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Supplementary Methods

Sepsis and pneumonia cohorts

Sepsis and pneumonia cohorts in critical care were selected from UK Biobank including 431,365 individuals of European ancestry. The population-based cohort was recruited from assessment centers throughout the United Kingdom between 2006 and 2010 [1, 2]. The definition of sepsis was based on international classification of diseases (ICD) codes formulated by the study team from collaborators with expertise in sepsis epidemiology, infectious diseases, critical care, and pediatrics [3]. The ICD-9 and ICD-10 main or secondary diagnosis codes from critical care inpatient records were used to define the sepsis phenotype. Similarly, the diagnosis of pneumonia was confirmed by abnormal chest radiography images and other evidence, such as relevant clinical manifestations and laboratory tests [4]. The ICD-10 primary or secondary diagnosis codes from critical care inpatient records were used to define the pneumonia phenotype.

Single nucleotide polymorphism selection procedure

Genotype data were imputed by standard quality control with reference to the 1000 Genomes Project. A linear regression model was used to estimate the genetic associations by adjusting for sex, age, and principal components [5]. A more detailed description of GWAS data is available at https://gwas.mrcieu.ac.uk/datasets/. To select single nucleotide polymorphism (SNP) for drug targets of Cholesteryl ester transfer protein (CETP), we used the following protocol. First, we imputed genotypes within ±100kb windows and a physical distance threshold of 250kb from the CETP referenced by 1000 Genomes Project. Those SNPs deviating from Hardy-Weinberg equilibrium ($p < 1 \times 10^{-6}$), with a call rate < 95% or with a minor allele frequency < 0.05 were removed in our study. Second, we used a linear regression model to test the association between the screening SNPs and high-density lipoprotein cholesterol (HDL-C) levels. Those associated with HDL-C levels with a threshold of P value less than 5×10^{-8} was selected as candidate SNPs. Third, we used a linkage disequilibrium clumping approach to remove correlated SNPs by setting a threshold of r2 less than 0.2. If the selected SNPs less than 3, the linkage disequilibrium r^2 threshold would be relaxed to 0.40 to increase the proportion of variance explained by genetic instruments. We also constructed genetically-proxied drug targets of HMGCR, PCSK9, and NPC1L1 inhibition by a similar protocol, as described previously [6].

Extended Mendelian randomization models

In our study, we also used alternative Mendelian randomization models to test the robustness of the results. First, we used MR-Egger regression which can provide a valid statistical method when the instrumental variable assumptions do not hold, but a weaker assumption is satisfied. The intercept from MR-Egger regression tested with a $p < 0.05$ would indicate evidence of average directional pleiotropy [7]. Generally, the MR-Egger method is considered conservative in the presence of pleiotropic variants and suffers from less precise estimates. Second, we used the weighted median method, which give more weight to more precise instrumental variables under the condition of at least 50% of the information contributing to the analysis comes from valid SNPs [8]. The weighted median method did not rely Instrument Strength Independent of Direct Effect (InSIDE) assumption, which is complementary to the recent MR-Egger regression method. Third, weighted mode method was also applied in our study. The weighted mode weights the number of SNPs within each cluster by the inverse variance of the SNP-outcome association and generates a final casual estimate based on the cluster with the largest weighted number of SNPs. The weighted mode method would generate an unbiased estimate of the causal effect in the condition of the SNPs within the cluster are all valid SNPs [9].

Multivariable Mendelian randomization

Multivariable Mendelian randomization is an elevated technique for estimating the causal effect of multiple exposure variables on a health outcome. Compared with conventional Mendelian randomization, multivariable Mendelian randomization has an advantage that it can estimate directly causal associations between exposures and outcomes by adjusting for confounding factors [10]. In the present study, we systematically searched for potential confounding factors associated with cholesterol levels and sepsis risk. Finally, we identified 3 potential confounding factors (body mass index, alcohol consumption, smoking) in our analyses. For anthropometric traits, summary statistics of body mass index were obtained from GWAS meta-analysis of Genetic Epidemiology Research on Adult Health and Aging (GERA) combined with Genetic Investigation of Anthropomorphic Traits (GIANT) consortium, which totally included 315,347 European populations [11]. For alcohol consumption, we extracted SNPs associated with drinks per week from the European GWAS including 335,394 individuals conducted by GSCAN [12]. For smoking, we extracted SNPs associated with smoking per day from a GWAS including 249,752 European populations conducted by GSCAN [12]. Univariable Mendelian randomization analyses were performed to evaluate whether there was a causal association between genetically-proxied drug targets and the three factors. If there was evidence of a causal association between drug targets and the three risk factors ($P <0.05$) in univariable Mendelian randomization analyses, then the multivariable Mendelian randomization would be conducted to adjust for the risk factors.

Colocalization analysis

Colocalization analysis was to test whether two or mor traits shared causal variants. The existence of shared causal variants may affect the assessment of direct causal association between traits by allelic heterogeneity. In order to test whether SNPs proxied inhibition CETP and sepsis traits shared causal variants, we used the multitrait Colocalization (HyPrColoc) package to conducted the colocalization analysis [13]. The HyPrColoc algorithm was based on a Bayesian framework, which can identify whether SNPs share causal pathways among exposure factors and disease outcomes with each other. Genomic regions were defined as ±100 kb windows from the drug-target gene. A cutoff threshold of the posterior probability (PP) > 0.8 [14] was used to suggest the existence of a shared causal variant between exposure factors and disease outcomes.

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Table S1. Characteristics of genetic variants in LDL-C, HDL-C, TC, BMI, alcohol consumption and smoking instruments.

SNP	EA/NA	EAF	Effect (95% CI)	P-value
LDL-C				
rs12721109	A/G	0.02	-0.446 (-0.482,-0.41)	2.99×10^{-122}
rs6511720	T/G	0.1	-0.221 (-0.233,-0.209)	1.00×10^{-200}
rs2965157	C/T	0.02	-0.189 (-0.211,-0.167)	7.29×10^{-62}
rs2228603	T/C	0.07	-0.104 (-0.118,-0.09)	4.43×10^{-44}
rs72902576	G/T	0.04	-0.093 (-0.119,-0.067)	9.58×10^{-12}
rs964184	C/G	0.84	-0.086 (-0.101,-0.07)	2.01×10^{-26}
rs6544713	C/T	0.71	-0.081 (-0.089,-0.073)	4.84×10^{-83}
rs6693893	C/T	0.04	-0.077 (-0.103,-0.051)	2.88×10^{-08}
rs1800961	T/C	0.03	-0.069 (-0.089,-0.048)	6.03×10^{-10}
rs2954029	T/A	0.47	-0.056 (-0.063,-0.049)	2.10×10^{-50}
rs6709904	G/A	0.11	-0.055 (-0.072,-0.038)	4.58×10^{-10}
rs247616	T/C	0.29	-0.055 (-0.063,-0.047)	2.57×10^{-37}
rs174583	T/C	0.37	-0.052 (-0.06,-0.045)	7.00×10^{-41}
rs1408272	G/T	0.05	-0.052 (-0.068,-0.036)	3.68×10^{-09}
rs10490626	A/G	0.08	-0.051 (-0.064,-0.037)	1.70×10^{-12}
rs2886232	C/T	0.88	-0.045 (-0.058,-0.033)	3.88×10^{-11}
rs3780181	G/A	0.05	-0.045 (-0.059,-0.03)	1.76×10^{-09}
rs7640978	T/C	0.11	-0.039 (-0.053,-0.026)	9.84×10^{-09}
rs12066643	T/C	0.12	-0.039 (-0.051,-0.026)	1.06×10^{-08}
rs3757354	T/C	0.21	-0.038 (-0.047,-0.03)	2.09×10^{-17}
rs13206249	A/G	0.22	-0.038 (-0.05,-0.026)	4.53×10^{-08}
rs6016373	G/A	0.37	-0.035 (-0.042,-0.028)	7.95×10^{-19}
rs13277801	T/C	0.65	-0.034 (-0.041,-0.026)	3.99×10^{-17}
rs17404153	T/G	0.14	-0.034 (-0.044,-0.023)	1.83×10^{-09}
rs267733	G/A	0.14	-0.033 (-0.043,-0.023)	5.29×10^{-09}
rs2737252	A/G	0.26	-0.031 (-0.039,-0.023)	7.04×10^{-14}
rs2419604	G/A	0.68	-0.03 (-0.038,-0.022)	7.49×10^{-14}
rs1883025	T/C	0.24	-0.03 (-0.038,-0.021)	6.14×10^{-11}
rs9875338	A/G	0.39	-0.027 (-0.034,-0.02)	2.21×10^{-11}
rs6909746	T/C	0.39	-0.026 (-0.034,-0.019)	7.86×10^{-11}
rs4942486	C/T	0.54	-0.024 (-0.032,-0.017)	2.26×10^{-11}
rs314253	C/T	0.34	-0.024 (-0.032,-0.017)	3.44×10^{-10}
rs10195252	C/T	0.42	-0.024 (-0.031,-0.016)	3.81×10^{-08}
rs6818397	G/T	0.59	-0.022 (-0.03,-0.015)	1.68×10^{-08}
rs2030746	C/T	0.6	-0.021 (-0.029,-0.014)	8.60×10^{-09}
rs2390536	G/A	0.63	-0.022 (-0.03,-0.015)	2.04×10^{-08}
rs2710642	G/A	0.38	-0.024 (-0.031,-0.016)	6.09×10^{-09}
rs1250229	T/C	0.21	-0.024 (-0.033,-0.016)	3.13×10^{-08}
rs364585	A/G	0.37	-0.025 (-0.032,-0.017)	4.28×10^{-10}

