

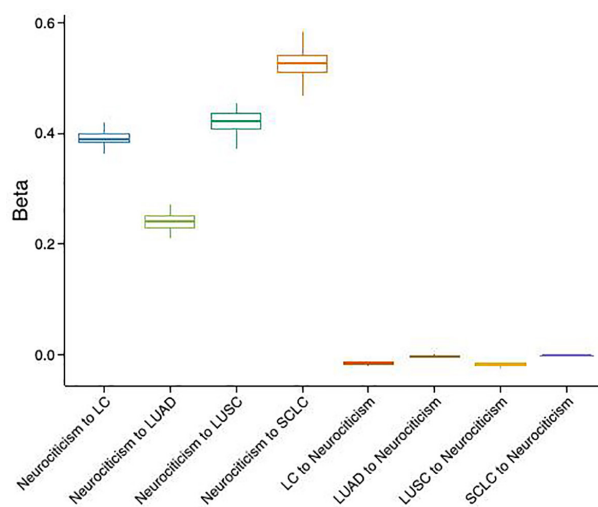


Figure S1 Box plot of the leave-one-out analysis. Each SNP was systematically removed at a time, and IVW analysis was performed using the remaining SNPs. Beta, effect allele beta coefficient; IVW, inverse-variance weighted; LC, lung cancer; LUAD, lung adenocarcinoma; LUSC, lung squamous cell carcinoma; SCLC, small-cell lung cancer; SNP, single nucleotide polymorphism.

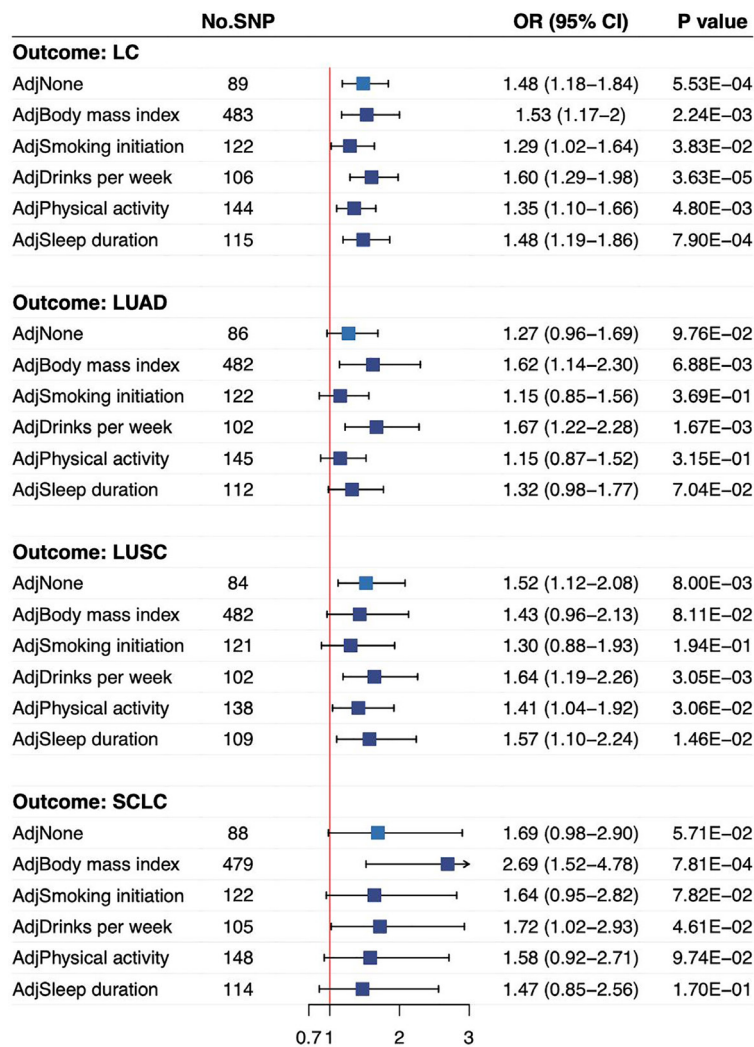


Figure S2 MVMR of genetically predicted neuroticism on LC. The estimated effect sizes were adjusted for each potential confounder separately. The y-axis indicates the genetically predicted confounder for which adjustment was made. “adjNone” refers to the point estimates of the causal effects of genetically predicted neuroticism on LC using univariable MR. CI, confidence interval; LC, lung cancer; LUAD, lung adenocarcinoma; LUSC, lung squamous cell carcinoma; MR, Mendelian randomization; MVMR, multivariable Mendelian randomization; OR, odds ratio; SCLC, small-cell lung cancer; SNP, single nucleotide polymorphism.

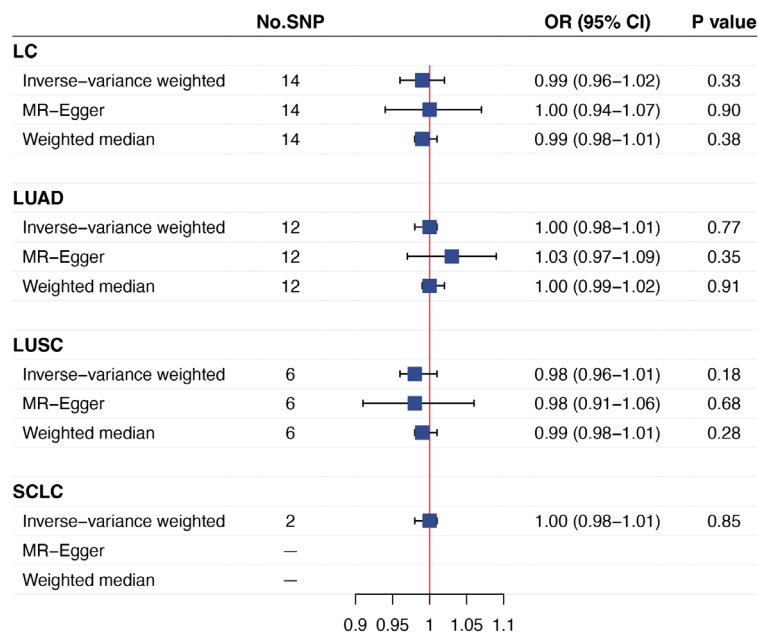


Figure S3 Estimates of causal effect sizes of LC on neuroticism using all LC-associated SNPs. IVW approach was used as the primary outcome, while MR-Egger and weighted median were applied as complementary analyses. CI, confidence interval; IVW, inverse-variance weighted; LC, lung cancer; LUAD, lung adenocarcinoma; LUSC, lung squamous cell carcinoma; MR, Mendelian randomization; OR, odds ratio; SCLC, small-cell lung cancer; SNP, single nucleotide polymorphism.

