVW			MR-Egger		Weighted median		MR-Egger intercept		Cochran's Q test	
	SNPs	OR (95%CI)	*P*	OR (95%CI)	*P*	OR (95%CI)	*P*	Intercept	*P*	Q	*P*
HDL-C	75	0.86(0.78-0.94)	**8.00×10^{-4}**	0.99(0.83-1.17)	0.882	0.90(0.81-1.00)	0.053	-0.01	0.055	196.03	5.54×10^{-13}
LDL-C	69	1.46(1.36-1.56)	**1.27×10^{-26}**	1.59(1.40-1.80)	1.06×10^{-9}	1.47(1.35-1.62)	5.25×10^{-17}	-4.90×10^{-3}	0.134	101.07	0.006
Triglyceride	50	1.33(1.20-1.46)	**1.61×10^{-8}**	1.25(1.08-1.46)	0.005	1.26(1.14-1.38)	2.73×10^{-6}	3.79×10^{-3}	0.327	131.71	1.67×10^{-9}

Abbreviations: LDL-C, Low density lipoprotein cholesterol; HDL-C, high density lipoprotein cholesterol.

Table S7. Mendelian randomization analysis of 3 lipid traits with the risk of chronic obstructive pulmonary disease.

Exposures	MR analysis							Sensitivity analysis			
	IVW			MR-Egger		Weighted median		MR-Egger intercept		Cochran's Q test	
	SNPs	OR (95%CI)	*P*	OR (95%CI)	*P*	OR (95%CI)	*P*	Intercept	*P*	Q	*P*
GLGC											
HDL-C	83	0.99(0.93-1.06)	0.854	0.97(0.85-1.09)	0.582	0.97(0.89-1.07)	0.558	1.54×10^{-3}	0.591	109.85	0.022
LDL-C	79	0.90(0.85-0.95)	**1.50×10^{-4}**	0.92(0.85-0.99)	0.038	0.90(0.84-0.97)	0.004	-1.83×10^{-3}	0.489	119.19	0.002
Triglyceride	54	0.98(0.91-1.06)	0.561	0.98(0.87-1.11)	0.796	0.99(0.89-1.10)	0.853	-4.10×10^{-4}	0.896	77.33	0.016
UK Biobank											
HDL-C	316	1.00(0.94-1.06)	0.882	0.99(0.90-1.09)	0.863	1.01(0.92-1.11)	0.803	1.39×10^{-4}	0.919	470.81	2.80×10^{-8}
LDL-C	151	0.87(0.81-0.93)	**7.26×10^{-5}**	0.89(0.81-0.99)	0.027	0.88(0.80-0.97)	0.009	-1.25×10^{-3}	0.501	211.22	0.001
Triglyceride	279	0.99(0.93-1.05)	0.701	0.92(0.84-1.01)	0.071	1.01(0.92-1.10)	0.910	2.99×10^{-3}	0.036	427.63	1.94×10^{-8}

Abbreviations: LDL-C, Low density lipoprotein cholesterol; HDL-C, high density lipoprotein cholesterol; GLGC, Global Lipids Genetics Consortium.

Table S8. Mendelian randomization analysis of chronic obstructive pulmonary disease on 3 lipid traits.

Outcomes	MR analysis							Sensitivity analysis			
	IVW			MR-Egger		Weighted median		MR-Egger intercept		Cochran's Q test	
	SNPs	OR (95%CI)	*P*	OR (95%CI)	*P*	OR (95%CI)	*P*	Intercept	*P*	Q	*P*
HDL-C	12	0.98(0.94-1.02)	0.247	0.94(0.87-1.02)	0.154	0.96(0.93-0.99)	0.024	4.41×10^{-3}	0.296	23.85	0.013
LDL-C	11	1.02(0.98-1.06)	0.295	1.03(0.95-1.11)	0.536	1.02(0.99-1.06)	0.195	-6.12×10^{-4}	0.881	15.84	0.104
Triglyceride	12	1.04(1.01-1.07)	0.021	1.04(0.97-1.10)	0.281	1.03(1.00-1.07)	0.049	-9.16×10^{-5}	0.977	12.92	0.298

Abbreviations: LDL-C, Low density lipoprotein cholesterol; HDL-C, high density lipoprotein cholesterol.

Table S9. Genetic variants that were used as instruments variables for 11 lipid-lowering drug target genes.

