

Table S1 Details of GWAS summary data

Phenotype	N _{cases}	N _{controls}	No. SNPs	Consortium	Population	Year	PubMed ID
Gastroesophageal reflux disease	78,707	288,734	2,324,711	UKBB and QSKIN	European	2022	34187846
Lung cancer	29,266	56,450	7,884,164	ILCCO	European	2017	28604730
Lung adenocarcinoma	11,273	55,483	7,876,477	ILCCO	European	2017	28604730
Lung squamous cell carcinoma	7,426	55,627	7,865,405	ILCCO	European	2017	28604730
Small-cell lung cancer	2,664	21,444	7,644,095	ILCCO	European	2017	28604730

GWAS, genome-wide association study; UKBB, UK Biobank; QSKIN, Queensland Sun and Health Study; ILCCO, International Lung Cancer Consortium.

Table S2 Partitioned genetic correlation between GERD and LC

Functional category	Phenotype1	Phenotype2	r_g	r_{g_se}	P value
Coding regions	GERD	LC	0.1894	0.0707	7.40E-03
		LUAD	0.0705	0.0804	3.81E-01
		LUSC	0.1565	0.0974	1.08E-01
		SCLC	0.2891	0.1249	2.06E-02
Conserved regions	GERD	LC	0.3838	0.0804	1.81E-06
		LUAD	0.2950	0.0899	1.00E-03
		LUSC	0.3790	0.1031	2.00E-04
		SCLC	0.3974	0.0787	4.36E-07
DNaseI digital genomic foot-printing region	GERD	LC	0.3156	0.0482	5.78E-11
		LUAD	0.2166	0.0521	3.23E-05
		LUSC	0.2957	0.0633	3.05E-06
		SCLC	0.3121	0.0679	4.35E-06
DNase I hypersensitive site	GERD	LC	0.3329	0.0441	4.48E-14
		LUAD	0.2266	0.0482	2.62E-06
		LUSC	0.3382	0.0603	2.00E-08
		SCLC	0.3616	0.0649	2.51E-08
Fetal DNase I hypersensitive site	GERD	LC	0.3043	0.0454	2.08E-11
		LUAD	0.2138	0.0516	3.47E-05
		LUSC	0.2988	0.0554	6.82E-08
		SCLC	0.2987	0.0600	6.52E-07
H3K4me1	GERD	LC	0.3236	0.0439	1.74E-13
		LUAD	0.2103	0.0616	6.00E-04
		LUSC	0.3301	0.0588	1.94E-08
		SCLC	0.2309	0.0594	1.00E-04
H3K4me3	GERD	LC	0.3039	0.0490	5.47E-10
		LUAD	0.2087	0.0576	3.00E-04
		LUSC	0.3147	0.0635	7.26E-07
		SCLC	0.3612	0.0910	7.22E-05
H3K9ac	GERD	LC	0.3458	0.0760	5.30E-06
		LUAD	0.2325	0.0844	5.90E-03
		LUSC	0.3123	0.0928	8.00E-04
		SCLC	0.3873	0.1314	3.20E-03
H3K27ac	GERD	LC	0.2823	0.0675	2.89E-05
		LUAD	0.1364	0.0750	6.91E-02
		LUSC	0.2944	0.0885	9.00E-04
		SCLC	0.2639	0.1071	1.38E-02
Intron	GERD	LC	0.2579	0.1141	2.37E-02
		LUAD	0.0567	0.1363	6.77E-01
		LUSC	0.3125	0.1331	1.89E-02
		SCLC	0.2177	0.1617	1.78E-01

Table S2 (continued)

Table S2 (continued)

Functional category	Phenotype1	Phenotype2	r_g	r_{g-se}	P value
Promotor	GERD	LC	0.3382	0.0693	1.05E-06
		LUAD	0.2164	0.0767	4.80E-03
		LUSC	0.3014	0.0849	4.00E-04
		SCLC	0.4093	0.1180	5.00E-04
Super enhancer	GERD	LC	0.1664	0.1340	2.14E-01
		LUAD	0.1466	0.1619	3.65E-01
		LUSC	0.2087	0.1694	2.18E-01
		SCLC	0.3248	0.3265	3.20E-01
Transcription factor-binding sites	GERD	LC	0.3097	0.0478	8.78E-11
		LUAD	0.2209	0.0518	2.02E-05
		LUSC	0.3184	0.0631	4.45E-07
		SCLC	0.3117	0.0652	1.77E-06
Transcribed regions	GERD	LC	0.3106	0.0472	4.55E-11
		LUAD	0.1881	0.0520	3.00E-04
		LUSC	0.3539	0.0585	1.46E-09
		SCLC	0.3474	0.0679	3.08E-07

r_g , genetic correlation; se, standard error; GERD, gastroesophageal reflux disease; LC, lung cancer; LUAD, lung adenocarcinoma; LUSC, lung squamous cell carcinoma; SCLC, small-cell lung cancer.