rs676388	T/C	0.54	-0.027 (-0.034,-0.019)	1.31×10^{-11}
rs3184504	T/C	0.47	-0.027 (-0.034,-0.019)	4.20×10^{-12}
rs6504872	C/T	0.53	-0.027 (-0.035,-0.02)	3.48×10^{-13}
rs4530754	G/A	0.42	-0.028 (-0.035,-0.02)	3.58×10^{-12}
rs2328223	A/C	0.75	-0.03 (-0.04,-0.02)	5.63×10^{-09}
rs8017377	G/A	0.54	-0.03 (-0.038,-0.023)	2.52×10^{-15}
rs4253776	A/G	0.88	-0.031 (-0.043,-0.02)	3.35×10^{-08}
rs10832962	C/T	0.28	-0.032 (-0.04,-0.024)	6.62×10^{-14}
rs10903129	A/G	0.46	-0.033 (-0.04,-0.026)	3.03×10^{-17}
rs4970712	A/C	0.19	-0.034 (-0.043,-0.025)	2.46×10^{-13}
rs7832643	G/T	0.6	-0.034 (-0.041,-0.026)	2.67×10^{-17}
rs11563251	C/T	0.87	-0.035 (-0.047,-0.022)	4.50×10^{-08}
rs2642438	A/G	0.25	-0.035 (-0.043,-0.027)	7.32×10^{-16}
rs1169288	A/C	0.67	-0.038 (-0.045,-0.03)	6.45×10^{-21}
rs16831243	C/T	0.82	-0.038 (-0.049,-0.027)	9.06×10^{-12}
rs2587534	G/A	0.47	-0.039 (-0.046,-0.032)	8.06×10^{-25}
rs6065311	T/C	0.54	-0.042 (-0.049,-0.035)	1.66×10^{-30}
rs6882076	T/C	0.33	-0.046 (-0.053,-0.038)	3.31×10^{-31}
rs7551981	G/T	0.41	-0.047 (-0.055,-0.04)	1.36×10^{-33}
rs1564348	T/C	0.85	-0.048 (-0.058,-0.038)	2.76×10^{-21}
rs2073547	A/G	0.81	-0.049 (-0.058,-0.039)	1.92×10^{-21}
rs12748152	C/T	0.93	-0.05 (-0.063,-0.037)	3.21×10^{-12}
rs10947332	G/A	0.87	-0.05 (-0.061,-0.039)	6.97×10^{-18}
rs10893499	G/A	0.86	-0.052 (-0.062,-0.042)	3.86×10^{-21}
rs2000999	G/A	0.82	-0.065 (-0.074,-0.056)	4.22×10^{-41}
rs112201728	C/T	0.94	-0.068 (-0.088,-0.047)	8.51×10^{-10}
rs9987289	A/G	0.08	-0.071 (-0.084,-0.058)	8.53×10^{-24}
rs12916	T/C	0.57	-0.073 (-0.081,-0.066)	7.79×10^{-78}
rs5763662	C/T	0.97	-0.077 (-0.1,-0.053)	1.19×10^{-08}
rs16891156	A/C	0.98	-0.097 (-0.13,-0.063)	8.23×10^{-09}
rs1801689	A/C	0.96	-0.103 (-0.13,-0.076)	9.81×10^{-12}
rs2315065	C/A	0.91	-0.11 (-0.141,-0.079)	5.23×10^{-12}
rs1367117	G/A	0.71	-0.119 (-0.126,-0.111)	9.48×10^{-183}
rs75687619	G/T	0.98	-0.174 (-0.205,-0.142)	8.05×10^{-24}
HDL-C				
rs3822072	A/G	0.49	-0.025 (-0.032,-0.018)	4.06×10^{-12}
rs1279840	C/T	0.75	-0.03 (-0.038,-0.022)	2.14×10^{-12}
rs998584	A/C	0.51	-0.026 (-0.033,-0.019)	2.27×10^{-11}
rs2278236	A/G	0.54	0.033 (0.026,0.04)	3.18×10^{-18}
rs6509859	T/C	0.27	-0.033 (-0.042,-0.024)	8.95×10^{-11}
rs4148005	G/T	0.3	-0.028 (-0.035,-0.021)	5.74×10^{-14}
rs4969178	G/A	0.63	0.026 (0.019,0.033)	1.53×10^{-12}
rs11065987	G/A	0.42	-0.022 (-0.029,-0.015)	1.23×10^{-09}
rs289745	A/C	0.6	0.028 (0.02,0.036)	2.28×10^{-20}

rs2642438	G/A	0.75	0.03 (0.023,0.038)	7.78×10^{-14}
rs4846914	A/G	0.58	0.048 (0.041,0.055)	3.51×10^{-41}
rs4983559	A/G	0.62	-0.02 (-0.027,-0.013)	9.57×10^{-09}
rs6031587	T/C	0.07	-0.049 (-0.063,-0.034)	1.92×10^{-09}
rs702485	G/A	0.45	0.024 (0.018,0.031)	6.45×10^{-12}
rs12748152	T/C	0.07	-0.051 (-0.063,-0.038)	9.74×10^{-16}
rs970548	C/A	0.28	0.026 (0.018,0.033)	1.71×10^{-10}
rs765548	T/C	0.27	0.107 (0.099,0.114)	7.03×10^{-153}
rs16842	C/T	0.25	-0.03 (-0.037,-0.023)	3.82×10^{-14}
rs13099479	A/G	0.09	0.036 (0.024,0.048)	1.82×10^{-08}
rs2925979	C/T	0.7	0.035 (0.028,0.042)	1.32×10^{-19}
rs9457931	G/A	0.07	-0.055 (-0.07,-0.041)	7.30×10^{-13}
rs17145738	T/C	0.12	0.041 (0.03,0.051)	4.95×10^{-13}
rs12740374	T/G	0.21	0.034 (0.026,0.042)	1.69×10^{-15}
rs4939883	C/T	0.82	0.08 (0.071,0.089)	1.80×10^{-66}
rs12145743	G/T	0.33	0.02 (0.013,0.027)	1.80×10^{-08}
rs676210	A/G	0.23	0.066 (0.058,0.074)	2.34×10^{-54}
rs12286037	T/C	0.06	-0.105 (-0.119,-0.091)	2.80×10^{-47}
rs174535	C/T	0.36	-0.039 (-0.046,-0.032)	9.04×10^{-28}
rs499974	A/C	0.18	-0.026 (-0.035,-0.018)	1.12×10^{-08}
rs2160669	T/C	0.91	0.094 (0.081,0.108)	1.84×10^{-36}
rs10761771	C/T	0.47	0.02 (0.013,0.026)	4.12×10^{-09}
rs11045163	G/A	0.41	0.022 (0.015,0.029)	3.20×10^{-09}
rs4465830	G/A	0.2	-0.06 (-0.068,-0.051)	5.17×10^{-40}
rs492571	C/T	0.04	-0.066 (-0.084,-0.049)	1.27×10^{-12}
rs2288911	G/T	0.51	0.03 (0.023,0.037)	2.84×10^{-15}
rs7306660	A/G	0.37	-0.035 (-0.042,-0.027)	3.34×10^{-19}
rs2972146	T/G	0.62	-0.032 (-0.039,-0.025)	1.85×10^{-17}
rs2293889	G/T	0.59	0.031 (0.024,0.038)	4.27×10^{-17}
rs2066714	C/T	0.12	0.045 (0.031,0.059)	7.26×10^{-10}
rs2602836	G/A	0.57	-0.019 (-0.026,-0.013)	4.96×10^{-08}
rs10087900	A/G	0.44	-0.023 (-0.03,-0.016)	2.17×10^{-09}
rs10808546	T/C	0.45	0.041 (0.034,0.048)	4.11×10^{-30}
rs4240624	A/G	0.92	0.082 (0.07,0.093)	1.32×10^{-45}
rs2240327	G/A	0.51	0.024 (0.018,0.031)	1.11×10^{-11}
rs12133576	G/A	0.65	-0.024 (-0.031,-0.017)	6.15×10^{-11}
rs1689797	A/C	0.3	-0.036 (-0.043,-0.029)	2.85×10^{-21}
rs2290547	A/G	0.21	-0.03 (-0.039,-0.021)	3.69×10^{-09}
rs4650994	A/G	0.48	-0.021 (-0.028,-0.014)	6.70×10^{-09}
rs2255141	G/A	0.68	-0.034 (-0.041,-0.026)	2.35×10^{-17}
rs12412743	T/C	0.15	-0.029 (-0.038,-0.02)	1.31×10^{-09}
rs17173637	C/T	0.1	-0.036 (-0.047,-0.025)	1.90×10^{-08}
rs838876	G/A	0.67	-0.049 (-0.057,-0.042)	7.32×10^{-33}
rs326214	A/G	0.69	-0.061 (-0.07,-0.052)	2.17×10^{-36}