SNP	Chr	Pos	Alt	Ref	Beta	Se	Eaf	Pval	Samplesize	R^2	F-statistic
LDLR											
rs1010679	19	11207102	C	T	-0.1017	0.0063	0.1794	3.51E-54	83043	0.00304527	254
rs12983316	19	11114352	G	A	0.0514	0.0052	0.1689	7.44E-22	164630	0.000741719	122
rs1433099	19	11242658	C	T	0.0357	0.0043	0.7098	2.51E-16	171474	0.000525049	90
rs36005514	19	11190764	A	G	0.0626	0.0096	0.0752	7.06E-10	83044	0.00054506	45
rs3786721	19	11146499	C	T	-0.0468	0.0038	0.5383	2.89E-31	163605	0.001088694	178
rs3786722	19	11161537	A	C	-0.0754	0.0043	0.2427	5.52E-63	171335	0.002089827	359
rs379309	19	11284302	T	C	-0.0313	0.0039	0.4974	1.39E-13	166821	0.000489832	82
rs5742911	19	11243445	G	A	-0.0606	0.0057	0.2678	4.83E-24	77573	0.001440176	112
rs6511720	19	11202306	T	G	-0.2209	0.0061	0.09763	1.00E-200	170608	0.00859784	1480
rs6511727	19	11315817	G	T	-0.0266	0.0038	0.6148	1.84E-11	170239	0.00033513	57
rs688	19	11227602	T	C	0.054	0.0037	0.4472	1.01E-43	166792	0.001441741	241
rs7188	19	11275139	C	A	0.0521	0.0043	0.3259	9.39E-31	144557	0.001192653	173
rs73015030	19	11207516	A	G	-0.1517	0.0148	0.02507	2.62E-22	83049	0.001124939	94
rs892114	19	11266584	G	A	-0.0353	0.0047	0.7731	7.63E-13	156312	0.000437169	68
HMGCR											
rs10066707	5	74560579	A	G	0.0497	0.0054	0.4169	2.97E-19	89888	0.00120093	108
rs10515198	5	74641560	A	G	0.0599	0.0061	0.1029	5.99E-22	173012	0.00066243	115
rs12659791	5	74757758	C	T	0.0433	0.005	0.1557	1.42E-18	173018	0.000492937	85
rs12916	5	74656539	C	T	0.0733	0.0038	0.4314	7.79E-78	168357	0.002635876	445
rs3804231	5	74696779	A	G	0.0642	0.0053	0.1319	1.88E-29	173020	0.000943875	163
rs3857388	5	74620377	C	T	0.0421	0.0059	0.128	2.20E-11	172939	0.000395659	68
rs72633962	5	74569028	C	T	0.06	0.0072	0.1412	3.33E-15	83103	0.00087309	73

NPC1L1											
rs2073547	7	44582331	G	A	0.0485	0.0049	0.1939	1.92E-21	169889	0.000735326	125
rs217386	7	44600695	A	G	-0.0363	0.0038	0.4077	1.20E-19	173021	0.000636393	110
rs7791240	7	44602589	C	T	0.0425	0.0065	0.09103	1.84E-10	161845	0.000298911	48
PCSK9											
rs10493176	1	55538552	G	T	-0.0776	0.0102	0.1148	2.54E-14	86056	0.001223874	105
rs11206510	1	55496039	C	T	-0.0831	0.005	0.1544	2.38E-53	172812	0.001803202	312
rs11206514	1	55516004	A	C	0.0507	0.0041	0.6108	9.95E-33	172996	0.001222131	212
rs11583974	1	55551718	A	G	0.0646	0.0117	0.03034	3.95E-09	99955	0.000245544	25
rs11591147	1	55505647	T	G	-0.497	0.018	0.01715	8.57E-143	77417	0.008327107	650
rs12067569	1	55528629	A	G	0.0885	0.01	0.0343	1.97E-17	164264	0.000518863	85
rs2479394	1	55486064	A	G	-0.0386	0.0041	0.715	1.58E-19	172953	0.000607233	105
rs2479409	1	55504650	A	G	-0.0642	0.0041	0.6675	2.51E-50	172970	0.001829544	317
rs2495495	1	55496556	C	T	-0.0342	0.0059	0.8654	3.52E-08	162403	0.000272486	44
rs4927193	1	55509872	C	T	-0.0352	0.0056	0.1306	4.27E-11	173009	0.00028137	49
rs572512	1	55517344	T	C	0.0478	0.0047	0.3456	5.31E-26	150564	0.001033482	156
rs585131	1	55524116	T	C	0.0637	0.005	0.8153	2.70E-35	167769	0.001222062	205
APOB											
rs10164442	2	21205563	G	A	0.0286	0.0039	0.3206	7.78E-13	173004	0.000356329	62
rs10198175	2	21133883	G	A	-0.0768	0.0063	0.91557	1.45E-32	172977	0.000911886	158
rs12691202	2	21249716	T	C	-0.0966	0.0114	0.05145	8.22E-19	109096	0.000910814	99
rs12720796	2	21261998	C	A	0.0909	0.0141	0.02243	1.68E-10	153714	0.000362356	56
rs12720842	2	21257927	C	T	0.0993	0.0116	0.02111	1.88E-15	161300	0.000407522	66
rs13392272	2	21217490	T	C	0.0875	0.0037	0.4129	1.46E-118	172951	0.003711958	644
rs1367117	2	21263900	A	G	0.1186	0.004	0.2876	9.48E-183	173007	0.005763843	1003
rs17398765	2	21270751	G	A	0.0916	0.0076	0.0686	3.54E-32	168107	0.001072214	180