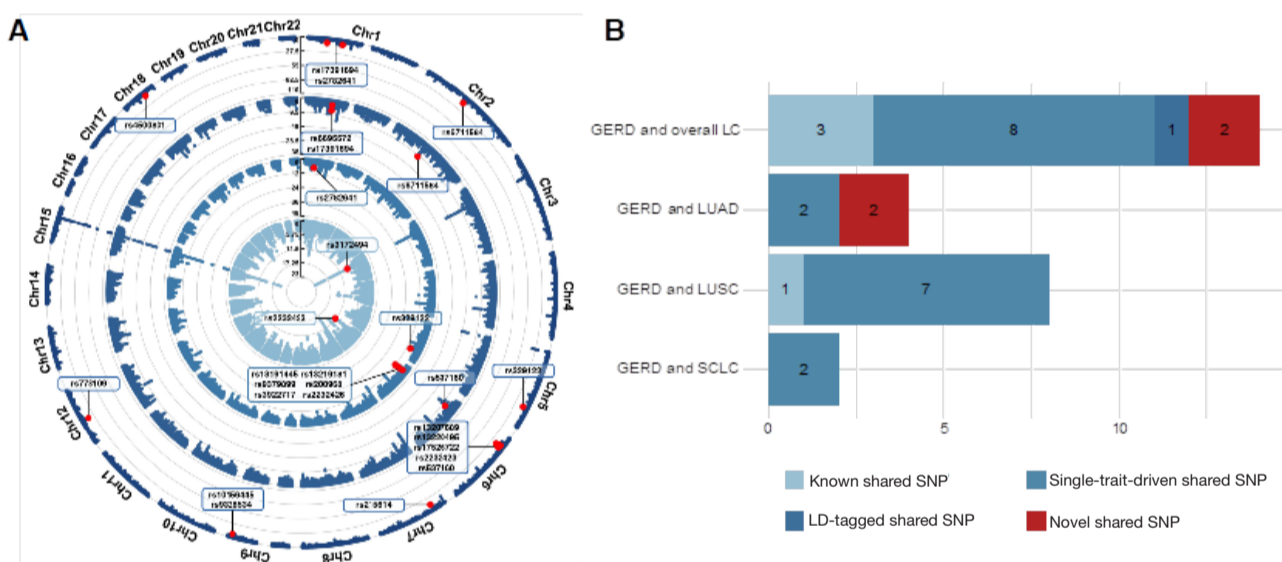


Figure S1 Cross-trait meta-analysis between GERD and LC. (A) Pleiotropic loci shared between GERD and LC. From periphery to center, each circular Manhattan plot represents results of the cross-trait meta-analysis between GERD and LC, as well as subtype-specific LC (LUAD, LUSC, and SCLC). The red dots represent significant pleiotropic loci in the cross-trait meta-analysis ($P_{CPASSOC} < 5 \times 10^{-8}$ and $P_{single-trait} < 1 \times 10^{-3}$ in both traits). (B) Bar plot of significant pleiotropic loci between GERD and LC. SNPs are categorized into four groups based on their single-trait and cross-trait characteristics: (I) “known” shared SNPs, referring to SNPs that reached genome-wide significance in both traits ($P_{GERD} < 5 \times 10^{-8}$ and $P_{LC} < 5 \times 10^{-8}$); (II) “single-trait-driven” shared SNPs, referring to SNPs reaching genome-wide significance in one of the two traits, either $P_{GERD} < 5 \times 10^{-8}$ or $P_{LC} < 5 \times 10^{-8}$; (III) “LD-tagged” shared SNPs, referring to SNPs not reaching genome-wide significance in both traits ($P_{GERD} > 5 \times 10^{-8}$ and $P_{LC} > 5 \times 10^{-8}$), but showing LD ($r^2=0.2$) with index SNPs previously identified by single-trait GWAS; and (IV) novel shared SNPs, referring to significant pleiotropic SNPs that did not reach genome-wide significance in both traits ($1 \times 10^{-3} < P_{single-trait} < 5 \times 10^{-8}$) and were not in LD with previously identified SNPs in single-trait GWAS ($r^2 < 0.2$). GERD, gastroesophageal reflux disease; LC, lung cancer; LUAD, lung adenocarcinoma; LUSC, lung squamous cell carcinoma; SCLC, small-cell lung cancer; SNP, single nucleotide polymorphism; CPASSOC, cross-phenotypic association; GWAS, genome-wide association study; LD, linkage disequilibrium.

Table S3 List of SNPs in the 99% credible set identified from fine-mapping analysis for each CPASSOC-identified locus shared between GERD and overall LC