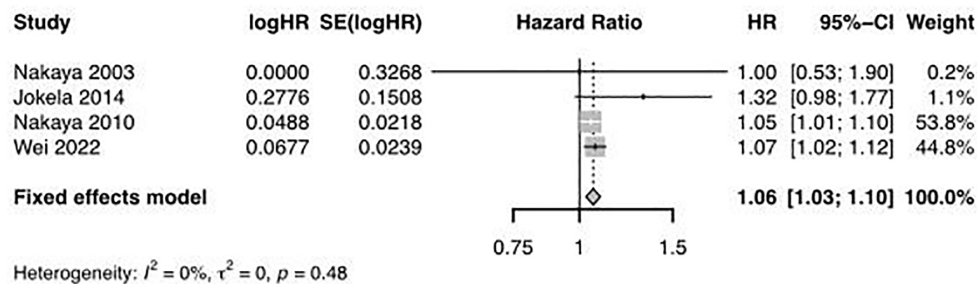


Figure S4 Forest plot of pooled risk of incident LC with neuroticism. Square represents the estimate of rate ratio for each study, with the size of square representing the weight of each study with respect to the overall estimate; horizontal line represents the 95% CIs, and diamond represents the overall estimate and its 95% CIs. CI, confidence interval; HR, hazard ratio; LC, lung cancer; SE, standard error.

Table S1 Genome-wide genetic correlations between neuroticism and LC

Trait 1	Trait 2	Unconstrained LDSC			Constrained LDSC		
		r_g	SE	P value	r_g	SE	P value
Neuroticism	Overall LC	0.15	0.04	2.24×10^{-5}	0.1	0.02	6.20×10^{-7}
	LUAD	0.07	0.04	0.085	0.05	0.02	3.28×10^{-2}
	LUSC	0.21	0.05	3.39×10^{-6}	0.13	0.02	1.38×10^{-7}
	SCLC	0.16	0.05	2.50×10^{-3}	0.12	0.03	1.72×10^{-5}

LC, lung cancer; LUAD, lung adenocarcinoma; LUSC, lung squamous cell carcinoma; SCLC, small-cell lung cancer; SE, standard error.

Table S2 Partitioned genetic correlation between neuroticism and LC

Phenotypes	Functional category	r_g	SE	P value
Neuroticism_LC	Conserved	0.1410	0.0644	0.0285
	DGF	0.1588	0.0454	0.0005
	DHS	0.1492	0.0412	0.0003
	Fetal DHS	0.1770	0.0460	0.0001
	H3K4me1	0.1745	0.0426	<0.0001
	H3K4me3	0.1890	0.0521	0.0003
	H3K9ac	0.2573	0.0877	0.0033
	H3K27ac	0.2462	0.0901	0.0063
	Promotor	0.1032	0.0738	0.1616
	TFBS	0.1693	0.0525	0.0012
	Transcribed	0.1346	0.0493	0.0064
Neuroticism_LUAD	Conserved	0.1157	0.0698	0.0975
	DGF	0.1356	0.0517	0.0087
	DHS	0.0986	0.0448	0.0279
	Fetal DHS	0.1311	0.0500	0.0087
	H3K4me1	0.1357	0.0488	0.0055
	H3K4me3	0.1395	0.0600	0.0201
	H3K9ac	0.1610	0.1012	0.1115
	H3K27ac	0.1681	0.1158	0.1465
	Promotor	0.0416	0.0937	0.6573
	TFBS	0.1422	0.0592	0.0163
	Transcribed	0.1063	0.0542	0.0496
Neuroticism_LUSC	Conserved	0.1304	0.0879	0.1379
	DGF	0.1501	0.0564	0.0078
	DHS	0.1545	0.0553	0.0052
	Fetal DHS	0.1773	0.0523	0.0007
	H3K4me1	0.1467	0.0505	0.0037
	H3K4me3	0.2044	0.0663	0.0020
	H3K9ac	0.2634	0.1071	0.0140
	H3K27ac	0.1769	0.1132	0.1183
	Promotor	0.0902	0.0873	0.3012
	TFBS	0.1526	0.0523	0.0035
	Transcribed	0.1529	0.0613	0.0126

Table S2 (continued)

Table S2 (*continued*)

Phenotypes	Functional category	r_g	SE	P value
Neuroticism_SCLC	Conserved	0.1308	0.0690	0.0581
	DGF	0.0563	0.0721	0.4349
	DHS	0.1151	0.0610	0.0590
	Fetal DHS	0.1276	0.0586	0.0295
	H3K4me1	0.0504	0.0576	0.3814
	H3K4me3	0.0842	0.0877	0.3367
	H3K9ac	0.0657	0.1505	0.6627
	H3K27ac	0.0318	0.1478	0.8299
	Promotor	0.0256	0.1369	0.8515
	TFBS	0.0663	0.0621	0.2857
	Transcribed	0.0403	0.0662	0.5424

DGF, DNase I digital genomic footprinting; DHS, DNase I hypersensitive sites; LC, lung cancer; LUAD, lung adenocarcinoma; LUSC, lung squamous cell carcinoma; SCLC, small-cell lung cancer; SE, standard error; TFBS, transcription factor-binding sites.

Table S3 Results from colocalization analysis for each pleiotropic locus

Index SNP	Chromosome	BP	Neuroticism		LC		P _{CPASSOC}	PP.H3.abf	PP.H4.abf
			Beta	P value	Beta	P value			
Neuroticism and LC									
rs6545684	2	58740603	0.0162	2.06E−08	0.0516	5.40E−04	8.12E−10	0.07	0.42
rs1043618	6	31783507	−0.0115	9.88E−07	0.0471	9.38E−05	3.55E−08	1.00	0.00
rs13213152	6	28349698	0.0193	1.71E−07	−0.1463	5.58E−12	8.32E−12	0.25	0.75
rs148696809	6	28934352	0.0188	2.21E−07	−0.1459	2.57E−12	3.71E−12	0.04	0.96
rs2523573	6	31328988	0.0147	1.06E−05	−0.1572	3.18E−17	2.70E−17	0.04	0.96
rs2769345	6	167366394	0.0111	1.72E−06	−0.0633	9.55E−08	1.07E−08	0.20	0.78
rs501942	6	31840477	−0.0171	8.38E−07	0.1699	8.40E−19	5.94E−19	1.00	0.00
rs6456701	6	25774130	0.0126	6.14E−04	−0.1177	1.77E−08	3.64E−08	0.95	0.04
rs12903078	15	47503469	0.0129	3.54E−08	0.0606	3.17E−07	1.39E−10	0.10	0.90
Neuroticism and LUAD									
rs1150753	6	32059867	0.0177	3.91E−07	−0.1003	2.69E−04	3.76E−08	0.16	0.49
rs2854275	6	32628428	−0.0171	1.64E−07	0.1009	8.58E−04	1.96E−08	0.06	0.67
rs113661667	17	43791610	−0.0323	3.74E−31	0.0740	2.77E−04	3.44E−34	0.11	0.60
rs916888	17	44863133	−0.0263	1.37E−22	0.0692	3.50E−04	5.86E−25	0.01	0.84
Neuroticism and LUSC									
rs13201782	6	26651053	−0.0173	4.59E−06	0.1996	1.62E−08	8.66E−09	0.28	0.71
rs13213986	6	28358009	−0.0193	1.72E−07	0.2225	6.88E−11	1.78E−11	0.16	0.84
rs148696809	6	28934352	0.0188	2.21E−07	−0.2213	3.77E−11	8.97E−12	0.04	0.96
rs2853999	6	31326074	0.0147	1.06E−05	−0.2458	3.51E−16	1.64E−17	0.04	0.96
rs36109883	6	26133070	−0.0171	1.39E−05	0.2537	6.16E−12	1.14E−12	0.94	0.06
rs4713570	6	32626040	−0.0113	1.44E−05	0.1424	2.04E−08	1.12E−08	0.31	0.61
rs501942	6	31840477	−0.0171	8.38E−07	0.2604	3.06E−17	1.00E−18	1.00	0.00
rs707938	6	31729359	0.0135	3.34E−08	−0.0720	3.35E−04	6.56E−10	1.00	0.00
rs1327938	13	59833252	−0.0127	2.49E−07	−0.0709	3.52E−04	7.63E−09	0.23	0.46
Neuroticism and SCLC									
rs4530683	4	139053569	−0.0129	3.43E−08	−0.1038	5.60E−04	1.59E−08	0.08	0.66
rs12903078	15	47503469	0.0129	3.54E−08	0.1052	4.50E−04	1.61E−08	0.08	0.84

LC, lung cancer.