rs1942880	T/C	0.34	-0.023 (-0.03,-0.016)	1.29×10^{-08}
rs731839	A/G	0.66	0.022 (0.015,0.029)	3.44×10^{-09}
rs634869	C/T	0.56	0.023 (0.017,0.03)	1.00×10^{-10}
rs10282707	T/C	0.4	-0.025 (-0.032,-0.018)	1.02×10^{-11}
rs12328675	C/T	0.15	0.045 (0.035,0.055)	2.13×10^{-15}
rs2606736	T/C	0.61	-0.025 (-0.033,-0.016)	4.80×10^{-08}
rs2454722	G/A	0.15	0.035 (0.026,0.044)	3.31×10^{-14}
rs4379922	C/T	0.35	0.025 (0.018,0.032)	9.56×10^{-12}
rs3936511	G/A	0.17	-0.031 (-0.04,-0.022)	2.96×10^{-09}
rs16942887	A/G	0.13	0.083 (0.073,0.093)	8.28×10^{-54}
rs2241210	G/A	0.55	0.033 (0.026,0.04)	2.49×10^{-20}
rs2075650	G/A	0.13	-0.055 (-0.065,-0.045)	9.72×10^{-26}
rs737337	C/T	0.07	-0.057 (-0.068,-0.045)	4.56×10^{-17}
rs13107325	T/C	0.08	-0.071 (-0.086,-0.056)	1.06×10^{-15}
rs4660293	G/A	0.24	-0.035 (-0.043,-0.027)	2.86×10^{-18}
rs686030	A/C	0.86	0.055 (0.045,0.065)	4.29×10^{-27}
rs633695	G/A	0.29	0.089 (0.078,0.099)	7.82×10^{-58}
rs10468017	T/C	0.28	0.118 (0.11,0.125)	1.21×10^{-188}
rs9491696	G/C	0.45	-0.02 (-0.027,-0.014)	5.21×10^{-10}
rs4917014	G/T	0.34	0.022 (0.015,0.029)	1.03×10^{-08}
rs3996352	G/A	0.46	0.03 (0.023,0.036)	3.59×10^{-17}
rs205262	G/A	0.27	-0.028 (-0.036,-0.021)	3.88×10^{-13}
rs1047891	A/C	0.3	-0.027 (-0.035,-0.019)	8.73×10^{-10}
rs6805251	C/T	0.62	-0.02 (-0.027,-0.013)	1.33×10^{-08}
rs181362	T/C	0.2	-0.032 (-0.044,-0.021)	4.36×10^{-08}
rs931992	T/G	0.67	0.029 (0.019,0.038)	1.69×10^{-07}
BMI				
rs10063334	C/T	0.1	0.027 (0.018,0.035)	1.90×10^{-09}
rs10132280	A/C	0.32	-0.022 (-0.027,-0.016)	6.20×10^{-15}
rs10182181	G/A	0.49	0.031 (0.026,0.036)	3.20×10^{-35}
rs10192119	G/T	0.21	0.018 (0.012,0.024)	2.80×10^{-08}
rs10460960	A/G	0.9	0.025 (0.017,0.032)	1.30×10^{-10}
rs10499694	G/A	0.5	-0.014 (-0.019,-0.009)	3.60×10^{-08}
rs10733682	G/A	0.55	-0.019 (-0.024,-0.014)	7.50×10^{-13}
rs10742752	C/T	0.64	0.015 (0.01,0.02)	3.90×10^{-09}
rs1074657	C/T	0.41	-0.017 (-0.023,-0.011)	7.70×10^{-09}
rs10840100	G/A	0.69	0.018 (0.013,0.023)	5.10×10^{-12}
rs10866869	G/A	0.9	-0.028 (-0.037,-0.019)	3.50×10^{-09}
rs10883521	T/A	0.22	0.023 (0.016,0.029)	4.90×10^{-11}
rs10909880	T/C	0.46	-0.015 (-0.02,-0.01)	1.00×10^{-08}
rs10920678	G/A	0.6	-0.017 (-0.021,-0.012)	6.80×10^{-11}
rs10929925	A/C	0.38	-0.014 (-0.019,-0.009)	1.80×10^{-08}
rs10938397	G/A	0.43	0.037 (0.032,0.042)	1.40×10^{-47}
rs10968576	G/A	0.29	0.025 (0.02,0.031)	6.50×10^{-21}

rs11057405	A/G	0.09	-0.029 (-0.038,-0.02)	2.90×10^{-10}
rs1106908	A/G	0.45	-0.018 (-0.023,-0.013)	1.60×10^{-12}
rs11074452	G/C	0.47	-0.017 (-0.023,-0.012)	2.00×10^{-09}
rs11081818	A/G	0.44	0.016 (0.011,0.022)	6.40×10^{-09}
rs11165643	T/C	0.58	0.019 (0.014,0.024)	2.60×10^{-13}
rs11170468	C/A	0.2	-0.017 (-0.023,-0.011)	1.20×10^{-08}
rs11611246	T/G	0.18	0.022 (0.016,0.029)	1.80×10^{-12}
rs11655589	G/A	0.31	0.015 (0.01,0.02)	4.20×10^{-08}
rs11709077	A/G	0.09	0.024 (0.017,0.032)	1.70×10^{-10}
rs11727676	C/T	0.08	-0.029 (-0.038,-0.019)	7.20×10^{-09}
rs118067556	T/C	0.68	-0.044 (-0.058,-0.029)	5.60×10^{-09}
rs11851122	G/A	0.42	0.019 (0.013,0.024)	5.40×10^{-10}
rs12220375	C/T	0.07	0.033 (0.025,0.042)	5.10×10^{-15}
rs12286929	G/A	0.46	0.021 (0.016,0.026)	5.50×10^{-16}
rs12352785	C/A	0.73	-0.018 (-0.023,-0.013)	5.00×10^{-11}
rs12429545	A/G	0.11	0.032 (0.025,0.04)	4.60×10^{-18}
rs12887636	G/T	0.32	-0.017 (-0.022,-0.012)	2.20×10^{-10}
rs12939549	G/A	0.44	-0.017 (-0.022,-0.012)	2.60×10^{-11}
rs13021737	G/A	0.86	0.058 (0.051,0.064)	3.80×10^{-69}
rs13107325	T/C	0.1	0.051 (0.04,0.061)	3.20×10^{-21}
rs13191362	G/A	0.17	-0.025 (-0.033,-0.017)	2.10×10^{-10}
rs1396141	T/C	0.62	0.017 (0.011,0.023)	1.20×10^{-08}
rs1436351	T/G	0.73	0.016 (0.011,0.022)	1.40×10^{-08}
rs1441264	A/G	0.57	0.018 (0.013,0.023)	2.10×10^{-12}
rs144839874	G/A	0.72	-0.139 (-0.188,-0.09)	2.00×10^{-08}
rs1558902	A/T	0.43	0.079 (0.074,0.084)	1.00×10^{-200}
rs1561277	A/C	0.29	-0.017 (-0.022,-0.011)	3.00×10^{-09}
rs1561589	A/G	0.34	0.017 (0.011,0.022)	6.60×10^{-10}
rs17016673	G/C	0.11	0.028 (0.019,0.037)	5.10×10^{-10}
rs17024393	C/T	0.04	0.053 (0.039,0.068)	6.40×10^{-13}
rs17203016	G/A	0.19	0.02 (0.013,0.026)	1.10×10^{-09}
rs17405819	C/T	0.35	-0.025 (-0.03,-0.019)	9.20×10^{-20}
rs17630235	A/G	0.35	-0.016 (-0.021,-0.011)	5.00×10^{-10}
rs17759796	A/C	0.13	0.02 (0.013,0.027)	2.50×10^{-08}
rs1819844	G/A	0.83	-0.019 (-0.025,-0.013)	4.40×10^{-09}
rs188275	C/A	0.64	-0.021 (-0.029,-0.014)	1.50×10^{-08}
rs1928295	C/T	0.43	-0.016 (-0.021,-0.011)	1.10×10^{-10}
rs197374	T/C	0.45	0.016 (0.011,0.022)	1.60×10^{-08}
rs201468966	CA/C	0.6	0.032 (0.021,0.043)	2.90×10^{-09}
rs2033529	G/A	0.26	0.018 (0.013,0.024)	2.00×10^{-11}
rs2062332	A/G	0.43	0.015 (0.01,0.02)	7.90×10^{-09}
rs2112347	G/T	0.38	-0.027 (-0.032,-0.022)	3.00×10^{-26}
rs2145272	A/G	0.65	0.018 (0.012,0.023)	6.30×10^{-11}
rs215607	A/G	0.8	-0.024 (-0.031,-0.016)	2.00×10^{-10}