rs1801701	2	21228827	T	C	0.0638	0.0064	0.07916	2.30E-21	173030	0.000593419	103
rs3791981	2	21245367	G	A	-0.0939	0.0067	0.1201	2.03E-41	161484	0.001863535	301
rs4128553	2	21147179	T	C	0.0652	0.006	0.09894	2.30E-24	173025	0.000757968	131
rs4665788	2	21188488	C	T	-0.0667	0.0042	0.7744	1.12E-52	165208	0.001554483	257
rs515135	2	21286057	C	T	0.1394	0.0048	0.7823	1.09E-178	173029	0.006618923	1153
rs531593	2	21348574	G	A	-0.0694	0.0078	0.06464	7.03E-18	167282	0.00058241	97
rs6413458	2	21231592	A	G	-0.094	0.0139	0.02375	2.19E-10	159056	0.000409742	65
rs6547409	2	21190209	T	C	-0.1226	0.0087	0.05937	8.19E-45	167103	0.001678792	281
rs6725189	2	21219001	T	G	-0.0604	0.0045	0.2348	5.63E-40	173003	0.001310922	227
rs6754295	2	21206183	G	T	-0.0628	0.0042	0.2586	1.64E-47	173013	0.001512274	262
rs6756743	2	21301892	T	C	0.0553	0.0092	0.04222	4.97E-09	163843	0.000247323	41
rs7567653	2	21276962	A	G	-0.1145	0.0112	0.03694	3.37E-26	161178	0.000932806	150
ABCG5/ABCG8											
rs10208987	2	44043135	G	T	-0.0486	0.0068	0.08971	2.36E-12	173038	0.000385765	67
rs1025447	2	44022970	C	T	0.0418	0.0048	0.1583	3.78E-16	172270	0.000465608	80
rs17424122	2	44075217	A	T	0.0645	0.0091	0.06596	5.40E-12	152253	0.00051262	78
rs4148177	2	44057102	A	G	-0.0365	0.0051	0.4327	1.15E-11	83048	0.000654057	54
rs4148218	2	44099582	A	G	-0.0441	0.0047	0.1913	6.76E-21	173032	0.000601741	104
rs4953023	2	44074000	A	G	-0.1313	0.0074	0.08443	1.73E-66	170076	0.00266531	455
rs6544713	2	44073881	C	T	-0.0806	0.0041	0.7058	4.84E-83	172940	0.002697891	468
ANGPTL3											
rs1168032	1	62967747	G	A	0.0683	0.0035	0.6781	1.49E-80	177790	0.002036508	363
rs12039115	1	62995263	T	C	-0.0471	0.0051	0.1095	6.53E-21	177765	0.000432633	77
rs4587594	1	63133930	A	G	-0.0694	0.0035	0.31	3.50E-82	177772	0.002060439	367
rs67537755	1	63117328	A	G	0.0384	0.0064	0.2573	5.96E-09	55254	0.000563567	31
APOC3											

rs12294259	11	116637146	T	C	0.219	0.0069	0.05937	1.79E-200	172242	0.005356784	928
rs1263167	11	116677723	G	A	-0.0423	0.0049	0.1807	5.59E-17	146678	0.0005298	78
rs180326	11	116624703	T	G	-0.0839	0.0036	0.6372	6.27E-108	161659	0.003254595	528
rs2187126	11	116635784	G	A	-0.0543	0.0069	0.05409	2.90E-15	177773	0.000301715	54
rs5110	11	116691634	A	C	0.156	0.0124	0.06464	2.14E-34	81720	0.00294279	241
rs533556	11	116741572	C	A	-0.0596	0.0035	0.6306	1.61E-59	175877	0.001654906	292
rs61905084	11	116610294	C	T	-0.0563	0.0059	0.1649	2.55E-20	84257	0.000872983	74
rs6589574	11	116730638	G	A	-0.1283	0.0054	0.8786	3.03E-113	177776	0.003511504	626
rs7943309	11	116773653	A	G	-0.0605	0.0087	0.03958	1.16E-11	172721	0.000278277	48
rs888246	11	116724232	T	C	0.0707	0.0058	0.08179	8.99E-31	158795	0.000750777	119
LPL											
rs10102717	8	19756813	T	C	-0.0313	0.0034	0.409	9.66E-20	177735	0.000473619	84
rs10103634	8	19890612	A	G	-0.0517	0.0036	0.3298	8.09E-46	164013	0.001181588	194
rs117604010	8	19848396	A	G	-0.1371	0.017	0.01979	3.11E-15	81223	0.000729239	59
rs117910839	8	19822741	A	T	-0.1365	0.0141	0.03694	7.07E-20	86724	0.001325701	115
rs11986942	8	19867445	G	C	-0.098	0.0038	0.3245	3.17E-142	168500	0.004210389	712
rs12678919	8	19844222	G	A	-0.1702	0.0056	0.1214	1.82E-199	177750	0.00617958	1105
rs2410622	8	19854773	C	T	-0.0537	0.0051	0.8562	1.20E-26	172471	0.000710089	123
rs283	8	19815098	T	C	0.037	0.0044	0.2348	1.70E-16	169866	0.000491934	84
rs285	8	19815189	T	C	-0.054	0.0034	0.5277	4.80E-56	172996	0.001453525	252
rs301	8	19816934	C	T	-0.1089	0.0039	0.4274	1.86E-167	177741	0.005804591	1038
rs312	8	19817997	C	G	-0.0398	0.005	0.1201	4.93E-17	177672	0.00033479	60
rs3289	8	19823192	C	T	0.1447	0.0111	0.0277	3.67E-33	169504	0.001127839	191
rs3779788	8	19803093	T	C	-0.0916	0.0049	0.1306	4.66E-76	177663	0.001905389	339
rs3898938	8	19749390	T	C	-0.0244	0.0034	0.4393	1.22E-12	177607	0.000293293	52
rs4557718	8	19890654	C	T	0.0578	0.0059	0.1266	3.26E-24	170599	0.00073881	126