Table S4 TWAS-identified shared gene-tissue pairs between neuroticism and LC

Gene	Tissue type	CHR	SNP. Num	Neuroticism				LC			
				BEST. GWAS.ID	BEST. GWAS.Z	TWAS.P	FDR	BEST. GWAS.ID	BEST. GWAS.Z	TWAS.P	FDR
<i>CATSPER2</i>	Muscle_Skeletal	15	256	rs12912505	-4.02	3.13E-04	3.14E-02	rs8040336	-4.38	1.32E-03	2.31E-02
<i>CCDC9B</i>	Minor_Salivary_ Gland	15	390	rs1453184	-3.28	1.40E-03	3.28E-02	rs1992272	-3.99	2.03E-04	3.96E-03
<i>CCR6</i>	Esophagus_Mucosa	6	540	rs7749278	4.74	1.73E-06	2.75E-04	rs239935	5.69	6.34E-07	8.03E-05
<i>CEP43</i>	Adipose_Visceral_ Omentum	6	631	rs7749278	4.74	6.02E-05	4.06E-03	rs239935	5.69	4.39E-05	5.07E-03
	Adrenal_Gland	6	626	rs7749278	4.74	6.24E-06	1.37E-03	rs239935	5.69	3.28E-05	5.90E-03
	Colon_Sigmoid	6	631	rs7749278	4.74	2.15E-05	1.82E-03	rs239935	5.69	2.03E-05	5.14E-03
	Esophagus_Mucosa	6	630	rs7749278	4.74	2.17E-06	2.75E-04	rs239935	5.69	4.19E-07	8.03E-05
	Heart_Atrial_ Appendage	6	626	rs7749278	4.74	4.63E-06	4.77E-04	rs239935	5.69	5.24E-06	1.61E-03
	Heart_Left_Ventricle	6	631	rs7749278	4.74	2.40E-06	6.22E-04	rs239935	5.69	1.03E-06	2.67E-04
	Lung	6	631	rs7749278	4.74	1.29E-05	2.80E-03	rs239935	5.69	7.26E-06	1.31E-03
	Muscle_Skeletal	6	631	rs7749278	4.74	2.24E-06	8.31E-04	rs239935	5.69	1.52E-07	2.82E-05
	Skin_Not_Sun_ Exposed_Suprapubic	6	626	rs7749278	4.74	2.56E-06	4.32E-04	rs239935	5.69	3.57E-07	7.09E-05
	Skin_Sun_Exposed_ Lower_leg	6	626	rs7749278	4.74	1.70E-06	4.06E-04	rs239935	5.69	8.84E-08	3.83E-05
	Thyroid	6	631	rs7749278	4.74	2.39E-06	6.10E-04	rs239935	5.69	3.40E-06	7.91E-04
<i>CLN8-AS1</i>	Brain_Spinal_cord_ cervical_c-1	8	727	rs3812479	-4.89	2.90E-03	4.24E-02	rs4876082	4.43	7.16E-05	7.80E-03
<i>DDX6</i>	Artery_Tibial	11	362	rs7933963	3.90	1.27E-03	3.05E-02	rs4938499	-4.51	7.09E-04	4.33E-02
	Brain_Cortex	11	363	rs7933963	3.90	9.39E-04	1.50E-02	rs4938499	-4.51	5.13E-04	4.74E-02
	Esophagus_ Muscularis	11	363	rs7933963	3.90	2.96E-03	3.78E-02	rs4938499	-4.51	3.22E-04	4.05E-02
	Liver	11	363	rs7933963	3.90	2.22E-03	2.23E-02	rs4938499	-4.51	3.79E-04	1.68E-02
	Stomach	11	361	rs7933963	3.90	1.27E-03	2.80E-02	rs4938499	-4.51	7.09E-04	4.07E-02
<i>DVL3</i>	Small_Intestine_ Terminal_Ileum	3	488	rs12488922	-3.79	1.32E-03	2.32E-02	rs7371826	-3.84	2.43E-04	4.69E-02
<i>EFNA3</i>	Heart_Atrial_ Appendage	1	373	rs4845681	4.09	3.20E-04	1.76E-02	rs2990245	-4.52	5.31E-06	1.75E-03
<i>MED19</i>	Heart_Atrial_ Appendage	11	386	rs7117205	6.20	2.63E-09	2.49E-07	rs11229042	-4.88	6.28E-04	4.77E-02
	Heart_Left_Ventricle	11	386	rs7117205	6.20	2.31E-09	2.53E-07	rs11229042	-4.88	7.02E-04	3.15E-02

Table S4 (continued)

Table S4 (continued)

