Supplementary Materials

The relationship between serum alkaline phosphatase levels and sepsis: observational and Mendelian randomization studies

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Supplemental Fig. 1 The scatter plot of the MR analysis of serum ALP levels on sepsis.

Supplemental Fig. 2 The forest plot summarized the SNP-specific and overall MR estimates for the causal effects on sepsis using the separately selected SNPs associated with serum ALP levels.

Supplemental Fig. 3 The leave-one-out sensitivity analyses for causal effects of serum ALP levels on sepsis.

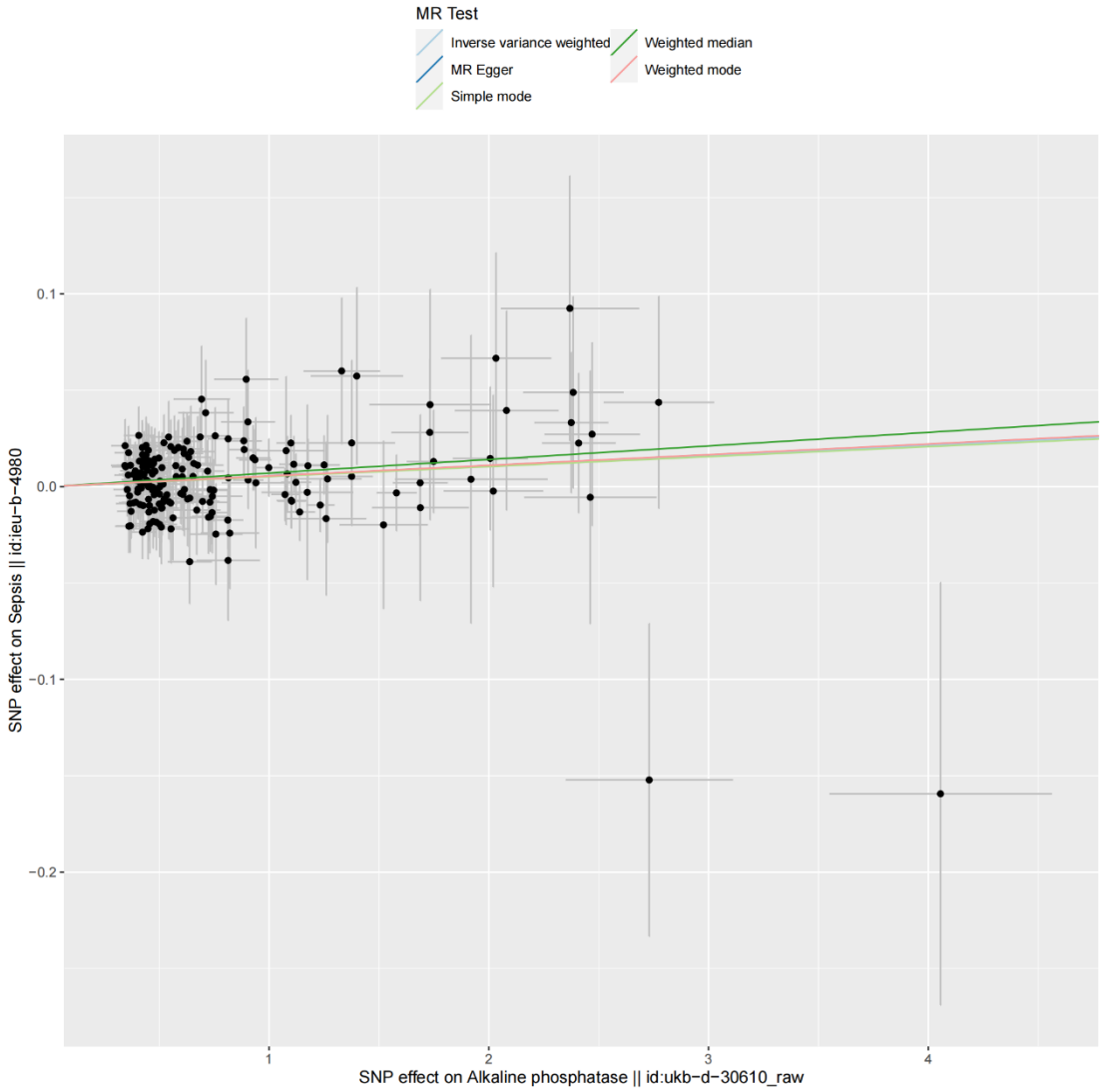
Supplemental Fig. 4 The funnel plot assessing heterogeneity.

Supplemental Table 1 Details of the GWASs included in the mendelian randomization study.