Index SNP	99% credible-set SNPs	Chromosome	Position	CumSum
rs17391694	rs17391694	1	78623626	0.9978
rs2782641	rs1013793	1	44207553	0.9874
rs2782641	rs10890281	1	44245939	0.9863
rs2782641	rs11210860	1	43982527	0.9387
rs2782641	rs11210869	1	44026040	0.8560
rs2782641	rs11577403	1	43989773	0.9286
rs2782641	rs11805774	1	44152715	0.8890
rs2782641	rs12410155	1	44188465	0.9467
rs2782641	rs17371903	1	44070691	0.8352
rs2782641	rs17401357	1	44153619	0.9040
rs2782641	rs2152113	1	43983569	0.7905
rs2782641	rs2270972	1	44158129	0.8735
rs2782641	rs2274465	1	44121557	0.9533
rs2782641	rs2782641	1	44013355	0.2861
rs2782641	rs2819333	1	44014573	0.7594
rs2782641	rs2819334	1	44014735	0.6716
rs2782641	rs2842185	1	44019731	0.3525
rs2782641	rs2842187	1	44014949	0.4727
rs2782641	rs2842188	1	44014280	0.5761
rs2782641	rs3791034	1	44145130	0.9837
rs2782641	rs3791035	1	44154479	0.9183
rs2782641	rs3791040	1	44202733	0.9820
rs2782641	rs3791043	1	44219546	0.9905
rs2782641	rs3791134	1	44049156	0.4183
rs2782641	rs3791136	1	44049947	0.5259
rs2782641	rs4660257	1	44148168	0.8136
rs2782641	rs4660740	1	44148617	0.9851
rs2782641	rs489319	1	44131794	0.9642
rs2782641	rs501299	1	44051834	0.6241
rs2782641	rs605709	1	44058467	0.7168
rs2782641	rs618678	1	44133299	0.9690
rs2782641	rs6429637	1	44198531	0.9802
rs2782641	rs660899	1	44117006	0.9588
rs2782641	rs6664485	1	44225532	0.9895
rs2782641	rs6673970	1	44199469	0.9784
rs2782641	rs673253	1	44062154	0.9729
rs2782641	rs7516647	1	44237465	0.9884
rs2782641	rs9787076	1	44141149	0.9764
rs6711584	rs17343925	2	104426377	0.8771
rs6711584	rs2678670	2	104469564	0.7454
rs6711584	rs2945452	2	104469422	0.5700
rs6711584	rs4347858	2	104423042	0.3914
rs6711584	rs6707445	2	104420858	0.9993
rs6711584	rs6711584	2	104421692	0.2127
rs329122	rs11242219	5	133848760	0.9941
rs329122	rs1476096	5	133837021	0.9594
rs329122	rs1981627	5	133838180	0.9463
rs329122	rs329117	5	133860101	0.9292
rs329122	rs329120	5	133861756	0.6415
rs329122	rs329122	5	133864599	0.3310
rs329122	rs329124	5	133865452	0.9065
rs329122	rs4958244	5	133845380	0.9887
rs329122	rs6891328	5	133851526	0.9722
rs329122	rs7701346	5	133828356	0.9812
rs13207689	rs10484399	6	27534528	0.9741
rs13207689	rs12190473	6	27024687	0.8650
rs13207689	rs12215241	6	27023081	0.9638
rs13207689	rs12215773	6	27039233	0.9704
rs13207689	rs13191227	6	27390115	0.5158

Table S3 (continued)

Table S3 (continued)

Index SNP	99% credible-set SNPs	Chromosome	Position	CumSum
rs13207689	rs13193542	6	27702425	0.9879
rs13207689	rs13194781	6	27815639	0.9723
rs13207689	rs13195040	6	27413924	0.7365
rs13207689	rs13195636	6	27509493	0.9552
rs13207689	rs13196692	6	27379119	0.6278
rs13207689	rs13199649	6	27868792	0.4014
rs13207689	rs13199906	6	27834139	0.9792
rs13207689	rs13202295	6	27698837	0.9203
rs13207689	rs13207082	6	27251379	0.9905
rs13207689	rs13207689	6	27369704	0.2241
rs13207689	rs13209332	6	27520752	0.9584
rs13207689	rs13210634	6	27646492	0.9683
rs13207689	rs13212318	6	27688841	0.9808
rs13207689	rs13215275	6	27647509	0.9661
rs13207689	rs13217620	6	27653120	0.8913
rs13207689	rs17695758	6	27837183	0.9776
rs13207689	rs17749927	6	27669976	0.9615
rs13207689	rs17750424	6	27701122	0.9865
rs13207689	rs17750747	6	27730334	0.9851
rs13207689	rs17751184	6	27775028	0.9759
rs13207689	rs200965	6	27866384	0.9301
rs13207689	rs200968	6	27859568	0.9418
rs13207689	rs200974	6	27855845	0.9469
rs13207689	rs200975	6	27855625	0.9519
rs13207689	rs200977	6	27854301	0.9822
rs13207689	rs200979	6	27852357	0.9360
rs13207689	rs3922717	6	27030924	0.8154
rs13207689	rs483143	6	27846744	0.9837
rs13207689	rs6904596	6	27491299	0.9060
rs13207689	rs6940638	6	27046250	0.9892
rs13220495	rs10484442	6	26555879	0.9680
rs13220495	rs1056667	6	26510564	0.9448
rs13220495	rs10946834	6	26533664	0.9366
rs13220495	rs12526680	6	26550954	0.9421
rs13220495	rs1321479	6	26501897	0.9631
rs13220495	rs1321481	6	26538210	0.9832
rs13220495	rs1407045	6	26476155	0.6332
rs13220495	rs1570059	6	26573325	0.8899
rs13220495	rs1570060	6	26573562	0.8804
rs13220495	rs1884946	6	26545308	0.9338
rs13220495	rs2024970	6	26497520	0.7693
rs13220495	rs2145318	6	26496603	0.3722
rs13220495	rs2179152	6	26325888	0.2660
rs13220495	rs2255070	6	26501777	0.9813
rs13220495	rs3736781	6	26505362	0.9879
rs13220495	rs3736782	6	26505403	0.9310
rs13220495	rs4145910	6	26313305	0.1380
rs13220495	rs4573	6	26546808	0.9892
rs13220495	rs4713006	6	26519872	0.9474
rs13220495	rs4713008	6	26538268	0.9133
rs13220495	rs4871	6	26545632	0.9751
rs13220495	rs6456733	6	26566804	0.9030
rs13220495	rs6456735	6	26574149	0.8635
rs13220495	rs6903973	6	26499942	0.9793
rs13220495	rs6918360	6	26577867	0.8751
rs13220495	rs6918506	6	26577857	0.8514
rs13220495	rs6918854	6	26577924	0.8945
rs13220495	rs6922824	6	26553815	0.9253
rs13220495	rs6926629	6	26499903	0.9655
rs13220495	rs6930120	6	26555484	0.9164