rs4599828	8	19709575	C	T	0.0241	0.0034	0.533	1.59E-11	177753	0.00028914	51
rs4922119	8	19874153	T	C	-0.0708	0.0034	0.4499	1.67E-95	172289	0.002481156	429
rs6586872	8	19715236	G	A	0.0339	0.0038	0.7441	4.09E-19	177730	0.000437654	78
rs6998248	8	19712564	T	C	0.0473	0.0079	0.8681	6.74E-10	91013	0.00051235	47
rs7003579	8	19728586	C	T	-0.0255	0.004	0.785	4.72E-10	177716	0.000219492	39
rs7005359	8	19870693	G	A	-0.0797	0.005	0.2058	1.86E-57	141560	0.002076452	295
rs7016529	8	19806631	C	T	0.1911	0.014	0.01319	3.57E-35	154015	0.00095067	147
rs7844579	8	19748603	C	T	0.0215	0.0034	0.5264	3.00E-10	174654	0.000230481	40
rs9644636	8	19824896	G	T	0.0415	0.0039	0.2639	2.02E-27	177570	0.000669118	119
CETP											
rs11076174	16	57003146	C	T	-0.1797	0.0075	0.1042	2.28E-127	174841	0.00602844	1060
rs1138429	16	56942921	T	A	-0.1156	0.0065	0.09763	9.52E-66	180290	0.002354581	426
rs117040820	16	57005762	T	C	0.1812	0.0216	0.01319	2.23E-14	86136	0.000854722	74
rs12446867	16	57052901	T	G	-0.0344	0.0042	0.2573	1.83E-16	185542	0.000452272	84
rs12597002	16	57002404	A	C	-0.0849	0.0039	0.2757	1.13E-102	185454	0.002878728	535
rs12708967	16	56993211	C	T	-0.1939	0.0047	0.1966	1.00E-200	185528	0.011876841	2230
rs12720917	16	57019392	C	T	0.0976	0.0055	0.1412	5.89E-68	175777	0.002310236	407
rs12928552	16	57048707	G	A	0.0498	0.0077	0.04222	2.17E-09	177294	0.000200573	36
rs12934552	16	57021433	G	A	-0.0541	0.0054	0.1266	8.71E-24	185547	0.000647249	120
rs13306677	16	56926195	A	G	0.09	0.0057	0.09894	1.35E-50	185551	0.001444244	268
rs150348	16	57116036	C	A	-0.0232	0.0035	0.628	7.41E-10	183750	0.000251483	46
rs16965220	16	57065121	A	C	0.0219	0.0037	0.2982	7.91E-09	185512	0.000200742	37
rs17370142	16	57050348	T	G	0.0342	0.0059	0.1161	1.19E-11	182488	0.000240059	44
rs1864163	16	56997233	A	G	-0.2247	0.0042	0.2678	1.00E-200	185418	0.019800513	3745
rs1875236	16	57033696	A	G	0.059	0.0065	0.09763	1.45E-18	185536	0.000613341	114
rs1991515	16	57034645	T	C	0.0225	0.0037	0.4565	5.62E-10	185480	0.000251209	47

rs247615	16	56984763	G	A	-0.0764	0.0044	0.219	2.93E-62	185538	0.001996696	371
rs289715	16	57008508	T	A	-0.1341	0.0064	0.8799	4.15E-98	163286	0.003800702	623
rs289719	16	57009941	C	T	-0.1129	0.0039	0.6715	5.37E-173	185439	0.005623404	1049
rs289723	16	57080528	A	C	-0.022	0.0038	0.252	4.08E-09	185478	0.000182464	34
rs289726	16	57074451	C	T	-0.0364	0.0037	0.6478	1.27E-22	185539	0.000604593	112
rs289745	16	57019532	A	C	0.0276	0.0041	0.6029	2.28E-20	182393	0.000364748	67
rs289748	16	57025063	G	A	-0.0387	0.005	0.4842	6.63E-17	92820	0.000748097	69
rs289751	16	57026775	A	G	-0.103	0.0103	0.95646	8.81E-25	153161	0.000883608	135
rs291040	16	57061189	C	T	-0.0305	0.0037	0.3377	8.21E-17	185511	0.000416117	77
rs3794650	16	56940513	C	T	-0.0687	0.005	0.1662	9.84E-41	181014	0.001308086	237
rs3829502	16	56896730	A	G	0.0482	0.0051	0.3945	1.46E-20	92820	0.001109904	103
rs5880	16	57015091	C	G	-0.3071	0.009	0.05937	1.00E-200	175234	0.010533568	1865
rs5883	16	57007353	T	C	0.1153	0.0084	0.06069	1.76E-31	167340	0.001515705	254
rs7198642	16	57032461	G	T	0.0352	0.0043	0.1675	3.06E-14	185530	0.000345553	64
rs7204044	16	56942709	G	A	-0.0388	0.004	0.7863	6.46E-20	185536	0.000505925	94
rs7204290	16	56968039	A	G	-0.0302	0.0038	0.3021	1.48E-14	185547	0.000384581	71
rs72786786	16	56985514	A	G	0.2174	0.0051	0.2955	1.00E-200	92706	0.019678299	1861
rs7499911	16	57036440	G	A	0.06	0.0111	0.06464	1.26E-08	92820	0.000435324	40
rs9938160	16	56984590	C	T	0.0599	0.0053	0.252	3.17E-25	92699	0.001352651	126
rs9989419	16	56985139	G	A	0.1473	0.0036	0.595	1.00E-200	177532	0.010457009	1876