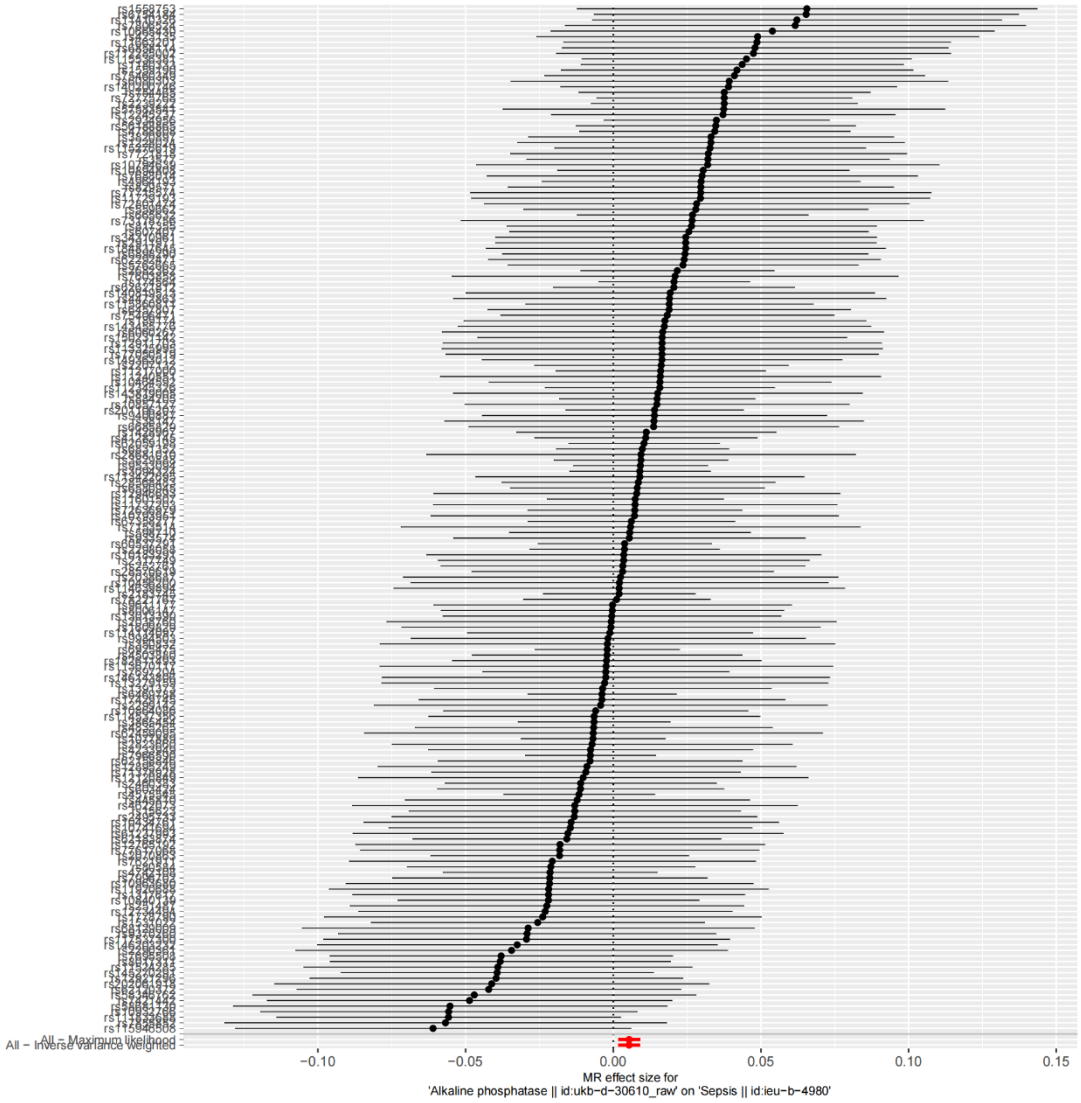
Supplemental Table 2 Characteristics of the SNPs filtering process in the Mendelian randomization study.

Supplemental Table 3 Summary information of the SNPs used as IVs in the MR study between serum ALP levels and sepsis.

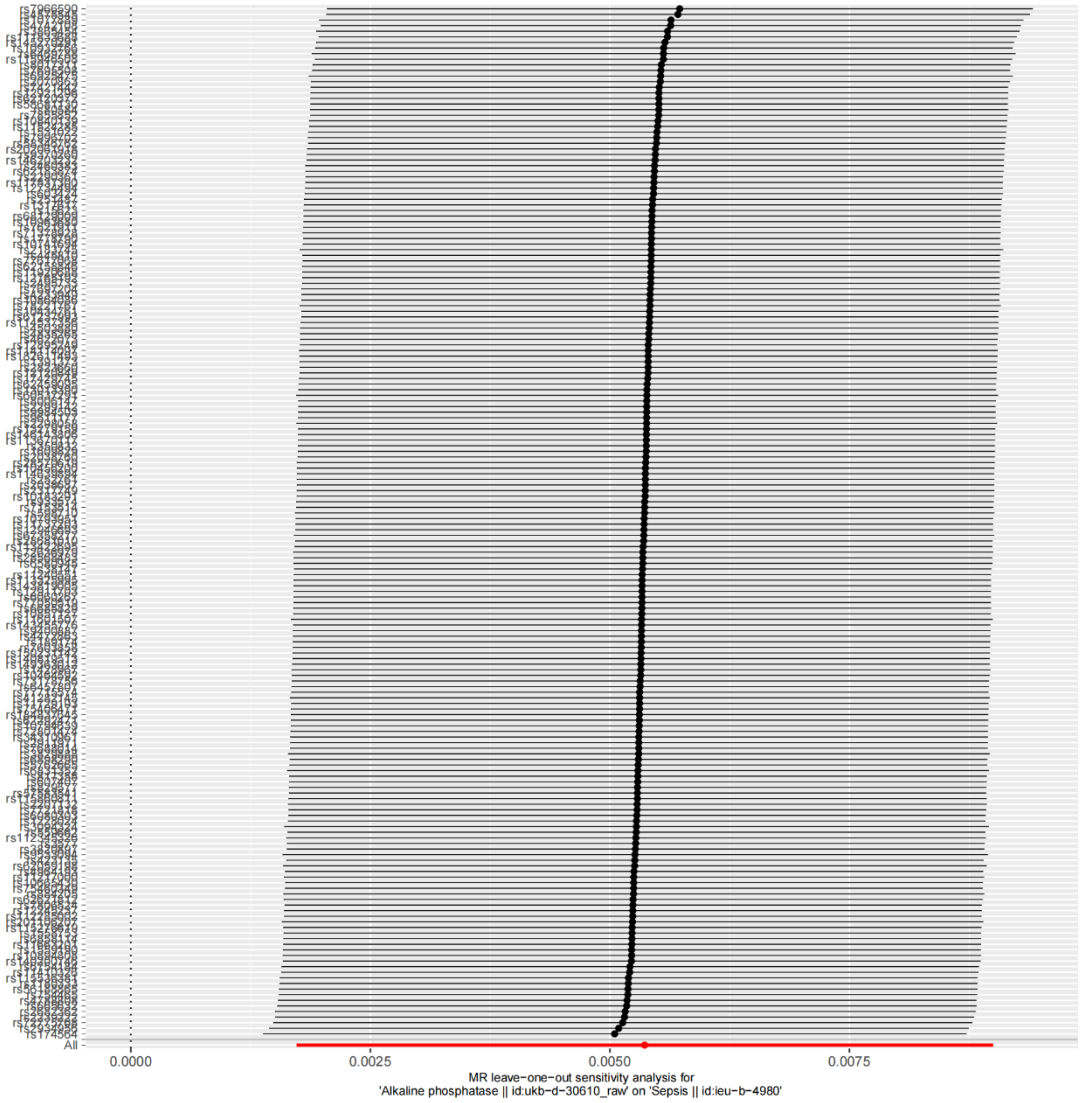
Supplemental Table 4 Pleiotropy and heterogeneity test of the mendelian randomization study.