Table S3 (continued)

Table S3 (continued)

Index SNP	99% credible-set SNPs	Chromosome	Position	CumSum
rs13220495	rs6933176	6	26540178	0.9580
rs13220495	rs6939048	6	26327953	0.5561
rs13220495	rs6940188	6	26562029	0.9194
rs13220495	rs6941022	6	26553531	0.9065
rs13220495	rs742090	6	26415637	0.9905
rs13220495	rs766406	6	26319588	0.8851
rs13220495	rs766407	6	26319534	0.4694
rs13220495	rs767471	6	26557854	0.9225
rs13220495	rs7753565	6	26560012	0.9865
rs13220495	rs7763910	6	26472655	0.8285
rs13220495	rs9295694	6	26512994	0.9606
rs13220495	rs9295695	6	26528250	0.9528
rs13220495	rs9357010	6	26527945	0.9704
rs13220495	rs9461267	6	26525455	0.9282
rs13220495	rs9461270	6	26544110	0.9772
rs13220495	rs9461271	6	26554968	0.9099
rs13220495	rs9461272	6	26579648	0.8693
rs13220495	rs9467703	6	26318903	0.7086
rs13220495	rs9467774	6	26505036	0.9394
rs13220495	rs9467779	6	26536687	0.9728
rs13220495	rs9467782	6	26542773	0.9849
rs13220495	rs9467791	6	26562486	0.9554
rs13220495	rs9467798	6	26575697	0.8989
rs13220495	rs9467800	6	26578525	0.8575
rs13220495	rs9467804	6	26583129	0.8453
rs13220495	rs9986382	6	26550619	0.9501
rs17526722	rs2179152	6	26325888	0.4994
rs17526722	rs4145910	6	26313305	0.2592
rs17526722	rs6939048	6	26327953	0.8447
rs17526722	rs766406	6	26319588	0.9952
rs17526722	rs766407	6	26319534	0.6820
rs17526722	rs9467703	6	26318903	0.9863
rs2232423	rs13204012	6	28201531	0.9815
rs2232423	rs13205211	6	28203056	0.9889
rs2232423	rs13208096	6	28225311	0.9736
rs2232423	rs13213152	6	28349698	0.9634
rs2232423	rs13213986	6	28358009	0.7324
rs2232423	rs13214023	6	28332141	0.8535
rs2232423	rs13217619	6	28306671	0.9915
rs2232423	rs2232423	6	28366151	0.2047
rs2232423	rs2232426	6	28360659	0.4072
rs2232423	rs2232429	6	28359632	0.5948
rs537160	rs1150754	6	32050758	1.0000
rs537160	rs1150755	6	32038550	0.4307
rs537160	rs1150758	6	32028149	0.7368
rs215614	rs1014242	7	32272305	0.9693
rs215614	rs10226228	7	32315613	0.9865
rs215614	rs10233045	7	32264492	0.9895
rs215614	rs10236197	7	32291761	0.9846
rs215614	rs10237329	7	32265725	0.9315
rs215614	rs10259431	7	32281397	0.9596
rs215614	rs10264177	7	32370862	0.9265
rs215614	rs1450869	7	32311672	0.9824
rs215614	rs215600	7	32333642	0.8983
rs215614	rs215605	7	32336965	0.8264
rs215614	rs215611	7	32341438	0.9407
rs215614	rs215614	7	32347335	0.5231
rs215614	rs215622	7	32357659	0.8705
rs215614	rs215625	7	32358313	0.8512
rs215614	rs215629	7	32360464	0.9630

Table S3 (continued)

Table S3 (continued)

Index SNP	99% credible-set SNPs	Chromosome	Position	CumSum
rs215614	rs215632	7	32368524	0.7112
rs215614	rs215634	7	32369148	0.9449
rs215614	rs215639	7	32373639	0.8889
rs215614	rs215669	7	32378979	0.9489
rs215614	rs215670	7	32379218	0.9069
rs215614	rs215695	7	32397908	0.9880
rs215614	rs215696	7	32398028	0.9364
rs215614	rs215697	7	32398041	0.9202
rs215614	rs4368879	7	32307925	0.9775
rs215614	rs4723147	7	32398156	0.9662
rs215614	rs6955346	7	32369553	0.9138
rs215614	rs7780515	7	32305274	0.9561
rs215614	rs7798739	7	32292961	0.9801
rs215614	rs7806224	7	32273107	0.9909
rs215614	rs7806397	7	32303339	0.9748
rs215614	rs929456	7	32293644	0.9721
rs215614	rs9771228	7	32322496	0.9526
rs10156445	rs10115938	9	128628571	0.2152
rs10156445	rs10118570	9	128476464	0.4374
rs10156445	rs10121853	9	128550854	0.6120
rs10156445	rs10156445	9	128617244	0.0607
rs10156445	rs10441758	9	128496337	0.7878
rs10156445	rs10513454	9	128673226	0.9182
rs10156445	rs10513456	9	128719849	0.9378
rs10156445	rs10739664	9	128684577	0.8977
rs10156445	rs10739665	9	128729977	0.9799
rs10156445	rs10760400	9	128524269	0.7591
rs10156445	rs10760401	9	128538841	0.7250
rs10156445	rs10760403	9	128608495	0.3092
rs10156445	rs10760404	9	128653015	0.1146
rs10156445	rs10760405	9	128711455	0.9871
rs10156445	rs10819079	9	128583899	0.7425
rs10156445	rs10819081	9	128629174	0.8119
rs10156445	rs10819082	9	128645617	0.4763
rs10156445	rs10819087	9	128695180	0.9518
rs10156445	rs10819089	9	128720289	0.9451
rs10156445	rs10986778	9	128263417	0.9291
rs10156445	rs10986780	9	128265664	0.9404
rs10156445	rs10986936	9	128569777	0.7999
rs10156445	rs10986965	9	128595268	0.5835
rs10156445	rs10986983	9	128620009	0.6621
rs10156445	rs10987017	9	128668715	0.9048
rs10156445	rs10987043	9	128689740	0.9322
rs10156445	rs10987054	9	128705227	0.9814
rs10156445	rs10987055	9	128707568	0.9351
rs10156445	rs1105727	9	128725543	0.9625
rs10156445	rs11789020	9	128616376	0.8550
rs10156445	rs11789188	9	128705012	0.9828
rs10156445	rs11791242	9	128705189	0.9768
rs10156445	rs11999260	9	128521473	0.8236
rs10156445	rs12336219	9	128732275	0.9641
rs10156445	rs12341976	9	128546359	0.8646
rs10156445	rs12345427	9	128732475	0.9557
rs10156445	rs12353435	9	128709253	0.9474
rs10156445	rs12552782	9	128564325	0.9101
rs10156445	rs12553980	9	128646863	0.8899
rs10156445	rs12686660	9	128335467	0.9913
rs10156445	rs13293667	9	128601761	0.8452
rs10156445	rs13299979	9	128625923	0.7063
rs10156445	rs1411350	9	128670179	0.7744