Gene	Tissue type	CHR	SNP. Num	Neuroticism				LC			
				BEST. GWAS.ID	BEST. GWAS.Z	TWAS.P	FDR	BEST. GWAS.ID	BEST. GWAS.Z	TWAS.P	FDR
<i>RNASET2</i>	Adipose_Subcutaneous	6	684	rs7749278	4.74	3.91E-05	5.47E-03	rs239935	5.69	1.14E-06	4.79E-04
	Adipose_Visceral_Omentum	6	684	rs7749278	4.74	3.67E-05	3.72E-03	rs239935	5.69	8.62E-07	2.89E-04
	Brain_Cerebellar_Hemisphere	6	678	rs7749278	4.74	4.73E-05	7.25E-03	rs239935	5.69	4.77E-05	5.99E-03
	Brain_Cerebellum	6	683	rs7749278	4.74	7.01E-05	6.40E-03	rs239935	5.69	5.30E-05	1.45E-02
	Brain_Nucleus_accumbens_basal_ganglia	6	683	rs7749278	4.74	1.05E-03	3.76E-02	rs239935	5.69	8.95E-07	1.92E-04
	Cells_Cultured_fibroblasts	6	680	rs7749278	4.74	5.68E-06	6.16E-04	rs239935	5.69	1.22E-07	5.28E-05
	Esophagus_Mucosa	6	683	rs7749278	4.74	4.58E-06	4.35E-04	rs239935	5.69	4.40E-07	8.03E-05
	Heart_Atrial_Appendage	6	679	rs7749278	4.74	1.48E-04	8.12E-03	rs239935	5.69	3.24E-05	4.99E-03
	Lung	6	684	rs7749278	4.74	2.67E-05	3.21E-03	rs239935	5.69	2.49E-07	8.96E-05
	Muscle_Skeletal	6	684	rs7749278	4.74	5.46E-06	1.01E-03	rs239935	5.69	3.53E-08	1.31E-05
	Nerve_Tibial	6	684	rs7749278	4.74	5.50E-06	1.35E-03	rs239935	5.69	3.36E-08	1.64E-05
	Pancreas	6	678	rs7749278	4.74	4.57E-06	1.12E-03	rs239935	5.69	3.84E-08	9.45E-06
	Skin_Not_Sun_Exposed_Suprapubic	6	679	rs7749278	4.74	2.42E-06	4.32E-04	rs239935	5.69	7.52E-08	2.99E-05
	Skin_Sun_Exposed_Lower_leg	6	679	rs7749278	4.74	2.94E-06	4.42E-04	rs239935	5.69	1.70E-07	3.83E-05
	Small_Intestine_Terminal_Ileum	6	684	rs7749278	4.74	1.33E-05	2.05E-03	rs239935	5.69	6.29E-07	9.69E-05
	Thyroid	6	684	rs7749278	4.74	2.62E-06	6.10E-04	rs239935	5.69	2.31E-08	1.07E-05
	Whole_Blood	6	684	rs7749278	4.74	1.13E-05	9.18E-04	rs239935	5.69	3.76E-08	4.05E-06
<i>SEMA6D</i>	Brain_Cerebellum	15	419	rs1563245	5.44	4.23E-04	2.58E-02	rs7165678	5.43	7.97E-07	4.86E-05
<i>SERPING1</i>	Thyroid	11	386	rs7117205	6.20	6.34E-08	4.91E-06	rs11229042	-4.88	1.59E-04	2.47E-02
	Whole_Blood	11	386	rs7117205	6.20	8.84E-10	1.02E-07	rs11229042	-4.88	1.87E-04	2.16E-02
<i>SKOR1</i>	Heart_Atrial_Appendage	15	350	rs4489954	4.40	8.36E-05	1.15E-02	rs1001870	-3.65	9.09E-04	2.08E-02
<i>SLC17A1</i>	Pituitary	6	654	rs198825	-5.75	9.00E-08	2.26E-05	rs2393592	6.48	2.50E-07	6.25E-05
<i>SLC17A4</i>	Pancreas	6	648	rs198825	-5.75	9.70E-05	7.95E-03	rs10946808	-5.97	1.66E-04	1.02E-02

Table S4 (continued)

Table S4 (*continued*)

Gene	Tissue type	CHR	SNP. Num	Neuroticism				LC			
				BEST. GWAS.ID	BEST. GWAS.Z	TWAS.P	FDR	BEST. GWAS.ID	BEST. GWAS.Z	TWAS.P	FDR
<i>SYT13</i>	Liver	11	554	rs8929	-5.23	3.78E-04	4.91E-03	rs751198	3.82	3.07E-04	1.68E-02
	Skin_Not_Sun_ Exposed_Suprapubic	11	556	rs8929	-5.23	2.81E-04	8.68E-03	rs751198	3.82	1.32E-04	1.87E-02
	Skin_Sun_Exposed_ Lower_leg	11	553	rs8929	-5.23	3.42E-04	9.70E-03	rs751198	3.82	1.16E-04	2.35E-02
<i>TMX2</i>	Nerve_Tibial	11	386	rs7117205	6.20	1.01E-09	2.16E-07	rs11229042	-4.88	1.49E-04	2.53E-02
<i>TTC36</i>	Esophagus_ Muscularis	11	444	rs7933963	3.90	2.79E-03	3.66E-02	rs1629083	-5.69	2.34E-04	3.99E-02
<i>YIPF4</i>	Artery_Aorta	2	314	rs2276592	4.30	1.73E-03	4.03E-02	rs458628	4.16	2.69E-05	6.16E-03
<i>ZDHHC5</i>	Artery_Aorta	11	393	rs7117205	6.20	1.29E-09	2.92E-07	rs11229042	-4.88	4.78E-04	4.39E-02
	Heart_Atrial_ Appendage	11	393	rs7117205	6.20	6.97E-10	1.10E-07	rs11229042	-4.88	1.82E-04	3.46E-02
	Heart_Left_Ventricle	11	393	rs7117205	6.20	1.29E-09	2.12E-07	rs11229042	-4.88	4.78E-04	2.62E-02
	Spleen	11	393	rs7117205	6.20	4.85E-10	8.17E-08	rs11229042	-4.88	6.48E-04	4.62E-02

LC, lung cancer.

Table S5 TWAS-identified shared gene-tissue pairs between neuroticism and LUAD

Gene	Tissue type	CHR	SNP Num	Neuroticism				LUAD			
				BEST. GWAS.ID	BEST. GWAS.Z	TWAS.P	FDR	BEST. GWAS.ID	BEST. GWAS.Z	TWAS.P	FDR
<i>ARHGAP27</i>	Cells_EBV-transformed_lymphocytes	17	180	rs8072451	11.63	9.30E-31	3.16E-29	rs173365	-3.42	2.26E-03	4.15E-02
<i>CCR6</i>	Esophagus_Mucosa	6	540	rs7749278	4.74	1.73E-06	2.75E-04	rs408918	4.22	1.27E-04	1.60E-02
<i>CEP43</i>	Esophagus_Mucosa	6	630	rs7749278	4.74	2.17E-06	2.75E-04	rs408918	4.22	2.94E-05	5.57E-03
	Heart_Left_Ventricle	6	631	rs7749278	4.74	2.40E-06	6.22E-04	rs408918	4.22	1.12E-04	1.45E-02
	Muscle_Skeletal	6	631	rs7749278	4.74	2.24E-06	8.31E-04	rs408918	4.22	9.64E-06	1.78E-03
	Skin_Not_Sun_Exposed_Suprapubic	6	626	rs7749278	4.74	2.56E-06	4.32E-04	rs408918	4.22	3.98E-05	8.16E-03
	Skin_Sun_Exposed_Lower_leg	6	626	rs7749278	4.74	1.70E-06	4.06E-04	rs408918	4.22	3.88E-05	8.75E-03
<i>CRHR1</i>	Thyroid	6	631	rs7749278	4.74	2.39E-06	6.10E-04	rs408918	4.22	2.18E-04	2.53E-02
	Brain_Spinal_cord_cervical_c-1	17	33	rs8072451	11.63	8.46E-30	2.43E-28	rs173365	-3.42	9.32E-04	4.61E-02
<i>IRF4</i>	Kidney_Cortex	17	33	rs8072451	11.63	1.33E-30	1.77E-29	rs173365	-3.42	2.12E-03	2.50E-02
	Whole_Blood	6	420	rs12203592	4.63	3.57E-06	5.80E-04	rs1050976	4.26	1.17E-04	9.51E-03
<i>KANSL1-AS1</i>	Brain_Hippocampus	17	29	rs8072451	11.63	7.82E-31	3.24E-29	rs173365	-3.42	1.98E-03	4.95E-02
	Brain_Spinal_cord_cervical_c-1	17	28	rs8072451	11.63	8.80E-31	3.56E-29	rs173365	-3.42	2.23E-03	4.61E-02
	Brain_Substantia_nigra	17	29	rs8072451	11.63	2.55E-31	2.67E-29	rs173365	-3.42	1.22E-03	3.72E-02
	Cells_EBV-transformed_lymphocytes	17	28	rs8072451	11.63	7.83E-31	3.16E-29	rs173365	-3.42	1.98E-03	4.15E-02
	Kidney_Cortex	17	28	rs8072451	11.63	8.84E-31	1.41E-29	rs173365	-3.42	2.19E-03	2.50E-02
	Small_Intestine_Terminal_Ileum	17	28	rs8072451	11.63	7.82E-31	2.56E-29	rs173365	-3.42	1.97E-03	4.62E-02
	Uterus	17	28	rs8072451	11.63	8.84E-31	2.81E-29	rs173365	-3.42	2.19E-03	3.33E-02
<i>LINC02210</i>	Vagina	17	29	rs8072451	11.63	7.82E-31	2.20E-29	rs173365	-3.42	1.97E-03	4.05E-02
	Brain_Spinal_cord_cervical_c-1	17	89	rs8072451	11.63	1.60E-30	5.36E-29	rs173365	-3.42	2.77E-03	4.61E-02
	Brain_Substantia_nigra	17	92	rs8072451	11.63	7.82E-31	2.67E-29	rs173365	-3.42	1.97E-03	3.72E-02
	Cells_EBV-transformed_lymphocytes	17	89	rs8072451	11.63	7.82E-31	3.16E-29	rs173365	-3.42	1.98E-03	4.15E-02
	Kidney_Cortex	17	89	rs8072451	11.63	7.82E-31	1.41E-29	rs173365	-3.42	1.97E-03	2.50E-02
	Small_Intestine_Terminal_Ileum	17	89	rs8072451	11.63	8.84E-31	2.56E-29	rs173365	-3.42	2.19E-03	4.62E-02
	Vagina	17	90	rs8072451	11.63	8.84E-31	2.20E-29	rs173365	-3.42	2.19E-03	4.05E-02
<i>LRRC37A</i>	Kidney_Cortex	17	75	rs8072451	11.63	6.78E-15	4.93E-14	rs173365	-3.42	4.15E-03	3.69E-02