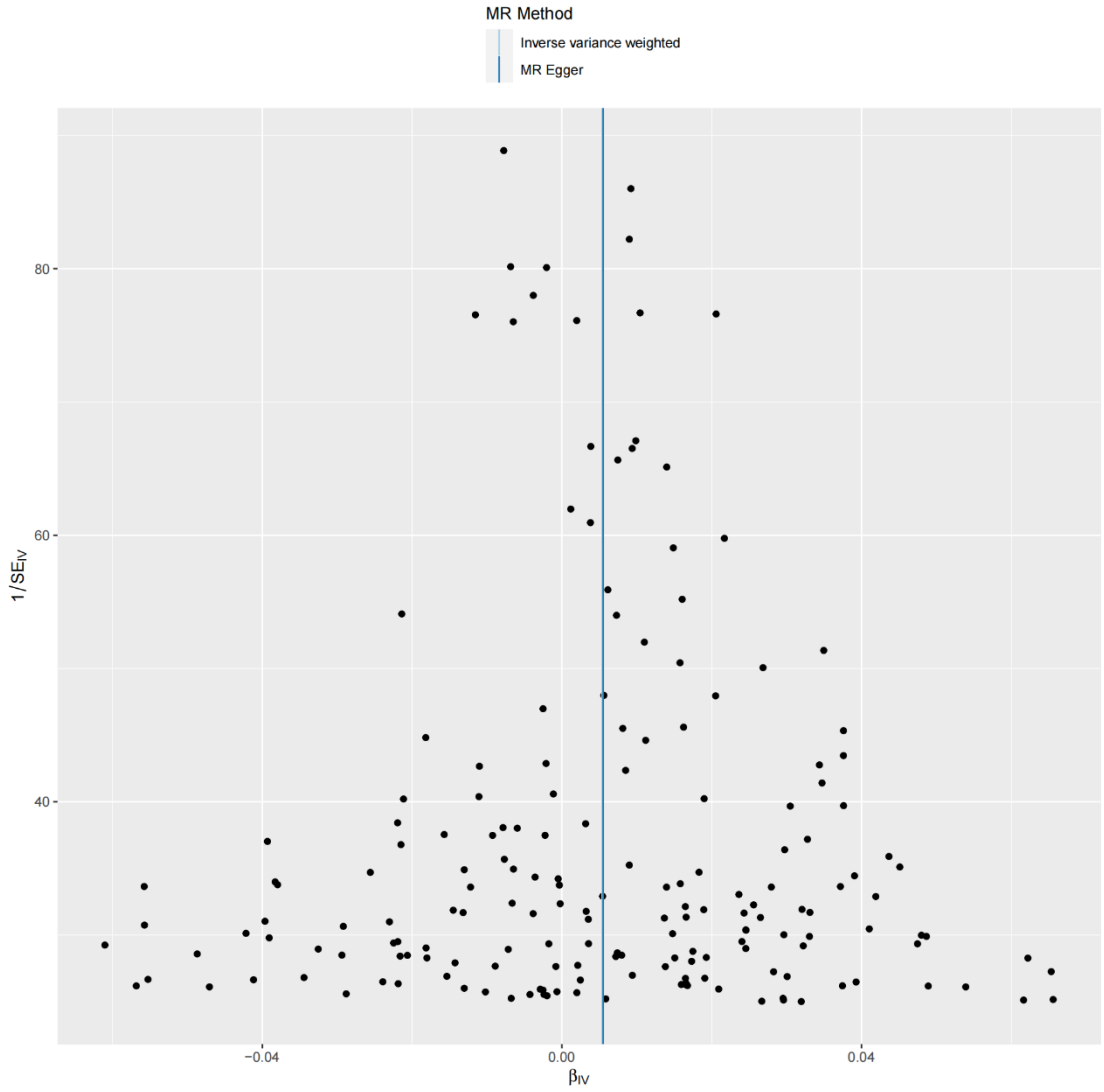
Supplemental Fig. 1 The scatter plot of the MR analysis of serum ALP levels on sepsis. The slope of each line represents the estimated Mendelian randomization (MR) effect via IVW, simple mode, weighted mode, weighted median, and MR-Egger regression methods. Each small black dot represents a selected SNP, and its horizontal and vertical lines represent the 95% confidence intervals of the exposure factor and outcome, respectively.



Supplemental Fig. 2 The forest plot summarized the SNP-specific and overall MR estimates for the causal effects on sepsis using the separately selected SNPs associated with serum ALP levels. The solid black circles represent the estimates of the causal effects for each single-nucleotide polymorphism (SNP), and the horizontal lines indicate the 95% confidence intervals (CIs). The solid red circles with the horizontal lines at the bottom of the forest plot show the result when all the individual SNPs are combined and averaged by the inverse variance weighted (IVW) method.