Table S10. Statistical power estimates for MR analyses

	LDL-C (GLGC)	LDL-C (UK Biobank)	*HMGCR*	*PCSK9*	*LPL*
R^2	0.096	0.061	0.007	0.019	0.035
OR	0.90	0.87	0.63	0.87	0.86
Statistical power	99.7%	99.8%	100%	77.5%	96%

Abbreviations: GLGC, Global Lipids Genetics Consortium; LDL-C, Low density lipoprotein cholesterol; OR, odds ratio.

Table S11. Mendelian randomization analysis of 11 lipid-lowering drug target genes with the risk of chronic obstructive pulmonary disease.

Exposures	MR analysis							Sensitivity analysis			
	IVW			MR-Egger		Weighted median		MR-Egger intercept		Cochran's Q test	
	SNPs	OR (95%CI)	*P*	OR (95%CI)	*P*	OR (95%CI)	*P*	Intercept	*P*	Q	*P*
LDLR	14	0.88(0.80-0.97)	0.007	0.95(0.81-1.13)	0.598	0.88(0.77-1.00)	0.057	-6.75×10^{-3}	0.276	12.57	0.482
HMGCR	7	0.63(0.54-0.75)	**4.92×10^{-8}**	0.74(0.30-1.79)	0.529	0.64(0.52-0.79)	1.92×10^{-5}	-9.10×10^{-3}	0.747	3.27	0.774
NPC1L1	3	0.69(0.50-0.95)	0.023	0.38(0.03-4.74)	0.592	0.70(0.49-1.01)	0.060	0.03	0.727	0.86	0.651
PCSK9	12	0.87(0.80-0.95)	**0.001**	0.90(0.79-1.01)	0.112	0.89(0.80-0.98)	0.018	-4.20×10^{-3}	0.482	4.84	0.938
APOB	20	0.94(0.87-1.02)	0.167	0.95(0.75-1.20)	0.662	0.97(0.87-1.07)	0.540	-3.35×10^{-4}	0.975	10.53	0.939
ABCG5	7	0.88(0.75-1.04)	0.129	0.83(0.57-1.23)	0.399	0.88(0.71-1.08)	0.211	3.78×10^{-3}	0.774	2.58	0.860
ABCG8	7	0.88(0.75-1.04)	0.129	0.83(0.57-1.23)	0.399	0.88(0.71-1.07)	0.203	3.78×10^{-3}	0.774	2.58	0.860
ANGPTL3	4	1.03(0.84-1.27)	0.792	0.83(0.35-1.97)	0.711	1.02(0.80-1.29)	0.884	0.01	0.664	1.33	0.722
APOC3	10	0.98(0.86-1.11)	0.741	0.92(0.69-1.22)	0.578	0.95(0.83-1.08)	0.428	0.01	0.638	14.10	0.118
LPL	24	0.86(0.79-0.94)	**6.37×10^{-4}**	0.90(0.76-1.05)	0.194	0.87(0.77-0.98)	0.017	-2.69×10^{-3}	0.608	11.61	0.976
CETP	36	1.02(0.98-1.07)	0.339	0.99(0.92-1.06)	0.773	1.02(0.96-1.09)	0.454	4.03×10^{-3}	0.254	30.67	0.677

Note: Statistically significant at $P<0.004$ (0.05/11) with Bonferrroni correction.

Figure S1 Scatter plot (A) and leave-one-out plot (B) of MR analysis between low density lipoprotein cholesterol from UK Biobank and chronic obstructive pulmonary disease.