rs2196618	G/A	0.75	0.019 (0.012,0.025)	9.90×10^{-09}
rs2216931	A/C	0.66	0.02 (0.014,0.026)	1.70×10^{-11}
rs2270204	G/T	0.3	0.018 (0.012,0.024)	4.50×10^{-09}
rs2365389	T/C	0.38	-0.02 (-0.025,-0.015)	3.40×10^{-15}
rs2372716	T/C	0.78	-0.017 (-0.023,-0.011)	3.10×10^{-08}
rs2481665	C/T	0.4	-0.018 (-0.023,-0.013)	1.40×10^{-12}
rs2528531	C/A	0.33	0.017 (0.011,0.023)	1.10×10^{-08}
rs2759315	A/C	0.51	0.019 (0.013,0.024)	5.20×10^{-11}
rs2820311	G/A	0.29	0.028 (0.022,0.034)	2.60×10^{-20}
rs2836754	C/T	0.63	0.017 (0.012,0.022)	7.40×10^{-11}
rs2862996	T/G	0.72	-0.018 (-0.023,-0.013)	4.30×10^{-11}
rs2890652	C/T	0.13	0.024 (0.017,0.032)	3.90×10^{-10}
rs29941	G/A	0.66	0.016 (0.011,0.021)	2.50×10^{-09}
rs3026101	C/T	0.25	0.02 (0.014,0.025)	2.70×10^{-13}
rs3101336	C/T	0.65	0.032 (0.027,0.037)	7.40×10^{-36}
rs3127553	A/G	0.63	-0.021 (-0.026,-0.016)	2.90×10^{-16}
rs34811474	A/G	0.6	-0.02 (-0.027,-0.014)	1.60×10^{-09}
rs34976806	T/C	0.46	-0.017 (-0.023,-0.012)	7.30×10^{-10}
rs3764400	C/T	0.16	0.027 (0.02,0.034)	6.00×10^{-13}
rs3817334	T/C	0.43	0.023 (0.018,0.028)	6.30×10^{-20}
rs4130548	C/T	0.39	0.022 (0.017,0.028)	2.40×10^{-16}
rs4671328	G/T	0.55	-0.024 (-0.03,-0.019)	4.90×10^{-18}
rs4715213	T/C	0.12	0.04 (0.034,0.047)	8.70×10^{-35}
rs4740619	C/T	0.47	-0.016 (-0.021,-0.011)	3.60×10^{-10}
rs4757142	A/G	0.65	0.019 (0.013,0.025)	1.20×10^{-10}
rs4776970	T/A	0.37	-0.026 (-0.031,-0.021)	3.50×10^{-24}
rs4788099	G/A	0.36	0.029 (0.024,0.034)	9.00×10^{-30}
rs4820408	G/T	0.64	-0.016 (-0.021,-0.011)	3.30×10^{-10}
rs4833079	C/T	0.36	-0.016 (-0.021,-0.011)	2.10×10^{-10}
rs487152	A/C	0.53	0.018 (0.013,0.023)	2.20×10^{-12}
rs492400	T/C	0.65	-0.014 (-0.019,-0.009)	4.10×10^{-08}
rs4926726	A/G	0.46	-0.016 (-0.021,-0.011)	1.00×10^{-08}
rs4986044	T/C	0.45	-0.015 (-0.02,-0.01)	3.20×10^{-08}
rs543874	G/A	0.24	0.048 (0.042,0.054)	4.20×10^{-52}
rs592483	T/C	0.6	-0.016 (-0.021,-0.011)	1.20×10^{-09}
rs6091540	T/C	0.28	-0.023 (-0.028,-0.017)	4.40×10^{-16}
rs6142096	A/G	0.54	0.016 (0.011,0.022)	1.10×10^{-08}
rs6265	T/C	0.18	-0.042 (-0.048,-0.035)	1.60×10^{-39}
rs6471932	A/T	0.87	-0.024 (-0.033,-0.016)	1.60×10^{-08}
rs6477694	T/C	0.64	-0.016 (-0.021,-0.011)	2.10×10^{-10}
rs6545714	A/G	0.62	-0.018 (-0.023,-0.013)	1.70×10^{-12}
rs6567160	C/T	0.27	0.052 (0.046,0.058)	6.80×10^{-70}
rs6569648	T/C	0.77	-0.016 (-0.022,-0.011)	4.30×10^{-08}
rs6676190	T/C	0.66	-0.015 (-0.021,-0.01)	2.70×10^{-08}

rs6713510	A/G	0.48	0.016 (0.011,0.021)	6.20×10^{-10}
rs6804842	G/A	0.58	0.017 (0.012,0.022)	5.70×10^{-12}
rs6864049	G/A	0.47	0.014 (0.009,0.019)	3.80×10^{-08}
rs6870983	T/C	0.19	-0.02 (-0.026,-0.014)	8.70×10^{-12}
rs687339	T/C	0.77	0.017 (0.011,0.023)	4.70×10^{-08}
rs7138803	A/G	0.42	0.027 (0.022,0.032)	6.10×10^{-27}
rs7143963	T/C	0.16	0.021 (0.015,0.027)	8.20×10^{-11}
rs7144011	T/G	0.25	0.029 (0.023,0.035)	3.00×10^{-20}
rs7161194	G/A	0.65	-0.019 (-0.025,-0.012)	1.50×10^{-09}
rs7239883	A/G	0.67	-0.016 (-0.021,-0.011)	6.80×10^{-10}
rs749671	A/G	0.39	-0.018 (-0.023,-0.013)	1.80×10^{-12}
rs756717	A/G	0.39	-0.015 (-0.02,-0.01)	2.40×10^{-08}
rs7580766	G/A	0.63	0.016 (0.01,0.021)	4.30×10^{-08}
rs758747	T/C	0.28	0.018 (0.012,0.024)	1.50×10^{-09}
rs7599312	A/G	0.28	-0.021 (-0.027,-0.016)	4.40×10^{-14}
rs7613875	A/C	0.57	0.02 (0.014,0.025)	6.90×10^{-14}
rs7629375	A/C	0.39	-0.021 (-0.026,-0.016)	3.50×10^{-17}
rs7647305	C/T	0.81	0.036 (0.03,0.042)	7.20×10^{-31}
rs77165542	T/C	0.69	-0.061 (-0.077,-0.046)	1.10×10^{-14}
rs7730898	A/G	0.73	0.016 (0.011,0.022)	5.10×10^{-09}
rs775709	C/A	0.58	-0.018 (-0.024,-0.012)	4.00×10^{-10}
rs7899106	G/A	0.05	0.039 (0.028,0.05)	2.70×10^{-11}
rs7903146	T/C	0.26	-0.021 (-0.027,-0.016)	3.30×10^{-14}
rs80255756	A/G	0.68	0.039 (0.026,0.051)	1.20×10^{-09}
rs8036171	C/A	0.6	-0.016 (-0.021,-0.011)	1.00×10^{-09}
rs809439	A/T	0.54	-0.017 (-0.023,-0.011)	2.60×10^{-09}
rs815610	G/C	0.52	-0.02 (-0.026,-0.014)	2.20×10^{-12}
rs879620	T/C	0.58	0.025 (0.018,0.031)	4.00×10^{-14}
rs889398	T/C	0.43	-0.016 (-0.021,-0.011)	1.70×10^{-10}
rs891389	T/C	0.32	0.021 (0.015,0.027)	1.90×10^{-12}
rs901630	T/C	0.45	-0.014 (-0.019,-0.009)	2.50×10^{-08}
rs935166	A/G	0.48	-0.017 (-0.023,-0.012)	5.40×10^{-10}
rs9400239	C/T	0.69	0.02 (0.015,0.026)	4.80×10^{-14}
rs9462027	A/G	0.26	0.02 (0.015,0.026)	4.80×10^{-13}
rs946711	C/A	0.29	0.018 (0.012,0.024)	3.50×10^{-09}
rs947612	A/G	0.74	-0.018 (-0.025,-0.012)	1.60×10^{-08}
rs9512699	A/G	0.38	-0.025 (-0.031,-0.018)	1.90×10^{-12}
rs9513140	T/C	0.41	0.019 (0.013,0.024)	3.10×10^{-11}
rs9527895	C/T	0.2	0.024 (0.016,0.031)	8.00×10^{-10}
rs9563576	T/C	0.2	-0.022 (-0.028,-0.016)	9.70×10^{-12}
rs972540	G/A	0.28	0.018 (0.012,0.023)	1.70×10^{-10}
rs9835772	T/A	0.59	0.02 (0.014,0.027)	3.90×10^{-10}
rs9856151	A/G	0.26	0.017 (0.011,0.022)	3.20×10^{-09}
Alcohol				