Table S5 (continued)

Table S5 (continued)

Gene	Tissue type	CHR	SNP. Num	Neuroticism				LUAD			
				BEST. GWAS.ID	BEST. GWAS.Z	TWAS.P	FDR	BEST. GWAS.ID	BEST. GWAS.Z	TWAS.P	FDR
MAPK8IP1P1	Brain_Hippocampus	17	58	rs8072451	11.63	1.16E-29	3.19E-28	rs173365	-3.42	1.68E-03	4.95E-02
	Brain_Spinal_cord_ cervical_c-1	17	56	rs8072451	11.63	3.25E-28	6.53E-27	rs173365	-3.42	1.97E-03	4.61E-02
	Brain_Substantia_nigra	17	59	rs8072451	11.63	1.81E-30	3.90E-29	rs173365	-3.42	2.22E-03	3.72E-02
	Kidney_Cortex	17	55	rs8072451	11.63	8.63E-27	8.63E-26	rs173365	-3.42	2.99E-03	2.99E-02
	Small_Intestine_ Terminal_Ileum	17	55	rs8072451	11.63	7.82E-31	2.56E-29	rs173365	-3.42	1.97E-03	4.62E-02
	Uterus	17	56	rs8072451	11.63	1.57E-30	3.67E-29	rs173365	-3.42	1.92E-03	3.33E-02
	Vagina	17	58	rs8072451	11.63	4.14E-27	7.71E-26	rs173365	-3.42	2.01E-03	4.05E-02
MAPT	Uterus	17	30	rs8072451	11.63	1.68E-30	3.67E-29	rs173365	-3.42	1.48E-03	3.33E-02
MAPT-IT1	Brain_Substantia_nigra	17	31	rs8072451	11.63	1.70E-30	3.90E-29	rs173365	-3.42	1.21E-03	3.72E-02
MMS22L	Prostate	6	332	rs9400737	-4.29	2.41E-04	1.87E-02	rs213861	-3.7	2.36E-04	2.01E-02
	Adipose_Subcutaneous	6	684	rs7749278	4.74	3.91E-05	5.47E-03	rs408918	4.22	1.02E-05	2.14E-03
	Adipose_Visceral_ Omentum	6	684	rs7749278	4.74	3.67E-05	3.72E-03	rs408918	4.22	2.38E-06	3.99E-04
	Brain_Cerebellar_ Hemisphere	6	678	rs7749278	4.74	4.73E-05	7.25E-03	rs408918	4.22	2.76E-05	6.93E-03
	Brain_Cerebellum	6	683	rs7749278	4.74	7.01E-05	6.40E-03	rs408918	4.22	2.99E-05	8.16E-03
	Brain_Nucleus_ accumbens_basal_ ganglia	6	683	rs7749278	4.74	1.05E-03	3.76E-02	rs408918	4.22	9.89E-06	2.13E-03
	Cells_Cultured_ fibroblasts	6	680	rs7749278	4.74	5.68E-06	6.16E-04	rs408918	4.22	4.88E-05	2.11E-02
	Esophagus_Mucosa	6	683	rs7749278	4.74	4.58E-06	4.35E-04	rs408918	4.22	1.30E-05	4.93E-03
	Lung	6	684	rs7749278	4.74	2.67E-05	3.21E-03	rs408918	4.22	1.23E-05	2.21E-03
	Muscle_Skeletal	6	684	rs7749278	4.74	5.46E-06	1.01E-03	rs408918	4.22	1.96E-05	2.42E-03
	Nerve_Tibial	6	684	rs7749278	4.74	5.50E-06	1.35E-03	rs408918	4.22	2.84E-05	6.94E-03
	Pancreas	6	678	rs7749278	4.74	4.57E-06	1.12E-03	rs408918	4.22	2.04E-05	2.51E-03
	Skin_Not_Sun_ Exposed_Suprapubic	6	679	rs7749278	4.74	2.42E-06	4.32E-04	rs408918	4.22	4.12E-05	8.16E-03
	Skin_Sun_Exposed_ Lower_leg	6	679	rs7749278	4.74	2.94E-06	4.42E-04	rs408918	4.22	2.19E-05	8.75E-03
	Small_Intestine_ Terminal_Ileum	6	684	rs7749278	4.74	1.33E-05	2.05E-03	rs408918	4.22	7.93E-06	6.11E-04
	Thyroid	6	684	rs7749278	4.74	2.62E-06	6.10E-04	rs408918	4.22	2.35E-05	3.63E-03
	Whole_Blood	6	684	rs7749278	4.74	1.13E-05	9.18E-04	rs408918	4.22	1.08E-05	3.51E-03
VCL	Esophagus_Muscularis	10	239	rs10824139	-4.55	4.41E-04	3.26E-02	rs3812625	3.76	2.52E-04	4.68E-02