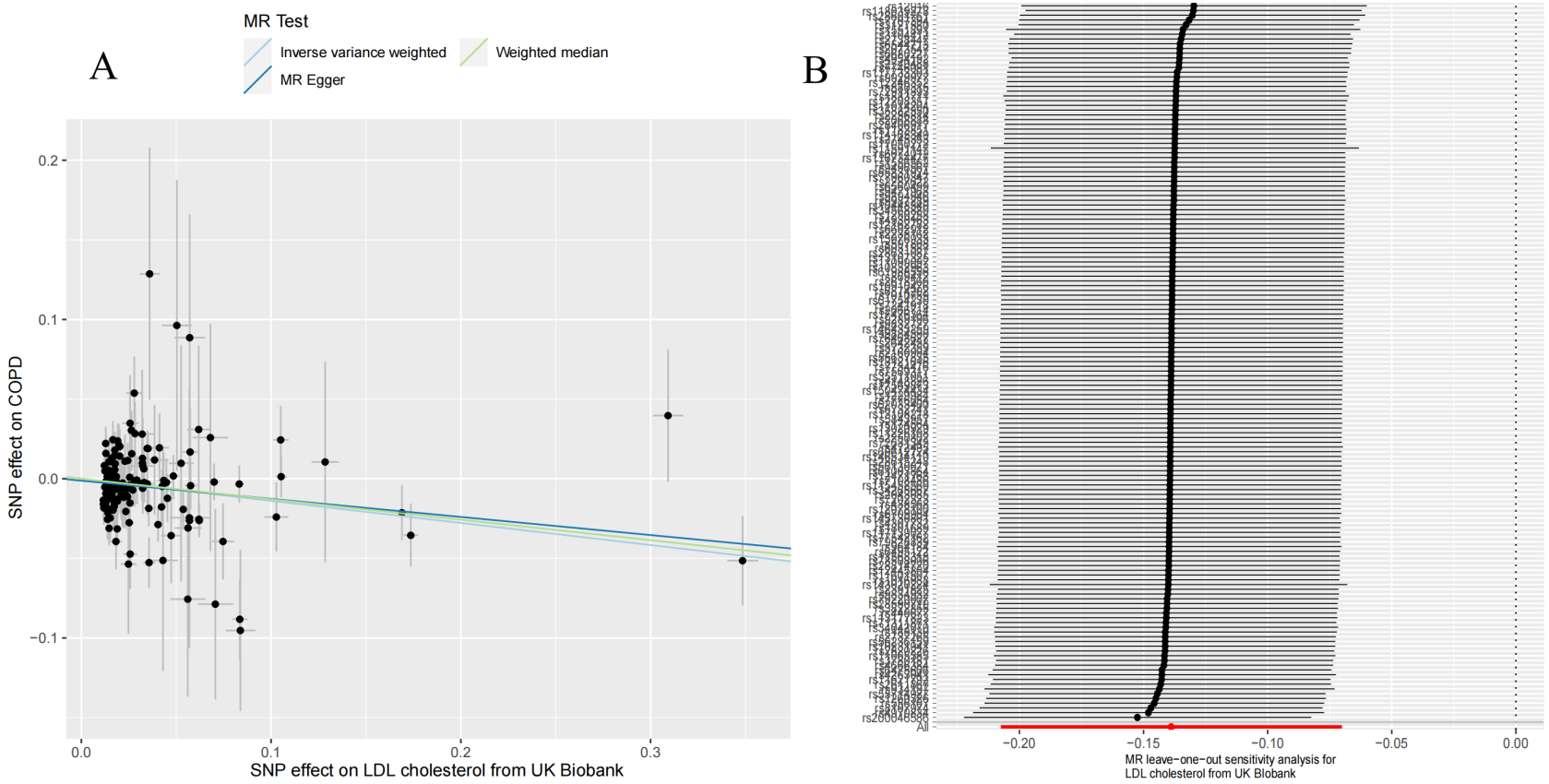

Figure S2 The direct causal effect of low density lipoprotein cholesterol on chronic obstructive pulmonary disease by adjusting several confounding factors.