rs10085696	G/A	0.2	-0.016 (-0.021,-0.011)	1.24×10^{-10}
rs11860773	C/T	0.18	-0.015 (-0.02,-0.01)	8.35×10^{-10}
rs1229984	C/T	0.95	0.188 (0.176,0.2)	1.00×10^{-200}
rs1260326	C/T	0.6	0.024 (0.02,0.028)	3.33×10^{-33}
rs13107325	T/C	0.07	-0.036 (-0.044,-0.029)	1.23×10^{-20}
rs13332432	G/C	0.3	0.014 (0.01,0.018)	5.94×10^{-11}
rs1387766	A/G	0.62	-0.011 (-0.015,-0.007)	4.79×10^{-08}
rs153106	C/T	0.41	-0.014 (-0.017,-0.01)	3.63×10^{-12}
rs16854020	A/G	0.13	0.018 (0.012,0.024)	4.82×10^{-10}
rs17542254	G/A	0.25	0.013 (0.009,0.017)	8.96×10^{-10}
rs2049045	C/G	0.19	-0.014 (-0.019,-0.009)	3.97×10^{-08}
rs2299409	A/G	0.49	-0.011 (-0.014,-0.007)	4.80×10^{-08}
rs28601761	G/C	0.41	0.011 (0.007,0.015)	7.60×10^{-09}
rs28680958	A/G	0.23	-0.014 (-0.018,-0.009)	9.78×10^{-09}
rs28712821	A/G	0.59	0.028 (0.024,0.032)	1.10×10^{-46}
rs28732378	G/A	0.73	-0.017 (-0.021,-0.012)	2.24×10^{-14}
rs28929474	T/C	0.02	-0.048 (-0.062,-0.034)	2.39×10^{-11}
rs331939	A/G	0.34	-0.012 (-0.016,-0.008)	4.50×10^{-09}
rs34121753	G/A	0.53	0.011 (0.007,0.015)	1.39×10^{-08}
rs4309187	C/A	0.7	0.015 (0.011,0.019)	1.37×10^{-12}
rs4752999	T/C	0.32	-0.015 (-0.019,-0.011)	2.03×10^{-12}
rs494904	C/T	0.43	0.015 (0.011,0.019)	1.41×10^{-14}
rs55872084	T/G	0.22	0.013 (0.008,0.017)	1.98×10^{-08}
rs55932213	G/A	0.7	0.012 (0.008,0.017)	1.80×10^{-08}
rs6106989	A/G	0.63	0.011 (0.007,0.015)	3.81×10^{-08}
rs6739804	C/T	0.66	-0.013 (-0.017,-0.009)	4.72×10^{-10}
rs676388	C/T	0.49	0.015 (0.011,0.019)	5.49×10^{-15}
rs6969458	A/G	0.46	0.013 (0.009,0.016)	5.20×10^{-11}
rs71404478	T/C	0.34	-0.013 (-0.017,-0.009)	3.83×10^{-10}
rs75120545	T/C	0.02	-0.033 (-0.044,-0.022)	7.59×10^{-09}
rs76640332	A/G	0.2	-0.021 (-0.026,-0.016)	1.47×10^{-18}
rs78234152	A/G	0.1	0.028 (0.022,0.034)	2.18×10^{-19}
rs79616692	C/G	0.11	0.019 (0.013,0.025)	2.38×10^{-09}
rs962961	T/C	0.33	-0.012 (-0.016,-0.008)	2.78×10^{-09}
rs9835772	T/A	0.24	0.013 (0.009,0.018)	3.90×10^{-09}
Smoking				
rs10226228	A/G	0.63	-0.011 (-0.014,-0.009)	2.00×10^{-15}
rs10282292	C/T	0.36	0.009 (0.006,0.012)	5.90×10^{-10}
rs1050847	C/T	0.43	0.008 (0.005,0.011)	1.40×10^{-08}
rs10819050	G/T	0.59	-0.011 (-0.014,-0.008)	2.20×10^{-15}
rs10823968	A/T	0.63	0.008 (0.005,0.011)	2.10×10^{-08}
rs10879871	T/G	0.34	-0.01 (-0.012,-0.007)	5.00×10^{-11}
rs10918701	G/A	0.37	0.008 (0.005,0.011)	2.10×10^{-08}
rs10922907	A/T	0.45	0.01 (0.007,0.013)	3.00×10^{-13}

rs11210229	A/G	0.38	0.012 (0.009,0.014)	2.00×10^{-16}
rs112282219	G/A	0.96	-0.023 (-0.03,-0.016)	3.80×10^{-11}
rs11255908	T/G	0.74	-0.01 (-0.013,-0.007)	2.30×10^{-10}
rs113382419	C/A	0.89	-0.028 (-0.033,-0.024)	3.00×10^{-37}
rs11768481	C/A	0.67	0.009 (0.006,0.012)	9.90×10^{-10}
rs11783093	C/T	0.84	0.016 (0.012,0.019)	1.20×10^{-16}
rs11801576	T/C	0.76	-0.01 (-0.013,-0.007)	2.30×10^{-10}
rs11861214	G/T	0.78	0.009 (0.006,0.013)	2.00×10^{-08}
rs11948770	T/C	0.77	-0.01 (-0.013,-0.007)	4.90×10^{-10}
rs12202536	A/G	0.51	-0.008 (-0.011,-0.006)	2.80×10^{-09}
rs1221148	C/G	0.59	0.009 (0.006,0.012)	7.30×10^{-11}
rs12244388	G/A	0.66	-0.013 (-0.016,-0.01)	1.40×10^{-19}
rs1246265	T/C	0.3	-0.009 (-0.012,-0.006)	4.20×10^{-09}
rs12481282	G/C	0.72	-0.009 (-0.012,-0.006)	7.80×10^{-09}
rs12623702	A/G	0.61	-0.01 (-0.013,-0.007)	7.70×10^{-12}
rs12708665	A/G	0.28	-0.009 (-0.012,-0.006)	3.50×10^{-09}
rs12831617	C/T	0.76	-0.009 (-0.012,-0.006)	1.90×10^{-08}
rs12967855	A/G	0.33	0.008 (0.005,0.011)	3.10×10^{-08}
rs13009008	A/G	0.33	0.009 (0.006,0.012)	4.60×10^{-09}
rs13106038	G/A	0.68	0.009 (0.006,0.012)	2.20×10^{-09}
rs13153393	A/G	0.88	-0.014 (-0.018,-0.009)	2.50×10^{-10}
rs136233	A/G	0.81	-0.01 (-0.013,-0.006)	1.80×10^{-08}
rs1403848	C/A	0.44	0.008 (0.005,0.011)	1.20×10^{-08}
rs147412694	G/A	0.85	-0.012 (-0.015,-0.008)	2.90×10^{-09}
rs17309874	G/A	0.74	-0.011 (-0.014,-0.008)	9.70×10^{-13}
rs17314832	C/T	0.64	0.009 (0.006,0.011)	3.70×10^{-09}
rs17553262	A/C	0.88	-0.013 (-0.017,-0.008)	5.30×10^{-09}
rs17576594	G/A	0.72	0.011 (0.008,0.014)	1.70×10^{-12}
rs17733784	T/C	0.62	0.008 (0.006,0.011)	4.60×10^{-09}
rs1922018	C/T	0.36	0.01 (0.007,0.013)	3.00×10^{-12}
rs1931263	G/T	0.51	-0.008 (-0.01,-0.005)	4.00×10^{-08}
rs202645	A/G	0.2	-0.01 (-0.014,-0.007)	3.90×10^{-09}
rs2080870	A/T	0.26	0.009 (0.006,0.012)	4.90×10^{-08}
rs2254710	C/A	0.24	0.009 (0.006,0.012)	3.50×10^{-08}
rs2401924	G/C	0.5	0.011 (0.008,0.013)	2.70×10^{-14}
rs245774	A/G	0.27	-0.009 (-0.012,-0.006)	7.40×10^{-09}
rs2675638	G/A	0.58	0.008 (0.006,0.011)	1.30×10^{-09}
rs2678670	A/T	0.49	0.009 (0.006,0.011)	3.10×10^{-10}
rs2838834	C/T	0.7	-0.009 (-0.012,-0.006)	6.30×10^{-10}
rs28485305	C/T	0.63	0.008 (0.005,0.011)	2.60×10^{-08}
rs28635466	G/A	0.7	0.008 (0.005,0.011)	2.00×10^{-08}
rs2867112	T/G	0.83	0.015 (0.011,0.018)	4.80×10^{-15}
rs2890772	G/T	0.41	-0.014 (-0.016,-0.011)	2.10×10^{-22}
rs2894808	T/A	0.92	-0.015 (-0.02,-0.01)	3.50×10^{-09}