Supplemental Fig. 3 The leave-one-out sensitivity analyses for causal effects of serum ALP levels on sepsis. Each black point represents the estimate of serum ALP levels (per standard deviation increase) on sepsis after the corresponding single-nucleotide polymorphism (SNP) was excluded. The error bars represent 95% confidence intervals (CIs). The red dot represents the inverse variance weighted (IVW) estimate using all SNPs.



Supplemental Fig. 4 The funnel plot assessing heterogeneity. The black dots represent the SNPs linked to serum ALP levels. The horizontal axis depicts each SNP's effect value (β_{IV}), while the vertical axis illustrates the estimation of causal effects for each SNP as the reciprocal of the standard error of calculation (SE) ($1/SE_{IV}$). The vertical line represents the estimated combined effect achieved by integrating the IVW and MR-Egger regression methods.

Supplemental Table 1 Details of the GWASs included in the mendelian randomization study.

Event	GWAS ID	Consortium	Year	Population	Sample size
ALP	ukb-d-30610_raw	Neale lab	2018	European	13,586,006
Sepsis	ieu-b-4980	UK Biobank	2021	European	11,643/474,841

Supplemental Table 2 Characteristics of the SNPs filtering process in the Mendelian randomization study.

SNPs correlated with exposure ($P < 5 \times 10^{-8}$)	SNPs not present in the outcome GWAS	Proxy SNPs (for SNPs not in outcome)	Horizontal pleiotropy	Palindromic SNPs	Confounders(events)	F ≤ 10	nSNPs in MR analysis
252	rs1062315	rs6698842(rs4459081)	rs2671541	rs5889386	rs10162642(Serum lipid)	rs149344982	184
	rs12092342	rs67564328(rs58712547)	rs12952704	rs1509396	rs10787429(Serum lipid)	rs28709106	
	rs12778436	rs17207494(rs62158846)	rs2919872	rs3772098	rs11621792(Serum lipid)	rs4654748	
	rs139269536	rs11099675(rs7697204)	rs4860987	rs5112	rs139974673(Serum lipid)	rs56222534	
	rs142738614	rs1960773(rs1531022)	rs36640	rs7115703	rs1408272(Serum lipid)	rs7949566	
	rs1984769	rs4576015(rs10857127)	rs1029709	rs764036	rs1601935(Serum lipid)	rs9414801	
	rs201772279	rs66492054(rs60537291)	rs61909599	rs9565082	rs2070895(Serum lipid)		
	rs28362459	rs35531907(rs72775768)	rs56397607		rs2000825(Serum lipid)		

rs376295566	rs7924036(rs9414801)	rs28601761	rs3918253(Serum lipid)
rs41265999	rs6589681(rs11217000)	rs12614487	rs55714927(Serum lipid)
rs71487834	rs676767(rs598710)	rs2272662	rs58542926(Serum lipid)
rs9391844	rs2909218(rs71378928)	rs4920192	rs2642438(Serum lipid)
rs9829214		rs10048745	rs79624003(Serum lipid)
rs9926191		rs2836881	rs550057(Serum lipid)
		rs28929474	rs3936510(Serum lipid)
		rs58712547	rs601338(Serum lipid)
			rs9302635(Serum lipid)
			rs9888986(Serum lipid)
			rs12133641(Circulating cytokines)
			rs1260326(Circulating cytokines)

		rs2393791(Circulating cytokines)
		rs4459081(Circulating cytokines)
		rs645040(Circulating cytokines)
		rs9987289(Circulating cytokines)
		rs9932007(Blood metabolites)

Supplemental Table 3 Summary information of the SNPs used as IVs in the MR study between serum ALP levels and sepsis.

SNP	chr	pos	EA	OA	EAF	beta.exposure	se.exposure	pval.exposure	beta.outcome	se.outcome	pval.outcome	samplesize	F
rs10794639	16	377367	G	A	0.472	0.343	0.063	3.98E-08	0.011	0.014	0.424	344292	21481
rs7153514	14	102269317	G	A	0.135	-0.503	0.091	3.51E-08	-0.003	0.020	0.883	344292	21583
rs7806524	7	98004997	T	G	0.474	-0.345	0.063	3.63E-08	-0.021	0.014	0.122	344292	21657
rs77715574	2	48656659	T	G	0.175	-0.453	0.083	3.98E-08	-0.013	0.018	0.457	344292	21692
rs73178756	20	56106400	A	G	0.164	0.465	0.084	3.61E-08	0.012	0.019	0.504	344292	21720
rs11729193	4	734351	G	A	0.550	0.347	0.063	2.99E-08	0.010	0.014	0.456	344292	21829
rs114639894	6	23982256	A	G	0.008	-1.919	0.346	2.97E-08	-0.004	0.075	0.959	344292	22175
rs113670117	14	36099366	T	C	0.088	-0.614	0.110	2.18E-08	0.001	0.024	0.951	344292	22214
rs1558753	3	186777789	A	T	0.068	-0.693	0.127	4.67E-08	-0.045	0.028	0.099	344292	22239
rs350832	19	4069426	A	G	0.771	0.415	0.075	2.72E-08	-0.001	0.016	0.960	344292	22285