Table S6 TWAS-identified shared gene-tissue pairs between neuroticism and LUSC

Gene	Tissue type	CHR	SNP. Num	Neuroticism				LUSC			
				BEST. GWAS.ID	BEST. GWAS.Z	TWAS.P	FDR	BEST. GWAS.ID	BEST. GWAS.Z	TWAS.P	FDR
<i>CCDC9B</i>	Minor_Salivary_ Gland	15	390	rs1453184	-3.28	1.40E-03	3.28E-02	rs1992272	-3.73	1.44E-03	2.81E-02
<i>RAD51AP2</i>	Heart_Atrial_ Appendage	2	408	rs17477667	4.43	2.06E-04	1.40E-02	rs13031455	-4.73	3.64E-05	1.73E-02
<i>SKOR1</i>	Heart_Left_Ventricle	2	408	rs17477667	4.43	2.06E-04	2.74E-02	rs13031455	-4.73	3.64E-05	1.53E-02
	Heart_Atrial_ Appendage	15	350	rs4489954	4.40	8.36E-05	1.15E-02	rs12905397	4.03	2.57E-04	1.77E-02
	Pancreas	15	351	rs4489954	4.40	3.52E-04	1.63E-02	rs12905397	4.03	2.82E-04	1.09E-02
	Skin_Not_ Sun_Exposed_ Suprapubic	15	341	rs4489954	4.40	6.84E-04	3.08E-02	rs12905397	4.03	3.89E-04	2.33E-02
<i>SLC17A1</i>	Pituitary	6	654	rs198825	-5.75	9.00E-08	2.26E-05	rs13212534	6.62	6.15E-10	1.54E-07
<i>SLC17A4</i>	Pancreas	6	648	rs198825	-5.75	9.70E-05	7.95E-03	rs13212534	6.62	6.52E-05	8.02E-03

Table S7 TWAS-identified shared gene-tissue pairs between neuroticism and SCLC

Gene	Tissue type	Chr	SNP. Num	Neuroticism				SCLC			
				BEST.GWAS. ID	BEST. GWAS.Z	TWAS.P	FDR	BEST.GWAS. ID	BEST. GWAS.Z	TWAS.P	FDR
<i>ASCC3</i>	Artery_Aorta	6	297	rs240769	-5.84	2.23E-05	3.82E-03	rs12524934	3.88	3.71E-04	3.89E-02
	Brain_Cerebellar_ Hemisphere	6	287	rs240769	-5.84	7.94E-04	3.40E-02	rs12524934	3.88	4.84E-04	4.03E-02
<i>C17orf58</i>	Pituitary	17	329	rs11656082	4.39	7.29E-03	4.64E-02	rs7216064	4.10	1.00E-04	2.81E-02
<i>NBN</i>	Heart_Atrial_ Appendage	8	375	rs218899	3.39	3.88E-04	2.35E-02	rs16902897	4.28	1.80E-04	4.37E-02
<i>SLC17A4</i>	Pancreas	6	648	rs198825	-5.75	9.70E-05	7.95E-03	rs9379780	3.96	7.40E-05	1.48E-02

Table S8 Details of IVs selected for neuroticism

SNP	Chr	BP	EA	OA	EAF	Beta	Se	Sample size	P value	R ²	F-statistic	Pleiotropic traits
rs12137398	1	7790548	T	C	0.1944	0.0179	0.0029	373492	1.02E-09	9.98E-05	37.28	
rs11263943	1	37198130	A	G	0.4288	0.0158	0.0023	376156	1.19E-11	1.22E-04	46.00	
rs12137936	1	72720357	C	G	0.6929	-0.0138	0.0025	379828	3.03E-08	8.08E-05	30.69	
rs17096778	1	75809970	A	G	0.9547	0.0321	0.0055	375649	7.60E-09	8.88E-05	33.37	
rs11184985	1	107313610	T	C	0.7305	0.0143	0.0026	379574	3.37E-08	8.03E-05	30.48	
rs12092768	1	174432882	A	G	0.2848	-0.0153	0.0025	378883	1.80E-09	9.55E-05	36.18	
rs2488401	1	197702401	T	C	0.2093	-0.0172	0.0029	369901	1.67E-09	9.82E-05	36.32	
rs4396680	2	10178236	A	G	0.2031	0.0168	0.0029	380060	4.00E-09	9.11E-05	34.62	Body height
rs2717043	2	58179019	T	C	0.6273	0.0152	0.0024	377478	1.88E-10	1.08E-04	40.59	
rs17619012	2	63893589	T	G	0.2168	-0.0156	0.0028	377066	2.26E-08	8.29E-05	31.26	
rs998884	2	148539852	A	G	0.5985	-0.0178	0.0024	373568	5.16E-14	1.52E-04	56.67	
rs59491086	2	157132879	A	G	0.7948	0.0188	0.0028	379865	3.27E-11	1.16E-04	44.01	
rs10497655	2	185462041	T	C	0.6857	0.0152	0.0025	380060	8.19E-10	9.92E-05	37.71	Insomnia
rs988867	2	215449018	T	G	0.8557	0.0183	0.0033	379828	2.00E-08	8.29E-05	31.49	
rs6737187	2	226360417	A	G	0.2995	-0.0141	0.0025	380060	1.69E-08	8.37E-05	31.82	Smoking cessation
rs6773869	3	16870340	A	G	0.6415	-0.0168	0.0024	371006	4.17E-12	1.29E-04	48.04	Educational attainment
rs1542212	3	35683935	T	G	0.6070	-0.0159	0.0024	375766	1.45E-11	1.21E-04	45.60	
rs4405857	3	65445527	C	G	0.5984	0.0134	0.0023	377766	1.20E-08	8.60E-05	32.49	
rs1282545	3	107199709	T	C	0.5637	-0.0168	0.0023	368649	8.84E-13	1.39E-04	51.08	
rs10935181	3	136098408	A	G	0.4241	-0.0165	0.0023	379500	1.06E-12	1.34E-04	50.74	
rs4585149	3	157493952	T	C	0.1771	-0.0175	0.0030	373895	7.16E-09	8.96E-05	33.49	
rs16854051	4	42123892	T	C	0.2132	-0.0156	0.0028	369969	3.66E-08	8.19E-05	30.32	
rs10005233	4	90743331	T	C	0.5216	0.0146	0.0023	377983	2.19E-10	1.07E-04	40.28	
rs4530683	4	139053569	A	G	0.4150	-0.0129	0.0023	375688	3.43E-08	8.10E-05	30.45	
rs10054419	5	46036965	T	G	0.5614	0.0131	0.0023	379525	1.40E-08	8.48E-05	32.18	
rs1422192	5	87959023	A	G	0.1656	0.0190	0.0031	380060	6.68E-10	1.00E-04	38.11	
rs11948261	5	107753691	A	T	0.2107	0.0178	0.0028	376764	3.01E-10	1.05E-04	39.66	
rs58007470	5	153666790	T	C	0.2185	0.0155	0.0028	374742	2.99E-08	8.20E-05	30.71	
rs10476484	5	164438264	A	G	0.7233	-0.0149	0.0026	380060	5.85E-09	8.91E-05	33.88	
rs77580167	5	166208982	T	G	0.1410	-0.0182	0.0033	378023	3.68E-08	8.02E-05	30.32	
rs10456089	6	11959836	A	G	0.0758	-0.0262	0.0044	361493	3.83E-09	9.60E-05	34.70	
rs28986304	6	29566082	T	C	0.8736	-0.0212	0.0035	380025	8.05E-10	9.93E-05	37.75	
rs2269426	6	32076499	A	G	0.3594	0.0184	0.0024	380060	1.25E-14	1.56E-04	59.46	
rs2503775	6	98521600	A	G	0.1311	0.0218	0.0034	379581	1.41E-10	1.08E-04	41.15	

Table S8 (continued)

Table S8 (continued)