rs317021	T/A	0.81	-0.012 (-0.015,-0.008)	1.10×10^{-10}
rs326341	G/A	0.52	0.009 (0.007,0.012)	1.20×10^{-11}
rs329120	C/T	0.58	0.01 (0.007,0.012)	6.30×10^{-12}
rs34866095	A/G	0.69	-0.009 (-0.012,-0.006)	1.20×10^{-08}
rs348809	A/G	0.35	-0.008 (-0.011,-0.005)	1.30×10^{-08}
rs35120974	A/G	0.58	-0.008 (-0.011,-0.006)	2.00×10^{-09}
rs35169606	T/G	0.61	0.009 (0.006,0.012)	1.20×10^{-09}
rs35175834	G/A	0.79	-0.016 (-0.02,-0.013)	4.60×10^{-22}
rs35343344	C/A	0.73	0.009 (0.006,0.012)	8.80×10^{-09}
rs35891966	G/A	0.93	0.016 (0.01,0.021)	6.90×10^{-09}
rs359243	T/C	0.39	-0.009 (-0.012,-0.006)	9.50×10^{-10}
rs369230	G/T	0.31	-0.009 (-0.012,-0.006)	1.80×10^{-09}
rs3742365	T/C	0.6	-0.011 (-0.014,-0.008)	2.50×10^{-14}
rs3769949	T/A	0.53	-0.008 (-0.011,-0.006)	2.50×10^{-09}
rs3811038	T/C	0.72	-0.01 (-0.013,-0.006)	8.90×10^{-10}
rs3896224	A/G	0.59	0.01 (0.007,0.012)	1.10×10^{-11}
rs421983	T/C	0.52	0.009 (0.006,0.011)	3.30×10^{-10}
rs4391802	A/G	0.71	0.01 (0.007,0.013)	1.40×10^{-11}
rs4473348	A/T	0.25	-0.01 (-0.014,-0.007)	6.40×10^{-11}
rs4543592	T/C	0.52	-0.009 (-0.011,-0.006)	4.50×10^{-10}
rs4568549	C/A	0.5	-0.008 (-0.01,-0.005)	3.90×10^{-08}
rs4571506	C/T	0.54	0.008 (0.005,0.011)	1.50×10^{-08}
rs4671357	T/C	0.52	-0.009 (-0.012,-0.007)	1.10×10^{-11}
rs4731925	C/T	0.32	-0.008 (-0.011,-0.005)	2.60×10^{-08}
rs4814873	C/T	0.77	0.01 (0.007,0.013)	2.90×10^{-09}
rs4949465	T/C	0.87	-0.012 (-0.016,-0.008)	1.70×10^{-08}
rs4957528	A/C	0.21	-0.01 (-0.013,-0.007)	4.20×10^{-09}
rs530916	A/G	0.44	-0.008 (-0.011,-0.005)	2.00×10^{-08}
rs549845	G/A	0.3	0.011 (0.008,0.014)	8.30×10^{-14}
rs57611503	G/A	0.48	0.008 (0.005,0.011)	4.00×10^{-08}
rs6050215	C/T	0.03	-0.026 (-0.034,-0.018)	5.70×10^{-11}
rs60952428	T/C	0.91	0.013 (0.009,0.018)	3.00×10^{-08}
rs6119897	G/A	0.76	-0.013 (-0.016,-0.01)	3.60×10^{-15}
rs61796681	A/T	0.91	-0.013 (-0.018,-0.009)	4.20×10^{-08}
rs62135536	C/T	0.97	0.024 (0.017,0.032)	8.00×10^{-10}
rs62155874	A/G	0.87	-0.017 (-0.021,-0.013)	5.20×10^{-16}
rs62175972	T/C	0.97	0.022 (0.014,0.029)	1.70×10^{-08}
rs62280815	A/G	0.84	-0.011 (-0.015,-0.007)	1.70×10^{-08}
rs624833	T/G	0.69	0.009 (0.006,0.012)	6.60×10^{-10}
rs6562474	C/G	0.65	0.008 (0.006,0.011)	1.00×10^{-08}
rs6598539	T/C	0.49	-0.008 (-0.011,-0.005)	4.50×10^{-09}
rs6665841	C/T	0.23	0.011 (0.007,0.014)	1.40×10^{-10}
rs6692614	C/G	0.42	-0.008 (-0.011,-0.005)	2.80×10^{-08}
rs6741228	T/C	0.43	0.008 (0.005,0.011)	1.60×10^{-08}

rs67596067	G/A	0.65	-0.009 (-0.012,-0.006)	1.20×10^{-09}
rs6778080	T/C	0.27	0.011 (0.008,0.014)	1.30×10^{-12}
rs6779302	G/T	0.63	-0.009 (-0.012,-0.006)	1.20×10^{-09}
rs6935954	A/G	0.42	0.01 (0.007,0.012)	8.20×10^{-12}
rs6962772	A/G	0.85	0.011 (0.007,0.015)	7.80×10^{-09}
rs7039819	G/A	0.43	0.009 (0.006,0.011)	5.10×10^{-10}
rs7077678	C/T	0.62	0.009 (0.006,0.011)	2.60×10^{-09}
rs71367545	G/A	0.79	-0.01 (-0.014,-0.007)	1.40×10^{-09}
rs71532325	C/T	0.68	0.008 (0.005,0.011)	2.30×10^{-08}
rs7155595	A/C	0.67	-0.009 (-0.012,-0.006)	2.50×10^{-09}
rs71627581	G/A	0.89	0.013 (0.009,0.018)	1.60×10^{-09}
rs72678864	G/A	0.83	0.012 (0.009,0.016)	1.60×10^{-11}
rs7297175	T/C	0.43	-0.008 (-0.011,-0.005)	6.60×10^{-09}
rs732083	G/A	0.33	0.008 (0.005,0.011)	1.50×10^{-08}
rs7333559	G/A	0.21	0.011 (0.007,0.014)	3.20×10^{-10}
rs74086911	G/A	0.93	0.015 (0.01,0.02)	2.10×10^{-08}
rs7528604	G/A	0.57	0.01 (0.007,0.012)	5.70×10^{-12}
rs7569203	A/C	0.69	-0.011 (-0.014,-0.008)	7.40×10^{-13}
rs75742406	G/A	0.74	0.01 (0.007,0.013)	1.30×10^{-09}
rs76608582	C/A	0.95	0.022 (0.015,0.028)	3.20×10^{-10}
rs77653640	G/A	0.81	-0.01 (-0.013,-0.006)	3.30×10^{-08}
rs7766610	C/A	0.18	0.013 (0.009,0.016)	2.20×10^{-12}
rs7807019	A/G	0.54	-0.01 (-0.013,-0.008)	6.70×10^{-14}
rs8042134	T/G	0.54	-0.01 (-0.013,-0.007)	1.30×10^{-12}
rs860326	C/T	0.43	0.008 (0.006,0.011)	2.70×10^{-09}
rs8614	C/A	0.82	-0.011 (-0.015,-0.008)	1.80×10^{-10}
rs889398	C/T	0.59	0.009 (0.006,0.012)	6.30×10^{-11}
rs9277988	T/C	0.8	-0.01 (-0.013,-0.006)	2.00×10^{-08}
rs9435340	T/A	0.34	0.008 (0.005,0.011)	1.20×10^{-08}
rs9842947	C/T	0.33	-0.009 (-0.012,-0.006)	3.10×10^{-09}
rs986391	G/A	0.37	0.011 (0.008,0.014)	9.40×10^{-15}
rs9919670	G/A	0.61	-0.015 (-0.018,-0.012)	7.60×10^{-27}

Abbreviations: BMI, body mass index; EA, Effect Allele; EAF, Effect Allele Frequency; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol; NA, Non-effect Allele.