rs68129009	17	2611471	C	G	0.109	-0.562	0.100	2.13E-08	0.016	0.022	0.461	344292	22457
rs12120849	1	68062148	T	C	0.085	-0.629	0.112	1.92E-08	0.006	0.024	0.793	344292	22540
rs2299142	7	42061523	T	C	0.428	0.354	0.063	2.13E-08	-0.002	0.014	0.913	344292	22555
rs2038760	6	2680732	T	C	0.170	-0.471	0.084	1.77E-08	0.000	0.018	0.986	344292	22971
rs58346762	10	103896322	A	C	0.050	0.813	0.143	1.33E-08	-0.038	0.031	0.219	344292	23063
rs13279159	8	129163047	G	A	0.266	0.404	0.071	1.21E-08	-0.001	0.016	0.940	344292	23363
rs4622073	1	93255073	G	A	0.606	0.365	0.064	1.20E-08	-0.005	0.014	0.735	344292	23401
rs10665430	17	72445839	GTTC	G	0.932	-0.711	0.125	1.12E-08	-0.038	0.027	0.159	344292	23423
rs7603858	2	172036699	A	T	0.297	0.391	0.069	1.27E-08	0.008	0.015	0.587	344292	23466
rs62459095	7	44267538	T	C	0.062	-0.742	0.134	2.89E-08	0.005	0.029	0.864	344292	23509
rs6060267	20	33734012	G	A	0.476	-0.359	0.062	9.15E-09	-0.006	0.014	0.660	344292	23618
rs57583541	8	30207179	G	T	0.209	-0.441	0.077	9.74E-09	-0.017	0.017	0.327	344292	23696

rs11920688	3	98755934	T	C	0.671	0.383	0.066	7.57E-09	-0.008	0.015	0.565	344292	23831
rs11240551	1	205641826	C	G	0.266	0.407	0.070	7.51E-09	0.006	0.015	0.675	344292	23837
rs423135	16	89740873	A	G	0.518	0.360	0.063	9.15E-09	0.018	0.014	0.201	344292	23848
rs7855852	9	124012631	C	T	0.461	-0.361	0.063	9.19E-09	0.021	0.014	0.137	344292	23909
rs12911703	15	89456948	A	G	0.281	-0.401	0.069	7.27E-09	-0.007	0.015	0.662	344292	23925
rs1778790	13	28437257	T	C	0.568	-0.367	0.063	6.30E-09	0.009	0.014	0.527	344292	24337
rs6080303	20	16554546	A	G	0.244	0.424	0.073	6.51E-09	0.017	0.016	0.298	344292	24398
rs202061918	8	71315856	CG	C	0.150	0.509	0.087	5.71E-09	-0.021	0.019	0.273	344292	24421
rs2038687	20	60707040	A	G	0.145	-0.517	0.089	5.22E-09	-0.001	0.019	0.948	344292	24424
rs4472863	10	96421416	G	A	0.214	0.445	0.076	4.43E-09	0.008	0.017	0.610	344292	24614
rs58681130	5	68391067	TG	T	0.461	-0.368	0.063	4.92E-09	0.020	0.014	0.141	344292	24904
rs61237993	9	34130435	A	G	0.127	-0.552	0.094	3.74E-09	0.008	0.021	0.679	344292	24934

rs2290361	7	134555127	T	G	0.425	-0.372	0.063	4.31E-09	0.013	0.014	0.356	344292	24958
rs7688014	4	103975060	C	T	0.534	-0.369	0.063	3.85E-09	-0.011	0.014	0.419	344292	24977
rs77050519	2	242163461	G	C	0.081	0.675	0.115	5.10E-09	0.011	0.025	0.659	344292	25019
rs28681010	15	90759849	A	G	0.322	-0.395	0.067	3.36E-09	-0.004	0.015	0.800	344292	25213
rs6754184	2	134856737	G	A	0.299	-0.407	0.068	2.36E-09	-0.027	0.015	0.075	344292	25652
rs72801474	5	132444128	A	G	0.093	-0.643	0.108	2.21E-09	-0.018	0.024	0.441	344292	25751
rs113325995	22	24291672	G	T	0.605	-0.382	0.066	8.51E-09	-0.006	0.015	0.664	344292	25829
rs10456200	6	15541024	C	T	0.042	-0.940	0.155	1.45E-09	-0.002	0.034	0.953	344292	26550
rs38147	7	20052543	A	G	0.338	0.400	0.066	1.36E-09	0.006	0.014	0.703	344292	26569
rs1609829	1	180909061	C	T	0.703	0.416	0.069	1.32E-09	0.000	0.015	0.982	344292	26871
rs10434761	5	115160053	A	G	0.144	0.543	0.089	1.05E-09	-0.008	0.019	0.691	344292	27039
rs12895249	14	73712922	C	T	0.201	0.477	0.079	1.38E-09	-0.004	0.017	0.806	344292	27144

rs146143806	1	22319471	G	A	0.028	-1.174	0.207	1.52E-08	0.003	0.045	0.948	344292	27852
rs143819005	7	150917891	C	T	0.116	-0.604	0.097	5.19E-10	-0.009	0.021	0.670	344292	27869
rs143455776	5	52112850	C	T	0.033	-1.077	0.174	5.86E-10	-0.019	0.038	0.627	344292	27904
rs7621911	3	47131595	A	G	0.576	0.393	0.063	4.35E-10	-0.008	0.014	0.557	344292	28090
rs140819513	20	3167805	C	G	0.174	0.512	0.082	4.94E-10	0.010	0.018	0.585	344292	28113
rs12765192	10	130899819	C	T	0.186	-0.500	0.080	5.23E-10	0.009	0.018	0.610	344292	28185
rs10963680	9	18629283	A	G	0.243	0.455	0.073	4.90E-10	-0.010	0.016	0.540	344292	28425
rs10793951	9	133496529	A	G	0.652	-0.411	0.066	4.56E-10	-0.003	0.014	0.838	344292	28632
rs11737203	4	151224817	G	A	0.268	-0.443	0.070	3.10E-10	-0.003	0.015	0.832	344292	28715
rs12946693	17	44084008	C	T	0.549	-0.395	0.063	4.27E-10	-0.003	0.014	0.820	344292	28883
rs189174	3	119818585	C	G	0.336	0.417	0.066	3.19E-10	0.007	0.014	0.615	344292	28953
rs117537300	8	10743939	A	G	0.062	-0.821	0.131	3.43E-10	0.024	0.029	0.403	344292	29297