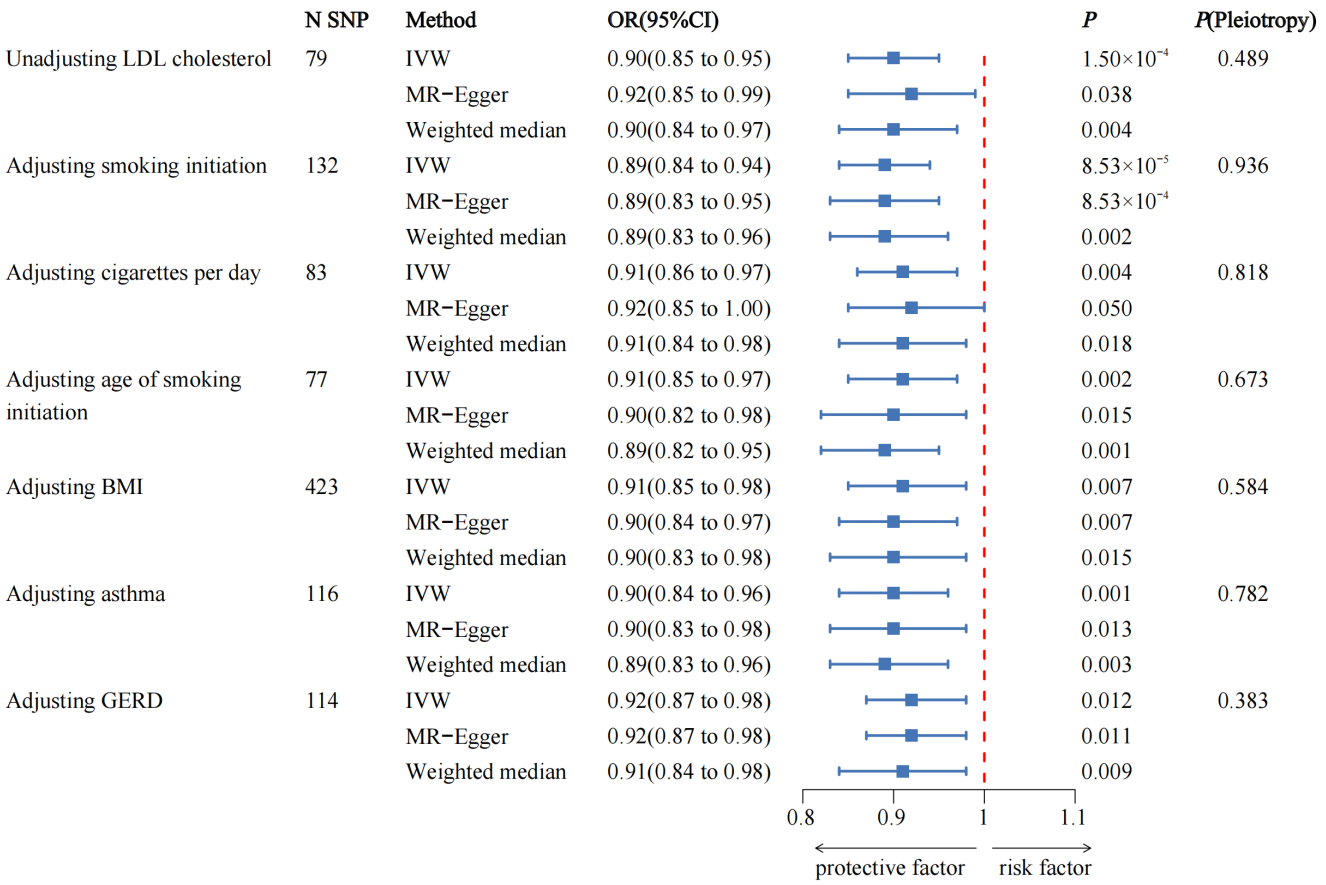

Figure S3 Scatter plot (A) and leave-one-out plot (B) of MR analysis between *HMGCR* and chronic obstructive pulmonary disease.