Table S3 (continued)

Table S3 (continued)

Index SNP	99% credible-set SNPs	Chromosome	Position	CumSum
rs10156445	rs1411352	9	128655115	0.1664
rs10156445	rs1477147	9	128736511	0.9538
rs10156445	rs1952669	9	128660676	0.6372
rs10156445	rs2026134	9	128680148	0.9428
rs10156445	rs2041943	9	128717131	0.9885
rs10156445	rs2058850	9	128731818	0.9843
rs10156445	rs2111358	9	128724683	0.9722
rs10156445	rs2149992	9	128738591	0.9591
rs10156445	rs2149993	9	128702846	0.9574
rs10156445	rs2416983	9	128730959	0.9658
rs10156445	rs3793622	9	128727170	0.9737
rs10156445	rs3829098	9	128727035	0.9753
rs10156445	rs4258094	9	128586487	0.3978
rs10156445	rs4515655	9	128616073	0.8347
rs10156445	rs4837022	9	128475379	0.5146
rs10156445	rs4838296	9	128591530	0.8733
rs10156445	rs4838298	9	128629488	0.6857
rs10156445	rs6478712	9	128514608	0.8817
rs10156445	rs7024493	9	128712242	0.9857
rs10156445	rs7026855	9	128724831	0.9784
rs10156445	rs7849076	9	128640702	0.2625
rs10156445	rs7849781	9	128736180	0.9220
rs10156445	rs7859110	9	128709600	0.9259
rs10156445	rs7862061	9	128731930	0.9496
rs10156445	rs7864769	9	128736041	0.9142
rs10156445	rs7868182	9	128721311	0.9899
rs10156445	rs7868811	9	128729746	0.9674
rs10156445	rs7869867	9	128675819	0.3543
rs10156445	rs7871599	9	128721828	0.9608
rs10156445	rs7875710	9	128597392	0.5509
rs10156445	rs872524	9	128723819	0.9706
rs10156445	rs888230	9	128724304	0.9690
rs9328534	rs10901120	9	134905524	0.7423
rs9328534	rs4145638	9	134880190	0.8844
rs9328534	rs4246173	9	134877278	0.4441
rs9328534	rs4246175	9	134930808	0.6184
rs9328534	rs4266768	9	134892125	0.6833
rs9328534	rs4287057	9	134898653	0.8353
rs9328534	rs4292819	9	134929122	0.5960
rs9328534	rs4363310	9	134890430	0.9603
rs9328534	rs4382592	9	134870755	0.2118
rs9328534	rs4402000	9	134891688	0.8519
rs9328534	rs4564007	9	134854280	0.9309
rs9328534	rs4592148	9	134917623	0.5725
rs9328534	rs4617289	9	134926958	0.7615
rs9328534	rs4962181	9	134880575	0.9001
rs9328534	rs6597540	9	134856576	0.4713
rs9328534	rs7019796	9	134863453	0.5239
rs9328534	rs7025089	9	134881443	0.3511
rs9328534	rs7025683	9	134865815	0.4142
rs9328534	rs7026534	9	134907263	0.2716
rs9328534	rs7032884	9	134858482	0.3836
rs9328534	rs7039772	9	134865891	0.4981
rs9328534	rs7040224	9	134886837	0.7032
rs9328534	rs7043386	9	134866354	0.3150
rs9328534	rs7048083	9	134858097	0.7806
rs9328534	rs7467596	9	134912678	0.5486
rs9328534	rs7858113	9	134853684	0.9156
rs9328534	rs9328534	9	134874805	0.1280
rs9328534	rs9328536	9	134914385	0.7232

Table S3 (continued)

Table S3 (continued)