rs7421442	2	21411649	G	A	0.735	0.449	0.072	4.13E-10	-0.022	0.016	0.164	344292	29306
rs2823660	21	17591139	C	A	0.581	-0.402	0.063	2.24E-10	0.003	0.014	0.836	344292	29374
rs77617068	4	37429097	C	T	0.098	0.671	0.105	1.81E-10	-0.012	0.023	0.599	344292	29676
rs146203232	6	160521885	T	C	0.075	0.758	0.119	2.09E-10	-0.025	0.026	0.347	344292	29696
rs7721818	5	88394669	A	G	0.386	0.409	0.064	1.55E-10	0.013	0.014	0.347	344292	29697
rs184837645	6	24372587	C	T	0.014	-1.733	0.276	3.27E-10	-0.043	0.060	0.477	344292	29961
rs115946508	7	150497496	A	C	0.111	-0.638	0.100	1.46E-10	0.039	0.022	0.074	344292	30235
rs9984503	21	36918405	C	G	0.362	-0.418	0.065	1.18E-10	0.001	0.014	0.959	344292	30260
rs112285002	19	48374320	T	C	0.164	0.542	0.084	1.18E-10	0.026	0.018	0.164	344292	30290
rs1317617	10	81096589	A	G	0.193	0.510	0.079	1.03E-10	-0.011	0.017	0.518	344292	30348
rs62292471	3	132429447	T	C	0.115	0.634	0.098	1.01E-10	0.015	0.021	0.478	344292	30572
rs10183291	2	181839944	G	A	0.387	0.415	0.064	1.18E-10	0.001	0.014	0.917	344292	30677

rs251487	3	142709233	A	C	0.593	-0.412	0.064	1.10E-10	0.009	0.014	0.509	344292	30686
rs1228024	11	47951353	A	C	0.660	-0.431	0.066	5.63E-11	-0.014	0.014	0.323	344292	31360
rs11663201	18	77218855	A	G	0.315	-0.440	0.067	5.41E-11	-0.021	0.015	0.146	344292	31378
rs11524285	9	136370101	T	C	0.790	0.502	0.077	5.86E-11	-0.020	0.017	0.244	344292	31397
rs6858114	4	77198465	A	G	0.377	0.423	0.064	4.63E-11	0.020	0.014	0.150	344292	31541
rs829577	2	30680450	G	C	0.242	-0.479	0.073	4.12E-11	-0.014	0.016	0.374	344292	31737
rs62120372	19	18305185	A	T	0.284	-0.457	0.069	3.98E-11	0.019	0.015	0.204	344292	31900
rs34310961	10	116623010	AT	A	0.399	0.425	0.064	2.61E-11	0.010	0.014	0.456	344292	32699
rs2911971	8	6607634	G	C	0.621	0.430	0.064	2.49E-11	0.011	0.014	0.456	344292	32799
rs11410326	10	64886721	CA	C	0.942	0.896	0.145	6.05E-10	0.056	0.032	0.079	344292	32995
rs9370260	6	53921674	C	T	0.691	-0.453	0.067	1.89E-11	0.013	0.015	0.371	344292	33004
rs10857127	4	129022203	T	C	0.601	-0.429	0.064	1.96E-11	-0.006	0.014	0.656	344292	33403

rs10932766	2	219122090	A	G	0.562	-0.424	0.063	1.65E-11	0.024	0.014	0.087	344292	33407
rs75460349	1	27180088	C	A	0.024	-1.399	0.208	1.83E-11	-0.057	0.046	0.211	344292	34240
rs12734494	1	211803881	A	G	0.494	0.427	0.063	1.08E-11	-0.010	0.014	0.476	344292	34453
rs2317749	3	101121980	G	A	0.625	0.442	0.065	7.80E-12	0.002	0.014	0.912	344292	34642
rs817355	20	62614338	G	A	0.487	-0.428	0.062	6.48E-12	-0.011	0.014	0.406	344292	34734
rs6685829	1	2330016	T	C	0.489	0.429	0.062	6.47E-12	0.006	0.014	0.669	344292	34824
rs6898290	5	158513546	C	T	0.427	0.437	0.063	3.90E-12	0.011	0.014	0.442	344292	35568
rs17429745	4	106038169	T	G	0.309	-0.469	0.068	4.53E-12	0.002	0.015	0.903	344292	35699
rs6457807	6	35142899	C	T	0.172	0.575	0.083	3.90E-12	0.011	0.018	0.546	344292	35746
rs10741694	11	16286183	C	T	0.628	0.451	0.065	2.78E-12	-0.007	0.014	0.644	344292	36200
rs252761	5	77380723	T	G	0.588	0.443	0.064	3.15E-12	0.001	0.014	0.918	344292	36250
rs3820897	2	3642361	C	T	0.820	-0.569	0.082	3.80E-12	-0.019	0.018	0.294	344292	36315

rs12921296	16	83972492	A	G	0.195	-0.553	0.081	1.01E-11	0.022	0.018	0.219	344292	36558
rs3577	20	39314670	A	G	0.152	-0.610	0.087	2.20E-12	-0.020	0.019	0.306	344292	36631
rs149363012	12	670520	T	C	0.026	1.376	0.195	1.54E-12	0.023	0.043	0.596	344292	37072
rs4835265	4	146821410	A	C	0.159	0.607	0.085	1.07E-12	-0.004	0.019	0.830	344292	37568
rs607407	1	234769499	A	C	0.674	0.474	0.067	1.65E-12	0.012	0.015	0.409	344292	37702
rs9611177	22	39840130	T	C	0.445	-0.451	0.064	1.34E-12	0.000	0.014	0.994	344292	38429
rs150231142	10	46132452	G	GA	0.320	-0.481	0.070	6.26E-12	-0.008	0.015	0.603	344292	38449
rs2495733	10	102339056	C	A	0.033	1.259	0.180	2.66E-12	-0.017	0.040	0.676	344292	38468
rs1559190	19	33856288	T	C	0.517	-0.450	0.062	5.27E-13	-0.019	0.014	0.168	344292	38796
rs933574	16	11792700	C	A	0.479	0.451	0.062	5.11E-13	0.002	0.014	0.858	344292	38875
rs5762665	22	28903360	G	A	0.621	0.467	0.064	3.98E-13	0.011	0.014	0.435	344292	39315
rs111833688	3	12173015	C	T	0.007	-2.730	0.379	5.99E-13	0.152	0.081	0.061	344292	39902