SNP	Chr	BP	EA	OA	EAF	Beta	Se	Sample size	P value	R ²	F-statistic	Pleiotropic traits
rs12660725	6	100978570	T	C	0.4738	0.0132	0.0023	377743	1.02E-08	8.69E-05	32.81	
rs11759026	6	126792095	A	G	0.7709	0.0151	0.0027	376800	3.68E-08	8.04E-05	30.30	Educational attainment
rs3996325	7	2053747	T	C	0.7554	0.0153	0.0027	378378	1.08E-08	8.64E-05	32.70	Sleep duration
rs11509880	7	12261911	A	G	0.3442	0.0157	0.0024	378729	8.92E-11	1.11E-04	42.04	
rs6970541	7	38963191	T	G	0.4914	0.0135	0.0023	374367	5.45E-09	9.09E-05	34.02	
rs802425	7	86294952	T	C	0.4400	-0.0131	0.0023	378705	1.34E-08	8.52E-05	32.26	
rs13226841	7	126389408	T	C	0.5239	-0.0172	0.0023	379972	7.13E-14	1.47E-04	56.04	
rs1731951	7	137075847	A	T	0.4400	-0.0137	0.0023	367589	6.07E-09	9.20E-05	33.81	Insomnia
rs2407746	8	4937757	C	G	0.6982	-0.0175	0.0025	374687	3.68E-12	1.29E-04	48.29	
rs11774503	8	10132291	A	G	0.5684	-0.0130	0.0023	371251	2.61E-08	8.34E-05	30.98	
rs7837935	8	65562019	T	G	0.1596	-0.0176	0.0031	379621	2.08E-08	8.27E-05	31.42	
rs6997840	8	141658361	T	C	0.3931	-0.0131	0.0024	372479	3.25E-08	8.20E-05	30.55	
rs2380937	9	4145781	T	C	0.6008	0.0133	0.0023	377601	1.54E-08	8.47E-05	32.00	
rs62550480	9	11449346	T	C	0.2142	-0.0181	0.0028	380060	9.32E-11	1.10E-04	41.96	
rs10811883	9	23291526	T	C	0.6263	-0.0173	0.0024	365932	9.32E-13	1.39E-04	50.98	
rs10119773	9	23736400	A	G	0.4660	-0.0161	0.0024	362077	8.33E-12	1.29E-04	46.69	
rs7033345	9	28717573	T	C	0.7209	0.0153	0.0026	376442	2.38E-09	9.46E-05	35.63	
rs11975	9	96327691	A	C	0.8557	-0.0216	0.0033	377873	4.14E-11	1.15E-04	43.55	
rs75614054	9	98275789	T	C	0.0864	0.0312	0.0041	377965	2.52E-14	1.54E-04	58.08	
rs2149351	9	120501644	T	G	0.2390	0.0186	0.0027	376531	5.15E-12	1.26E-04	47.62	
rs72759273	9	126973873	A	G	0.8055	0.0158	0.0029	380060	4.76E-08	7.84E-05	29.81	
rs7895261	10	58751054	T	G	0.7100	0.0142	0.0025	375329	2.33E-08	8.31E-05	31.20	
rs7912226	10	107652144	A	T	0.4009	-0.0132	0.0024	372662	2.20E-08	8.40E-05	31.30	
rs860626	10	119301703	T	G	0.7024	0.0152	0.0025	370116	2.06E-09	9.70E-05	35.92	
rs4757136	11	13281327	A	T	0.5712	-0.0166	0.0023	376976	8.56E-13	1.36E-04	51.15	
rs297346	11	16355771	A	G	0.3661	0.0156	0.0024	378364	6.56E-11	1.13E-04	42.64	
rs3026389	11	31813529	C	G	0.2111	0.0174	0.0028	379852	6.60E-10	1.00E-04	38.13	
rs11039182	11	47346723	T	C	0.7307	-0.0196	0.0026	380060	3.08E-14	1.52E-04	57.68	Fasting blood glucose measurement
rs10896636	11	57448032	C	G	0.6635	-0.0159	0.0024	373132	8.62E-11	1.13E-04	42.11	Educational attainment
rs674437	11	88689953	A	G	0.5149	-0.0145	0.0023	378851	2.74E-10	1.05E-04	39.85	
rs1884	11	112880597	C	G	0.2567	0.0166	0.0026	379494	2.46E-10	1.06E-04	40.06	
rs4245154	11	113388674	A	G	0.5689	0.0196	0.0023	375994	3.75E-17	1.89E-04	70.90	

Table S8 (continued)

Table S8 (continued)

SNP	Chr	BP	EA	OA	EAf	Beta	Se	Sample size	P value	R ²	F-statistic	Pleiotropic traits
rs73034263	11	133808038	C	G	0.8060	0.0162	0.0029	377135	2.78E-08	8.18E-05	30.86	
rs11608355	12	109879292	T	C	0.6832	-0.0196	0.0025	378137	2.44E-15	1.66E-04	62.66	
rs3124426	13	55937346	T	C	0.7695	-0.0153	0.0027	379969	1.88E-08	8.32E-05	31.62	
rs1892350	13	68080614	A	G	0.5094	-0.0142	0.0023	378178	7.00E-10	1.01E-04	38.02	Alcohol consumption
rs7338774	13	69344134	A	G	0.6702	-0.0148	0.0025	373129	1.85E-09	9.68E-05	36.13	Insomnia
rs9516861	13	97854889	A	T	0.1414	0.0184	0.0033	377206	2.48E-08	8.24E-05	31.08	
rs36006259	14	30268871	T	C	0.1577	-0.0179	0.0032	365810	2.41E-08	8.51E-05	31.14	
rs1778377	14	41694018	A	T	0.2712	-0.0156	0.0026	378079	1.53E-09	9.65E-05	36.49	
rs11627348	14	57295404	A	C	0.1514	0.0187	0.0032	373579	6.48E-09	9.02E-05	33.69	
rs4902704	14	69703588	C	G	0.6238	0.0142	0.0024	378906	2.38E-09	9.41E-05	35.64	Smoking cessation
rs10144845	14	75237770	T	C	0.6797	0.0182	0.0025	379924	1.41E-13	1.44E-04	54.69	
rs12902680	15	46316484	T	C	0.6189	-0.0134	0.0024	373788	1.77E-08	8.49E-05	31.73	
rs12903078	15	47503469	A	G	0.4062	0.0129	0.0023	379431	3.54E-08	8.01E-05	30.38	
rs3936093	15	78101909	A	G	0.4329	-0.0148	0.0023	374779	1.98E-10	1.08E-04	40.49	
rs4362360	15	86940622	T	C	0.5129	0.0126	0.0023	380060	3.57E-08	7.99E-05	30.37	
rs3785237	16	7667131	C	G	0.5032	0.0166	0.0023	373763	7.03E-13	1.38E-04	51.54	
rs62055866	16	30969557	C	G	0.6150	0.0148	0.0024	379511	3.19E-10	1.04E-04	39.55	
rs76082995	16	87426307	T	C	0.5620	-0.0136	0.0023	374546	5.81E-09	9.05E-05	33.90	
rs12938775	17	2574821	A	G	0.5003	-0.0157	0.0023	380060	8.00E-12	1.23E-04	46.76	Body height
rs35982947	17	38214275	A	C	0.6310	0.0136	0.0024	370627	1.52E-08	8.64E-05	32.02	
rs62062288	17	44096553	A	G	0.2115	0.0334	0.0028	370937	5.82E-32	3.73E-04	138.44	Alcohol consumption
rs56084168	17	79084574	T	C	0.1480	-0.0232	0.0032	378968	6.79E-13	1.36E-04	51.61	
rs4799723	18	31367050	T	G	0.4798	-0.0140	0.0023	373459	1.31E-09	9.85E-05	36.80	
rs11082011	18	35145122	T	C	0.6560	-0.0229	0.0024	375860	4.44E-21	2.36E-04	88.77	Educational attainment
rs17487484	18	50723283	T	G	0.4970	-0.0142	0.0023	380060	5.24E-10	1.02E-04	38.59	
rs1452789	18	53115879	A	T	0.6184	-0.0154	0.0024	378460	6.98E-11	1.12E-04	42.52	
rs2295094	20	33447915	A	G	0.1744	0.0173	0.0030	376087	1.29E-08	8.60E-05	32.35	
rs4578918	20	44721656	T	C	0.2568	0.0169	0.0026	378169	1.20E-10	1.10E-04	41.46	
rs11090045	22	41753603	A	G	0.3023	0.0193	0.0025	365483	3.93E-14	1.56E-04	57.20	Smoking cessation