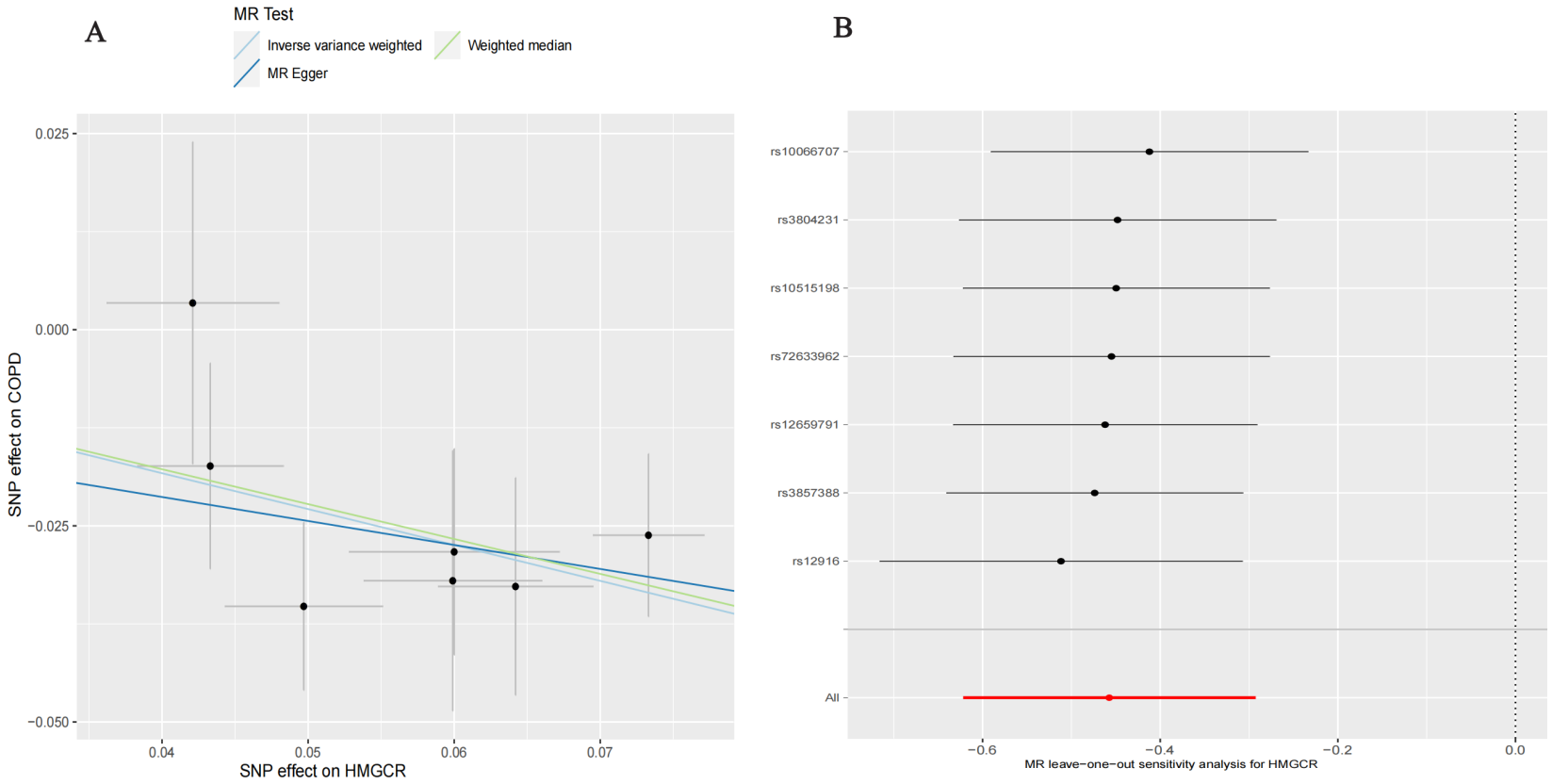

Figure S4 Scatter plot (A) and leave-one-out plot (B) of MR analysis between *PCSK9* and chronic obstructive pulmonary disease.

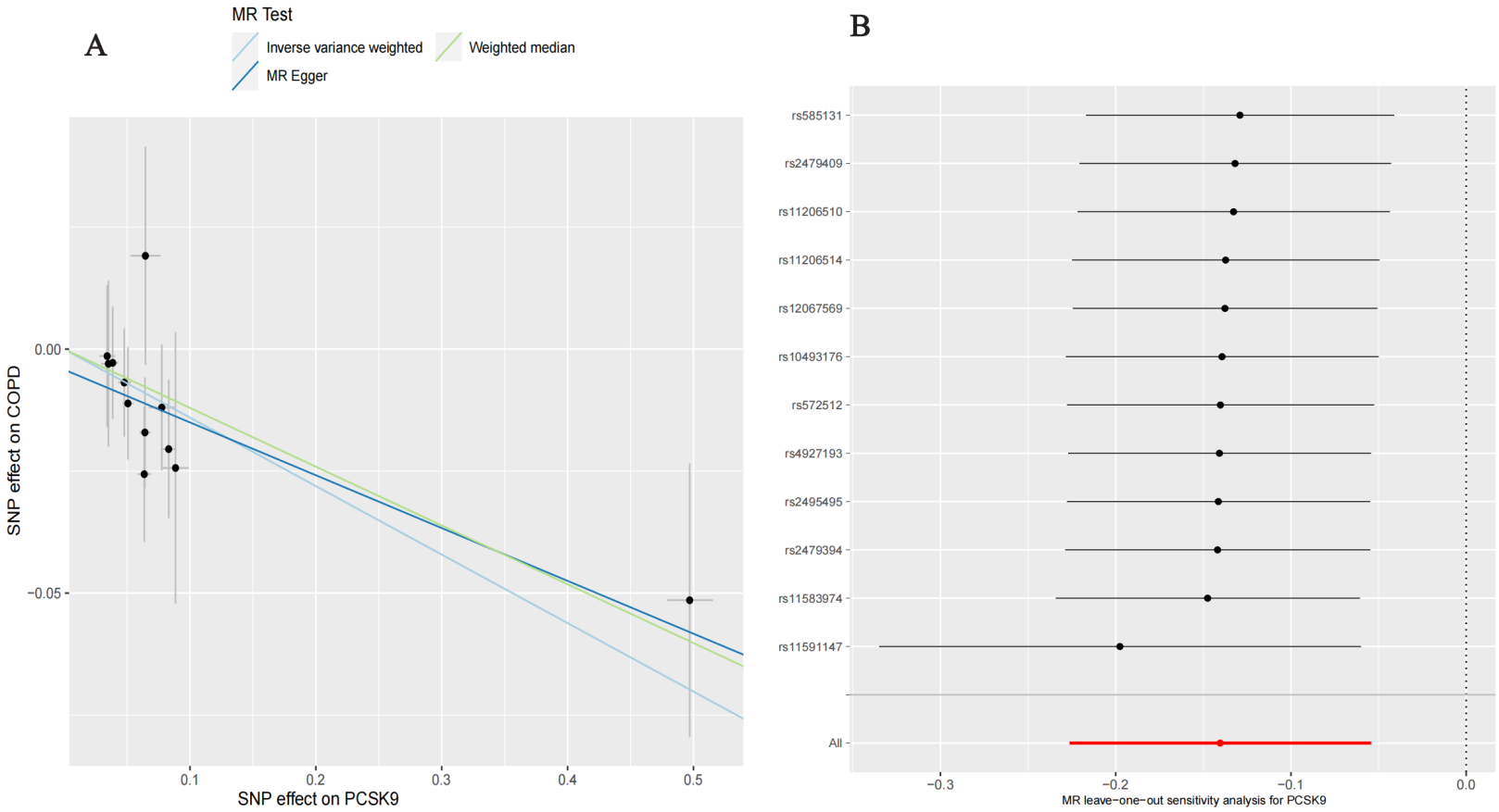

Figure S5 Scatter plot (A) and leave-one-out plot (B) of MR analysis between *LPL* and chronic obstructive pulmonary disease.