rs9400887	6	116421127	G	A	0.400	0.469	0.064	1.74E-13	0.007	0.014	0.639	344292	40581
rs559662	1	109634432	C	G	0.169	-0.613	0.083	2.06E-13	-0.017	0.018	0.348	344292	40612
rs7695508	4	111112610	G	A	0.339	-0.487	0.066	1.47E-13	0.018	0.014	0.200	344292	40900
rs445810	5	81731077	C	T	0.733	0.522	0.071	1.66E-13	-0.006	0.016	0.682	344292	41078
rs8006147	14	75430033	A	G	0.486	-0.464	0.063	1.37E-13	0.000	0.014	0.991	344292	41398
rs10464592	7	96230686	A	G	0.441	0.467	0.063	1.10E-13	0.007	0.014	0.593	344292	41494
rs12245237	10	26227401	T	C	0.071	-0.904	0.121	9.98E-14	-0.034	0.027	0.211	344292	41519
rs8017311	14	93105338	A	G	0.580	0.472	0.063	8.57E-14	-0.018	0.014	0.193	344292	41883
rs1391373	6	32603660	C	T	0.359	0.490	0.065	4.69E-14	-0.002	0.014	0.902	344292	42689
rs13013390	2	192126727	G	A	0.327	0.501	0.067	6.71E-14	0.000	0.015	0.987	344292	42856
rs140200746	9	104347086	T	C	0.010	-2.369	0.313	3.69E-14	-0.093	0.069	0.179	344292	43623
rs75406471	10	5257647	A	G	0.156	0.657	0.086	2.27E-14	0.012	0.019	0.525	344292	44123

rs1531022	4	69537154	A	G	0.475	-0.478	0.063	2.95E-14	0.012	0.014	0.375	344292	44199
rs114537356	1	22214279	A	C	0.021	1.688	0.219	1.23E-14	-0.011	0.048	0.821	344292	44983
rs15623	17	6978319	G	A	0.026	-1.521	0.199	2.40E-14	0.020	0.044	0.649	344292	45083
rs115536381	17	47957952	T	C	0.034	1.330	0.173	1.66E-14	0.060	0.038	0.113	344292	45146
rs113422695	7	107070208	A	T	0.229	-0.577	0.075	1.01E-14	-0.005	0.016	0.751	344292	45870
rs4233949	2	54659707	G	C	0.606	-0.501	0.064	5.23E-15	0.004	0.014	0.784	344292	46879
rs1180333	1	40020504	C	T	0.669	-0.521	0.066	3.55E-15	-0.023	0.015	0.117	344292	47087
rs4964193	12	107321748	T	C	0.503	-0.498	0.062	1.45E-15	-0.015	0.014	0.279	344292	48736
rs7996702	13	111108874	A	C	0.599	-0.513	0.064	7.33E-16	0.011	0.014	0.429	344292	49778
rs62183874	2	204106164	G	A	0.553	0.516	0.063	1.81E-16	-0.008	0.014	0.555	344292	52225
rs28570619	19	33517152	A	G	0.043	1.266	0.153	1.32E-16	0.004	0.033	0.903	344292	52848
rs145270291	1	20771550	A	G	0.004	-4.056	0.505	1.01E-15	0.159	0.110	0.146	344292	53037

rs62158846	2	113864010	T	G	0.384	0.535	0.065	1.21E-16	-0.004	0.014	0.765	344292	53901
rs10864086	1	214318748	A	C	0.743	-0.598	0.072	6.62E-17	0.004	0.016	0.821	344292	54402
rs10840139	11	8894838	G	T	0.154	0.724	0.086	5.02E-17	-0.016	0.019	0.399	344292	54444
rs115276619	1	184865132	A	T	0.017	-2.032	0.250	3.94E-16	-0.067	0.055	0.223	344292	54734
rs71378928	17	66464546	G	C	0.781	-0.639	0.075	2.69E-17	0.006	0.017	0.729	344292	55826
rs754465	10	79680514	A	C	0.596	0.552	0.063	3.32E-18	0.021	0.014	0.135	344292	59273
rs10894808	11	134256805	T	C	0.128	0.814	0.093	2.27E-18	0.025	0.021	0.227	344292	59781
rs182611493	19	19458388	G	A	0.012	-2.462	0.300	2.29E-16	0.006	0.066	0.933	344292	60321
rs603424	10	102075479	A	G	0.168	-0.731	0.083	1.80E-18	0.008	0.018	0.655	344292	60381
rs80584	22	36555794	T	C	0.829	0.732	0.083	8.81E-19	-0.015	0.018	0.395	344292	61795
rs115860811	1	22432154	C	G	0.018	-2.080	0.235	8.13E-19	-0.040	0.052	0.445	344292	63403
rs114114097	1	22072751	C	G	0.020	2.020	0.225	3.17E-19	-0.002	0.050	0.963	344292	64815