Index SNP	99% credible-set SNPs	Chromosome	Position	CumSum
rs9328534	rs9411331	9	134883419	0.8183
rs9328534	rs9411334	9	134896887	0.8684
rs9328534	rs9411335	9	134901224	0.9746
rs9328534	rs9411336	9	134901901	0.7995
rs9328534	rs9411337	9	134902172	0.9849
rs9328534	rs9411340	9	134943989	0.9929
rs9328534	rs9411424	9	134864382	0.6626
rs9328534	rs9411430	9	134907819	0.6407
rs9328534	rs9411433	9	134921485	0.9460
rs773109	rs1873914	12	56379427	0.9812
rs773109	rs705698	12	56384687	0.7284
rs773109	rs705699	12	56384804	0.9857
rs773109	rs705702	12	56390636	0.9653
rs773109	rs773107	12	56369506	0.8518
rs773109	rs773108	12	56369911	0.5324
rs773109	rs773109	12	56374695	0.2923
rs773109	rs773114	12	56379060	0.9741
rs773109	rs877636	12	56480583	0.9902
rs4500831	rs1020169	18	53066079	0.7585
rs4500831	rs12605773	18	53064423	0.9225
rs4500831	rs12607679	18	53059748	0.9417
rs4500831	rs1261097	18	52868977	0.5526
rs4500831	rs1348047	18	53050058	0.8670
rs4500831	rs1440477	18	53086455	0.8405
rs4500831	rs1452789	18	53115879	0.9888
rs4500831	rs1623427	18	53046319	0.8537
rs4500831	rs1788019	18	53050523	0.8905
rs4500831	rs1788025	18	53048678	0.9670
rs4500831	rs1942262	18	52873317	0.4951
rs4500831	rs2872041	18	53064491	0.7150
rs4500831	rs2919450	18	53084545	0.7757
rs4500831	rs2919451	18	53084300	0.9815
rs4500831	rs2924321	18	53125435	0.4291
rs4500831	rs2958163	18	53085412	0.6440
rs4500831	rs2958166	18	53087632	0.9120
rs4500831	rs2958169	18	53089138	0.6807
rs4500831	rs2958171	18	53072832	0.9594
rs4500831	rs2958175	18	53074958	0.7927
rs4500831	rs2958178	18	53069972	0.9322
rs4500831	rs2958186	18	53077795	0.6038
rs4500831	rs3794889	18	53061937	0.9510
rs4500831	rs3794891	18	53055212	0.9012
rs4500831	rs4374254	18	53092547	0.2546
rs4500831	rs4468713	18	53104019	0.9908
rs4500831	rs4500831	18	53097544	0.1278
rs4500831	rs4524013	18	53096708	0.8094
rs4500831	rs4801149	18	53063229	0.8257
rs4500831	rs4801150	18	53065110	0.7398
rs4500831	rs624244	18	53183396	0.9899
rs4500831	rs7228159	18	53104253	0.3461
rs4500831	rs9320010	18	53053897	0.9744
rs4500831	rs9320016	18	53095471	0.8791
rs4500831	rs9950000	18	53052169	0.9871

SNPs, single nucleotide polymorphisms; CPASSOC, cross-phenotypic association; GERD, gastroesophageal reflux disease; LC, lung cancer.

Table S4 List of SNPs in the 99% credible set identified from fine-mapping analysis for each CPASSOC-identified locus shared between GERD and LUAD

Index SNP	99% credible-set SNPs	Chromosome	Position	CumSum
rs6695572	rs10782651	1	77934335	0.8769
rs6695572	rs10873947	1	77986516	0.9825
rs6695572	rs11162350	1	77929479	0.8468
rs6695572	rs11162351	1	77944732	0.8905
rs6695572	rs11806197	1	77964855	0.9178
rs6695572	rs11811611	1	77982017	0.9619
rs6695572	rs12040471	1	77968401	0.9000
rs6695572	rs12042177	1	77986638	0.9554
rs6695572	rs12042881	1	77968443	0.9089
rs6695572	rs12047928	1	77932750	0.9675
rs6695572	rs12049202	1	77967523	0.9780
rs6695572	rs12093263	1	77964339	0.9899
rs6695572	rs12729914	1	77980235	0.9341
rs6695572	rs17384946	1	77978205	0.9260
rs6695572	rs1874819	1	77912969	0.9915
rs6695572	rs2088518	1	77951330	0.8132
rs6695572	rs2647506	1	77914159	0.9864
rs6695572	rs3113637	1	77927144	0.9845
rs6695572	rs6603950	1	77938087	0.9420
rs6695572	rs6695572	1	77945635	0.3824
rs6695572	rs6698295	1	77945965	0.7380
rs6695572	rs6704141	1	77932095	0.9803
rs6695572	rs7514937	1	77981099	0.9882
rs6695572	rs7522356	1	77951460	0.9730
rs6695572	rs7542588	1	77938165	0.9488
rs6695572	rs9324162	1	77954804	0.8632
rs17391694	rs17391694	1	78623626	0.9940
rs6711584	rs17343925	2	104426377	0.6405
rs6711584	rs2678670	2	104469564	0.9991
rs6711584	rs2945452	2	104469422	0.8904
rs6711584	rs4347858	2	104423042	0.4785
rs6711584	rs6707445	2	104420858	0.7798
rs6711584	rs6711584	2	104421692	0.2622
rs537160	rs1052248	6	31556581	0.9846
rs537160	rs1799964	6	31542308	0.7980
rs537160	rs2072633	6	31919578	0.6528
rs537160	rs2534671	6	31465661	0.9877
rs537160	rs2844480	6	31564821	0.9196
rs537160	rs3093661	6	31543758	0.9729
rs537160	rs3093668	6	31546495	0.8591
rs537160	rs3828917	6	31465917	0.7326
rs537160	rs389883	6	31947460	0.9799
rs537160	rs537160	6	31916400	0.5421
rs537160	rs589428	6	31848220	0.9903

SNPs, single nucleotide polymorphisms; CPASSOC, cross-phenotypic association; GERD, gastroesophageal reflux disease; LUAD, lung adenocarcinoma.