Table S2. **Variance explained by genetic instruments (R^2), F-statistics, I^2-statistics for genetic instruments, and statistical power (%) estimates for primary analyses**

Exposure	R^2 of IVs	F-statistics	I^2 -statistics	Power			
				Sepsis	Sepsis mortality	Pneumonia	Pneumonia mortality
CETP	0.0673	2317	0.99	100	68	100	96
HMGCR	0.0040	138.2	0.95	22	9	38	15
NPC1L1	0.0013	77.3	0.99	11	7	18	9
PCSK9	0.0170	190.7	0.99	68	23	93	46

Abbreviations: IVs, instrument variables;

*Power calculations represent statistical power to detect an odds ratio of OR 0.50 per 1 mmo/L increase in HDL cholesterol (target of CETP) or 1mmol/L reduction in LDL cholesterol (targets of HMGCR, NPC1L1, and PCSK9) at type I error of 5%.

Table S3. Estimating heterogeneity and pleiotropic effects results of genetically proxied drug target in sepsis and pneumonia

Exposure	MR-PRESSO	MR Egger intercept		Cochran's heterogeneity test			
	Global P value	Intercept value	P value	IVW-Q value	IVW-P value	Egger-Q value	Egger-P value
CETP							
Sepsis	0.735	0.045	0.718	3.523	0.619	3.373	0.497
Sepsis mortality	0.881	-0.134	0.596	1.736	0.884	1.407	0.843
Pneumonia	0.721	0.075	0.417	3.164	0.675	2.348	0.672
Pneumonia mortality	0.962	-0.014	0.942	0.979	0.964	0.973	0.914
HMGCR							
Sepsis	0.819	0.062	0.543	1.913	0.752	1.446	0.695
Sepsis mortality	0.967	0.026	0.893	0.573	0.966	0.552	0.907
Pneumonia	0.938	0.008	0.909	0.979	0.913	0.964	0.810
Pneumonia mortality	0.595	-0.119	0.473	3.503	0.477	2.833	0.418
NPC1L1							
Sepsis	0.424	-0.037	0.827	3.175	0.365	3.079	0.214
Sepsis mortality	0.499	0.266	0.381	3.052	0.384	1.811	0.404
Pneumonia	0.575	-0.062	0.536	1.836	0.607	1.288	0.525
Pneumonia mortality	0.580	0.029	0.891	2.095	0.553	2.071	0.355
PCSK9							
Sepsis	0.815	-0.037	0.195	5.898	0.824	3.942	0.915
Sepsis mortality	0.339	-0.009	0.876	11.79	0.299	11.76	0.227
Pneumonia	0.098	0.033	0.192	17.47	0.065	14.29	0.112
Pneumonia mortality	0.806	0.032	0.459	6.211	0.797	5.612	0.778

Abbreviations: IVW, inverse variance-weighted; MR, mendelian randomization; PRESSO pleiotropy residual sum and outlier; SNP, single-nucleotide polymorphism.

Table S4. Association of genetically-proxied inhibition of CETP with sepsis, pneumonia, and 28-day mortality in leave-one-out analysis

Outcome	SNP removed	OR (95% CI)	P-Value
Sepsis			
	rs12708967	0.84 (0.74, 0.97)	0.014
	rs1800775	0.83 (0.73, 0.94)	0.004
	rs1864163	0.83 (0.72, 0.97)	0.015
	rs289714	0.92 (0.78, 1.08)	0.299
	rs3764261	0.83 (0.73, 0.94)	0.004
	rs9929488	0.83 (0.73, 0.95)	0.005
	rs9989419	0.77 (0.66, 0.90)	0.001
Sepsis mortality			
	rs12708967	0.66 (0.51, 0.87)	0.003
	rs1800775	0.66 (0.50, 0.87)	0.003
	rs1864163	0.72 (0.54, 0.96)	0.024
	rs289714	0.73 (0.52, 1.01)	0.055
	rs3764261	0.67 (0.52, 0.88)	0.003
	rs9929488	0.68 (0.52, 0.87)	0.003
	rs9989419	0.67 (0.49, 0.93)	0.015
Pneumonia			
	rs12708967	0.80 (0.72, 0.88)	3.05e-06
	rs1800775	0.79 (0.72, 0.87)	4.51e-07
	rs1864163	0.76 (0.68, 0.84)	1.10e-07
	rs289714	0.79 (0.70, 0.88)	4.53e-05
	rs3764261	0.78 (0.71, 0.86)	2.51e-07
	rs9929488	0.78 (0.72, 0.86)	1.46e-07
	rs9989419	0.76 (0.68, 0.85)	1.83e-06
Pneumonia mortality			
	rs12708967	0.93 (0.75, 1.16)	0.519
	rs1800775	0.91 (0.74, 1.12)	0.381
	rs1864163	0.87 (0.69, 1.09)	0.234
	rs289714	0.93 (0.72, 1.21)	0.606
	rs3764261	0.91 (0.74, 1.12)	0.384
	rs9929488	0.91 (0.74, 1.12)	0.362
	rs9989419	0.89 (0.69, 1.15)	0.377

Effect estimate represents the change in outcome per genetically-proxied inhibition equivalent to a 1 mmol/L (15.5 mg/dL) increase in high density lipoprotein cholesterol.

Table S5. Association of genetically-proxied HDL and LDL cholesterol levels with sepsis, pneumonia and 28-day mortality in sensitivity analyses.

Outcome	**MR-Egger regression OR (95% CI) P-value**		**Weighted median estimator OR (95% CI) P-value**		**Weighted mode estimator OR (95% CI) P-value**	
	LDL	HDL	LDL	HDL	LDL	HDL
Sepsis	1.17 (0.88,1.54) 0.28	1.01 (0.73, 1.42) 0.94	1.15 (0.87,1.50) 0.33	0.91 (0.66,1.25) 0.57	1.17(0.90,1.51) 0.24	0.94 (0.71,1.23) 0.64
Sepsis mortality	0.74 (0.43,1.27) 0.28	1.28 (0.69,2.38) 0.44	0.92 (0.52,1.61) 0.76	1.08 (0.59, 1.99) 0.81	0.87(0.52,1.47) 0.61	1.09 (0.62,1.90) 0.77
Pneumonia	1.18 (0.95, 1.45) 0.13	0.85 (0.66,1.10) 0.22	1.04 (0.86,1.26) 0.66	0.81 (0.66,1.01) 0.06	1.11(0.94,1.31) 0.20	0.83 (0.68,1.01) 0.06
Pneumonia mortality	1.06 (0.69,1.64) 0.78	1.01 (0.54,1.89) 0.98	1.11(0.72, 1.71) 0.65	0.87 (0.53,1.44) 0.59	1.06 (0.73,1.56) 0.75	0.99 (0.62,1.58) 0.96

Table S6. Colocalization analysis of CETP variants and their association with HDL-C levels and risk and 28-day mortality of sepsis and pneumonia

Outcome	Posterior probability
Sepsis	0.01
Sepsis mortality	0.01
Pneumonia	0.12
Pneumonia mortality	0.01

Table S7. Association between genetically proxied lipid-modifying drug targets and previously reported risk factors for sepsis and pneumonia

Proposed risk factor	N	Effect estimate (95% CI) P-value			
		CETP	HMGCR	NPC1L1	PCSK9
Alcohol consumption	335,394	1.01 (1.00, 1.02)	1.00 (0.93,1.06)	1.01 (0.92,1.11)	1.00 (0.99, 1.02)
		0.06	0.89	0.87	0.86
Body mass index	315,347	1.01 (1.00,1.02)	0.80 (0.69,0.92)	1.00 (0.89,1.12)	1.01 (0.98,1.04)
		0.06	0.002	0.95	0.59
smoke	249,752	1.01 (0.99,1.02)	0.96 (0.80,1.15)	0.73 (0.57,0.92)	0.97 (0.93, 1.02)
		0.53	0.65	0.009	0.22

Table S8. Association of genetically-proxied inhibition of HMGCR and NPC1L1 with sepsis, pneumonia and 28-day mortality adjusted for body mass index and smoking.