rs56188865	1	247606276	C	T	0.370	-0.587	0.065	1.11E-19	-0.020	0.014	0.150	344292	66041
rs28568483	2	199216941	T	C	0.646	0.605	0.065	1.89E-20	0.005	0.014	0.719	344292	69101
rs4788808	16	71615613	T	C	0.522	-0.585	0.062	6.71E-21	-0.020	0.014	0.142	344292	70872
rs2460383	2	135014126	C	T	0.772	-0.697	0.075	9.21E-21	0.008	0.016	0.639	344292	71109
rs4503880	18	56084054	C	T	0.799	-0.732	0.078	6.16E-21	0.002	0.017	0.928	344292	71625
rs2239222	14	73011885	G	A	0.349	-0.626	0.066	1.77E-21	-0.024	0.014	0.102	344292	74619
rs1428967	5	36646915	G	A	0.236	0.720	0.073	1.08E-22	0.008	0.016	0.618	344292	79145
rs2070863	17	1648502	T	C	0.219	-0.740	0.075	8.53E-23	0.013	0.017	0.415	344292	79325
rs2207132	20	39142516	A	G	0.033	1.731	0.175	3.51E-23	0.028	0.038	0.459	344292	81207
rs72775768	9	139327143	T	C	0.290	0.686	0.069	3.12E-23	0.026	0.015	0.088	344292	82698
rs6580945	12	53698874	T	G	0.649	0.654	0.065	1.82E-23	0.005	0.014	0.711	344292	83168
rs7697204	4	148985104	T	C	0.743	0.748	0.071	1.01E-25	-0.002	0.016	0.906	344292	93529

rs598710	12	111975163	C	A	0.203	-0.814	0.078	9.21E-26	-0.005	0.017	0.788	344292	94091
rs62621812	7	127015083	A	G	0.020	-2.384	0.227	8.57E-26	-0.049	0.050	0.325	344292	101101
rs665632	13	43106514	C	T	0.187	0.885	0.080	4.01E-28	0.024	0.018	0.179	344292	107651
rs2934956	17	37830447	A	T	0.684	-0.755	0.067	2.50E-29	-0.026	0.015	0.073	344292	112337
rs112345326	1	22151854	A	G	0.017	-2.773	0.250	1.31E-28	-0.044	0.055	0.427	344292	122992
rs41282145	9	104249507	A	T	0.022	2.470	0.216	2.66E-30	0.027	0.048	0.567	344292	126083
rs4742108	9	5632130	T	G	0.294	0.812	0.068	1.47E-32	-0.017	0.015	0.248	344292	129755
rs72636979	11	296675	A	G	0.036	2.006	0.170	3.20E-32	0.015	0.037	0.694	344292	132952
rs11217000	11	118606521	G	A	0.216	-0.927	0.076	7.00E-34	-0.015	0.017	0.375	344292	141579
rs67358277	11	126251650	G	A	0.151	-1.083	0.088	1.32E-34	-0.007	0.019	0.732	344292	147941
rs884205	18	60054857	C	A	0.747	-0.936	0.072	1.86E-38	-0.014	0.016	0.380	344292	170434
rs2682362	1	21688141	C	T	0.677	0.886	0.068	2.64E-39	0.019	0.015	0.195	344292	180242

rs2298058	13	95248566	T	C	0.305	0.904	0.068	1.23E-40	0.003	0.015	0.816	344292	182849
rs78221767	10	104004653	G	T	0.068	-1.687	0.123	1.39E-42	-0.002	0.027	0.942	344292	196245
rs11601507	11	5701074	A	C	0.068	1.749	0.122	8.78E-47	0.013	0.027	0.624	344292	220022
rs201106207	2	169859883	C	CAA	0.036	-2.375	0.167	4.38E-46	-0.033	0.036	0.362	344292	225099
rs3829888	2	169888842	G	A	0.037	-2.409	0.166	8.31E-48	-0.023	0.036	0.533	344292	240822
rs60537291	6	24273461	C	T	0.127	-1.376	0.094	7.65E-49	-0.005	0.021	0.797	344292	248617
rs6831352	4	100063525	C	T	0.698	-0.999	0.068	6.08E-49	-0.010	0.015	0.508	344292	250040
rs3865454	19	41342459	G	T	0.665	-1.101	0.066	1.98E-62	0.007	0.014	0.622	344292	403740
rs174564	11	61588305	G	A	0.350	1.099	0.065	1.96E-63	0.023	0.014	0.115	344292	419930
rs4575545	16	79755446	A	G	0.307	1.139	0.068	2.28E-63	-0.013	0.015	0.377	344292	425114
rs2183745	9	104219175	A	T	0.674	-1.122	0.067	1.29E-62	-0.002	0.015	0.880	344292	426424
rs62059198	17	7220697	T	G	0.340	1.112	0.066	9.79E-64	0.012	0.015	0.423	344292	428950

rs6469788	8	119952750	C	A	0.542	1.072	0.063	1.12E-65	-0.004	0.014	0.766	344292	458034
rs1077889	20	25267893	G	A	0.443	-1.103	0.063	2.82E-69	0.008	0.014	0.583	344292	516315
rs6925475	6	24454679	A	G	0.141	-1.580	0.090	2.38E-69	0.003	0.020	0.870	344292	528178
rs3094324	9	136350150	C	T	0.720	1.250	0.069	9.02E-73	0.011	0.015	0.459	344292	588141
rs9533094	13	42965837	G	A	0.489	1.177	0.062	1.56E-79	0.011	0.014	0.428	344292	773384
rs7966590	12	570840	A	G	0.582	1.233	0.063	8.24E-85	-0.010	0.014	0.491	344292	974980

Supplemental Table 4 Pleiotropy and heterogeneity test of the mendelian randomization study.

Exposure	Outcome	Pleiotropy test				Heterogeneity test					
		MR Egger			PRESSO	MR Egger			IVW		
		Intercept	SE	P	P	Q	Q_df	Q_ P	Q	Q_df	Q_ P
ukb-d-30610_raw	ieu-b-4980	-0.0001	0.0028	0.9658	0.9999	125.5396	182	0.9995	125.5414	183	0.9996