Table S5 List of SNPs in the 99% credible set identified from fine-mapping analysis for each CPASSOC-identified locus shared between GERD and LUSC

Index SNP	99% credible-set SNPs	Chromosome	Position	CumSum
rs2782641	rs1013793	1	44207553	0.9865
rs2782641	rs10789442	1	44140075	0.9807
rs2782641	rs10890281	1	44245939	0.9823
rs2782641	rs11210860	1	43982527	0.9116
rs2782641	rs11210869	1	44026040	0.8064
rs2782641	rs11577403	1	43989773	0.9005
rs2782641	rs11805774	1	44152715	0.8892
rs2782641	rs12410155	1	44188465	0.9211
rs2782641	rs1472661	1	44209075	0.9878
rs2782641	rs17371903	1	44070691	0.8279
rs2782641	rs17401357	1	44153619	0.8602
rs2782641	rs1887402	1	44036085	0.7272
rs2782641	rs2152113	1	43983569	0.7607
rs2782641	rs2270972	1	44158129	0.8449
rs2782641	rs2274465	1	44121557	0.9300
rs2782641	rs2782640	1	44009033	0.2575
rs2782641	rs2782641	1	44013355	0.1587
rs2782641	rs2819333	1	44014573	0.6930
rs2782641	rs2819334	1	44014735	0.6575
rs2782641	rs2842185	1	44019731	0.3231
rs2782641	rs2842187	1	44014949	0.4322
rs2782641	rs2842188	1	44014280	0.4825
rs2782641	rs3791034	1	44145130	0.9702
rs2782641	rs3791035	1	44154479	0.8748
rs2782641	rs3791040	1	44202733	0.9770
rs2782641	rs3791043	1	44219546	0.9851
rs2782641	rs3791101	1	44366250	0.9905
rs2782641	rs3791134	1	44049156	0.3796
rs2782641	rs3791136	1	44049947	0.5317
rs2782641	rs4660257	1	44148168	0.7838
rs2782641	rs4660740	1	44148617	0.9791
rs2782641	rs489319	1	44131794	0.9381
rs2782641	rs501299	1	44051834	0.5753
rs2782641	rs605709	1	44058467	0.6168
rs2782641	rs618678	1	44133299	0.9460
rs2782641	rs6429637	1	44198531	0.9749
rs2782641	rs660899	1	44117006	0.9531
rs2782641	rs6673970	1	44199469	0.9726
rs2782641	rs673253	1	44062154	0.9664
rs2782641	rs7516647	1	44237465	0.9838
rs2782641	rs7520053	1	44226657	0.9892
rs2782641	rs9787076	1	44141149	0.9597
rs329122	rs10056247	5	133898136	0.9910
rs329122	rs11242219	5	133848760	0.9688
rs329122	rs1476096	5	133837021	0.8845
rs329122	rs1981627	5	133838180	0.8515
rs329122	rs2241699	5	133899872	0.9809
rs329122	rs329117	5	133860101	0.8101
rs329122	rs329120	5	133861756	0.5201
rs329122	rs329122	5	133864599	0.2687
rs329122	rs329124	5	133865452	0.7620
rs329122	rs4958241	5	133829990	0.9749
rs329122	rs4958244	5	133845380	0.9564

Table S5 (continued)

Table S5 (continued)