F-statistic was calculated using the following formulas: $R^2 = 2 \times \beta^2 \times \text{EAF} \times (1 - \text{EAF})$ and $F = R^2 (n - 2) / (1 - R^2)$, where R^2 represents the phenotypic variance explained by a genetic instrument, F represents F-statistic, n is the sample size, β is the estimated genetic association of SNP with the exposure. EAF, effect allele frequency; SNP, single nucleotide polymorphisms; IV, instrumental variable.

Table S9 Details of IVs selected for LC with neuroticism

Trait	SNP	Chr	BP	EA	OA	EAf	Beta	Se	Sample size	P value	R ²	F-statistic
LC	rs71658797	1	77967507	A	T	0.1034	0.1278	0.0193	85716	3.25E-11	5.13E-04	44.02
	rs7705526	5	1285974	A	C	0.3403	0.1171	0.0133	85716	1.01E-18	9.10E-04	78.03
	rs380286	5	1320247	A	G	0.4226	-0.1413	0.0119	85716	1.51E-32	1.64E-03	141.13
	rs2893843	6	26338697	G	A	0.3915	-0.0723	0.0121	85716	2.03E-09	4.19E-04	35.95
	rs501942	6	31840477	T	C	0.0986	0.1699	0.0192	85716	8.40E-19	9.14E-04	78.40
	rs239935	6	167411788	G	A	0.4785	0.0668	0.0118	85716	1.29E-08	3.77E-04	32.35
	rs11780471	8	27344719	A	G	0.0596	-0.1411	0.0250	85716	1.69E-08	3.71E-04	31.82
	rs1629083	11	118126576	C	T	0.4976	0.0670	0.0118	85716	1.25E-08	3.78E-04	32.41
	rs7953330	12	998819	C	G	0.3121	-0.0873	0.0127	85716	6.10E-12	5.51E-04	47.30
	rs11571833	13	32972626	T	A	0.0109	0.4722	0.0584	85716	6.12E-16	7.62E-04	65.39
	rs4774488	15	47491291	C	T	0.4042	0.0658	0.0119	85716	3.60E-08	3.54E-04	30.35
	rs77468143	15	49376624	G	T	0.2539	-0.0827	0.0135	85716	1.00E-09	4.35E-04	37.32
	rs55781567	15	78857986	G	C	0.3667	0.2604	0.0121	85716	3.08E-103	5.40E-03	465.51
	rs151118057	15	78988620	A	G	0.0177	-0.2939	0.0512	85716	9.56E-09	3.84E-04	32.93
	rs56113850	19	41353107	T	C	0.4404	-0.1228	0.0138	85716	5.02E-19	9.26E-04	79.41
LUAD	rs71658797	1	77967507	A	T	0.1026	0.1693	0.0269	66756	3.12E-10	5.93E-04	39.60
	rs13080835	3	189357199	T	G	0.4934	-0.1107	0.0162	66756	7.45E-12	7.02E-04	46.91
	rs7705526	5	1285974	A	C	0.3422	0.2222	0.0180	66756	3.80E-35	2.29E-03	153.01
	rs421629	5	1320136	A	G	0.4267	-0.1566	0.0163	66756	9.75E-22	1.37E-03	91.77
	rs4236709	8	32410110	G	A	0.2178	0.1243	0.0193	66756	1.28E-10	6.19E-04	41.34
	rs885518	9	21830157	G	A	0.1011	0.1545	0.0253	66756	9.96E-10	5.59E-04	37.33
	rs62560775	9	22052068	G	A	0.1065	0.1659	0.0277	66756	2.23E-09	5.35E-04	35.76
	rs11591710	10	105687632	C	A	0.1368	0.1506	0.0230	66756	6.30E-11	6.40E-04	42.72
	rs1056562	11	118125625	T	C	0.4731	0.1021	0.0162	66756	2.76E-10	5.96E-04	39.84
	rs77468143	15	49376624	G	T	0.2526	-0.1551	0.0188	66756	1.69E-16	1.02E-03	67.94
	rs55781567	15	78857986	G	C	0.3586	0.2440	0.0167	66756	2.83E-48	3.18E-03	213.12
	rs56113850	19	41353107	T	C	0.4446	-0.1143	0.0186	66756	8.64E-10	5.63E-04	37.61
	rs41309931	20	62326579	T	G	0.1170	0.1574	0.0259	66756	1.31E-09	5.51E-04	36.80
LUSC	rs467095	5	1336221	C	T	0.4269	-0.1788	0.0191	63053	6.73E-21	1.39E-03	87.95
	rs501942	6	31840477	T	C	0.0971	0.2604	0.0308	63053	3.06E-17	1.13E-03	71.30
	rs9273429	6	32627456	G	A	0.3366	-0.1342	0.0239	63053	2.03E-08	4.99E-04	31.46
	rs7953330	12	998819	C	G	0.3153	-0.1456	0.0203	63053	7.26E-13	8.16E-04	51.47
	rs11571818	13	32968810	C	T	0.0107	0.7539	0.0939	63053	9.77E-16	1.02E-03	64.47
	rs8040868	15	78911181	C	T	0.4135	0.2550	0.0189	63053	2.50E-41	2.87E-03	181.32
	rs56113850	19	41353107	T	C	0.4447	-0.1446	0.0222	63053	7.18E-11	6.73E-04	42.47

Table S9 (continued)

Table S9 (*continued*)

Trait	SNP	Chr	BP	EA	OA	EAF	Beta	Se	Sample size	P value	R ²	F-statistic
SCLC	rs11571833	13	32972626	T	A	0.0096	0.7858	0.1415	24108	2.82E-08	1.28E-03	30.83
	rs55853698	15	78857939	G	T	0.3599	0.2879	0.0306	24108	4.78E-21	3.66E-03	88.61

F-statistic was calculated using the following formulas: $R^2 = 2 \times \beta^2 \times \text{EAF} \times (1 - \text{EAF})$ and $F = R^2 (n - 2) / (1 - R^2)$, where R^2 represents the phenotypic variance explained by a genetic instrument, F represents F-statistic, n is the sample size, β is the estimated genetic association of SNP with the exposure. EAF, effect allele frequency; SNP, single nucleotide polymorphisms; IV, instrumental variable.