Drug targets	Proposed risk factor	Effect estimate P-value			
		Sepsis	Sepsis mortality	Pneumonia	Pneumonia mortality
HMGCR	Body mass index	2.72 (0.33,22.42) 0.35	4.58 (0.11,19.6) 0.43	1.57 (0.44,5.62) 0.49	10.31 (0.15,69.65) 0.28
NPC1L1	Smoking	2.99 (1.05,8.41) 0.04	0.19 (0.01,3.30) 0.25	0.41 (0.11,1.49) 0.18	3.14 (0.35,28.41) 0.31

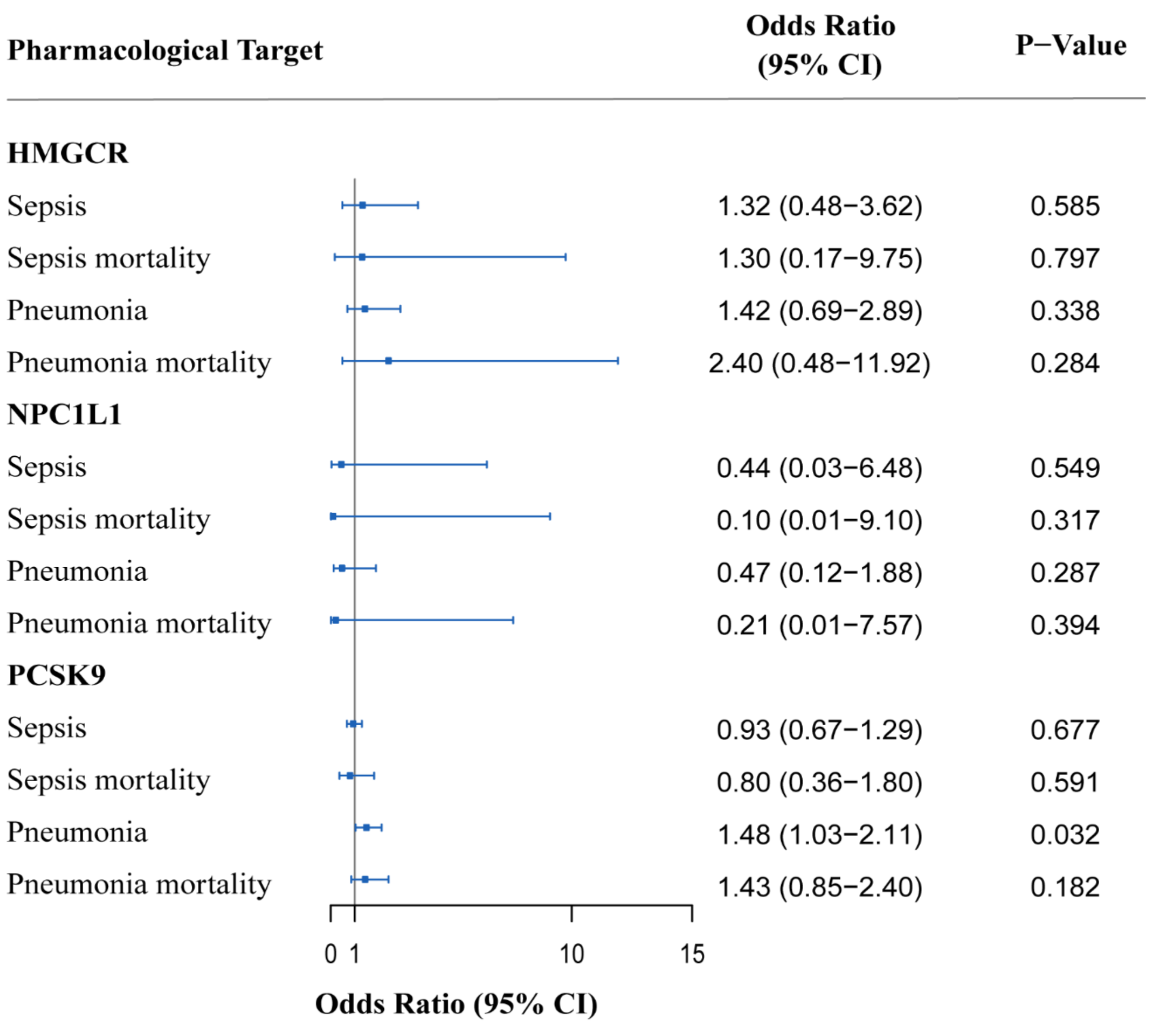

Fig. S1. Mendelian randomization estimates of the association between other genetically proxied inhibition of drug target (HMGCR, NPC1L1, PCSK9) and sepsis and pneumonia.

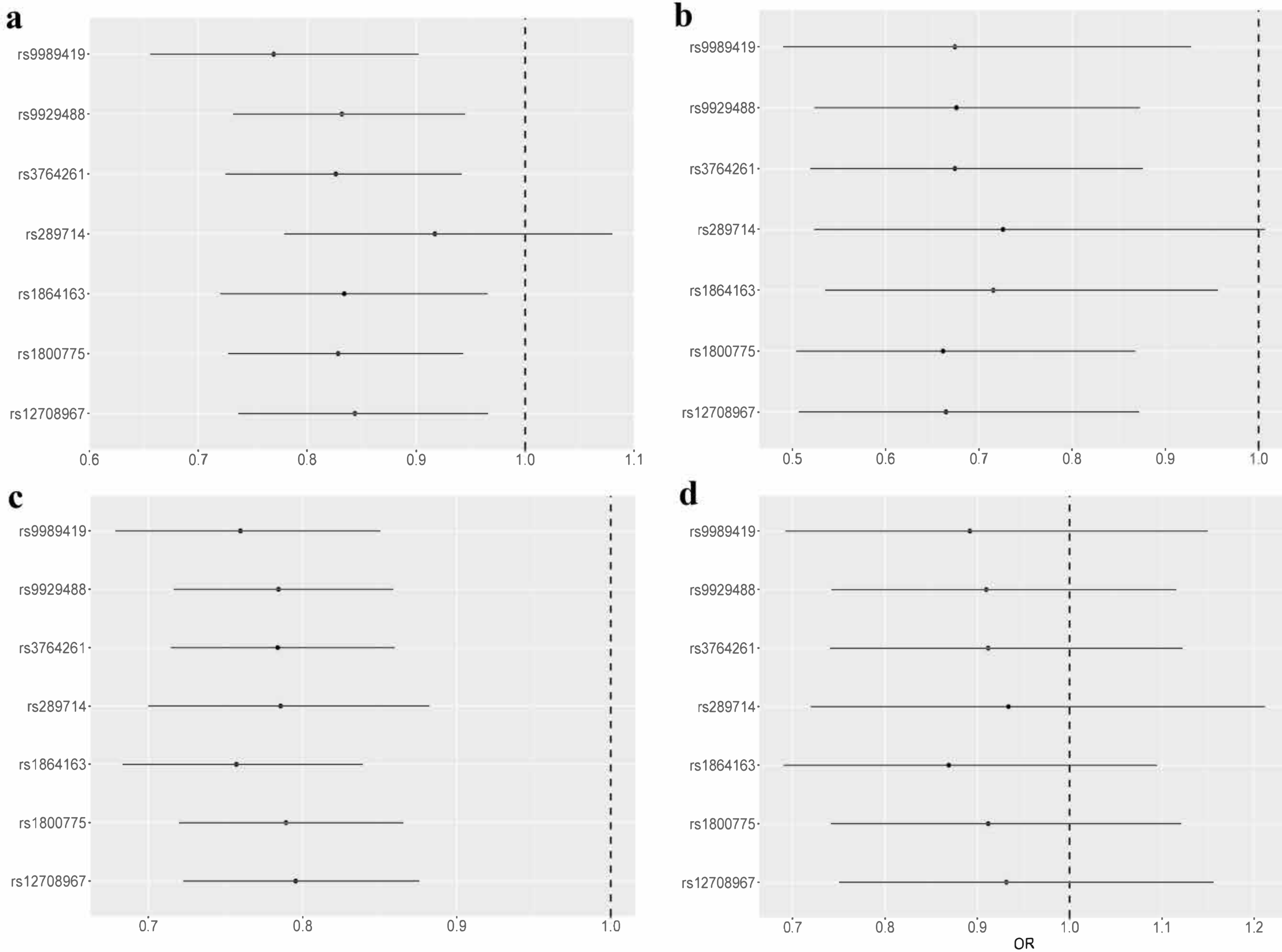

Fig. S2. Leave-one-out analysis of genetically proxied CETP inhibition on risk of sepsis and pneumonia. (a) CETP inhibition and risk of sepsis; (b) CETP inhibiti on and 28-day mortality from sepsis; (c) CETP inhibition and risk of pneumonia; (d) CETP inhibition and 28-day mortality from pneumonia