Index SNP	99% credible-set SNPs	Chromosome	Position	CumSum
rs329122	rs6871635	5	133830395	0.9862
rs329122	rs6891328	5	133851526	0.9129
rs329122	rs7701346	5	133828356	0.9390
rs13191445	rs10456045	6	26404958	0.9900
rs13191445	rs1056667	6	26510564	0.9267
rs13191445	rs13191445	6	26015489	0.9723
rs13191445	rs13202688	6	25993469	0.9855
rs13191445	rs13212534	6	25983010	0.9882
rs13191445	rs1321479	6	26501897	0.9491
rs13191445	rs13220495	6	26441640	0.9893
rs13191445	rs1407045	6	26476155	0.3564
rs13191445	rs1624440	6	26433329	0.9209
rs13191445	rs17526722	6	25918855	0.9869
rs13191445	rs1796520	6	26410800	0.9825
rs13191445	rs1796521	6	26421392	0.9760
rs13191445	rs2024970	6	26497520	0.4776
rs13191445	rs2145318	6	26496603	0.1869
rs13191445	rs2179152	6	26325888	0.6592
rs13191445	rs2255070	6	26501777	0.9681
rs13191445	rs3736781	6	26505362	0.9794
rs13191445	rs3736782	6	26505403	0.9381
rs13191445	rs4145910	6	26313305	0.5763
rs13191445	rs6903973	6	26499942	0.9637
rs13191445	rs6926629	6	26499903	0.9544
rs13191445	rs6939048	6	26327953	0.8525
rs13191445	rs742090	6	26415637	0.9150
rs13191445	rs766406	6	26319588	0.9592
rs13191445	rs766407	6	26319534	0.7289
rs13191445	rs7763910	6	26472655	0.7931
rs13191445	rs806973	6	26148326	0.9906
rs13191445	rs9295694	6	26512994	0.9324
rs13191445	rs9467703	6	26318903	0.9084
rs13191445	rs9467774	6	26505036	0.9438
rs9379899	rs10484442	6	26555879	0.9829
rs9379899	rs1056667	6	26510564	0.9864
rs9379899	rs10946834	6	26533664	0.9835
rs9379899	rs12190473	6	27024687	0.8085
rs9379899	rs12215241	6	27023081	0.8554
rs9379899	rs12215773	6	27039233	0.8324
rs9379899	rs12526680	6	26550954	0.9811
rs9379899	rs1321479	6	26501897	0.9901
rs9379899	rs1407045	6	26476155	0.8895
rs9379899	rs1570059	6	26573325	0.9712
rs9379899	rs1570060	6	26573562	0.9704
rs9379899	rs1624440	6	26433329	0.9847
rs9379899	rs1884946	6	26545308	0.9779
rs9379899	rs2024970	6	26497520	0.9171
rs9379899	rs2145318	6	26496603	0.8733
rs9379899	rs2179152	6	26325888	0.9345
rs9379899	rs3736782	6	26505403	0.9880
rs9379899	rs3922717	6	27030924	0.5104
rs9379899	rs4145910	6	26313305	0.9265
rs9379899	rs4713006	6	26519872	0.9858
rs9379899	rs4713008	6	26538268	0.9758
rs9379899	rs4871	6	26545632	0.9852
rs9379899	rs6456733	6	26566804	0.9694

Table S5 (continued)

Table S5 (continued)

Index SNP	99% credible-set SNPs	Chromosome	Position	CumSum
rs9379899	rs6456735	6	26574149	0.9685
rs9379899	rs6918360	6	26577867	0.9655
rs9379899	rs6918506	6	26577857	0.9645
rs9379899	rs6918854	6	26577924	0.9721
rs9379899	rs6922824	6	26553815	0.9751
rs9379899	rs6930120	6	26555484	0.9773
rs9379899	rs6933176	6	26540178	0.9817
rs9379899	rs6939048	6	26327953	0.9529
rs9379899	rs6940188	6	26562029	0.9786
rs9379899	rs6940638	6	27046250	0.9055
rs9379899	rs6941022	6	26553531	0.9729
rs9379899	rs742090	6	26415637	0.9799
rs9379899	rs766407	6	26319534	0.9411
rs9379899	rs767471	6	26557854	0.9765
rs9379899	rs7763910	6	26472655	0.9473
rs9379899	rs9295694	6	26512994	0.9874
rs9379899	rs9295695	6	26528250	0.9841
rs9379899	rs9357010	6	26527945	0.9896
rs9379899	rs9461267	6	26525455	0.9792
rs9379899	rs9461270	6	26544110	0.9891
rs9379899	rs9461271	6	26554968	0.9737
rs9379899	rs9461272	6	26579648	0.9675
rs9379899	rs9467703	6	26318903	0.9583
rs9379899	rs9467774	6	26505036	0.9885
rs9379899	rs9467779	6	26536687	0.9869
rs9379899	rs9467791	6	26562486	0.9805
rs9379899	rs9467798	6	26575697	0.9744
rs9379899	rs9467800	6	26578525	0.9665
rs9379899	rs9467804	6	26583129	0.9634
rs9379899	rs9986382	6	26550619	0.9823
rs3922717	rs10484442	6	26555879	0.9884
rs3922717	rs10946834	6	26533664	0.9891
rs3922717	rs12190473	6	27024687	0.8678
rs3922717	rs12215241	6	27023081	0.9181
rs3922717	rs12215773	6	27039233	0.8935
rs3922717	rs12526680	6	26550954	0.9865
rs3922717	rs13191227	6	27390115	0.9520
rs3922717	rs13195040	6	27413924	0.9628
rs3922717	rs13196692	6	27379119	0.9680
rs3922717	rs13207689	6	27369704	0.9464
rs3922717	rs1570059	6	26573325	0.9764
rs3922717	rs1570060	6	26573562	0.9755
rs3922717	rs1884946	6	26545308	0.9844
rs3922717	rs3922717	6	27030924	0.5479
rs3922717	rs4713008	6	26538268	0.9822
rs3922717	rs4871	6	26545632	0.9897
rs3922717	rs6456733	6	26566804	0.9745
rs3922717	rs6456735	6	26574149	0.9734
rs3922717	rs6904596	6	27491299	0.9790
rs3922717	rs6918360	6	26577867	0.9702
rs3922717	rs6918506	6	26577857	0.9691
rs3922717	rs6918854	6	26577924	0.9773
rs3922717	rs6922824	6	26553815	0.9814
rs3922717	rs6930120	6	26555484	0.9837
rs3922717	rs6933176	6	26540178	0.9872
rs3922717	rs6940188	6	26562029	0.9851
rs3922717	rs6940638	6	27046250	0.9354
rs3922717	rs6941022	6	26553531	0.9782
rs3922717	rs767471	6	26557854	0.9829

Table S5 (continued)

Table S5 (continued)

Index SNP	99% credible-set SNPs	Chromosome	Position	CumSum
rs3922717	rs9461271	6	26554968	0.9798
rs3922717	rs9461272	6	26579648	0.9724
rs3922717	rs9467779	6	26536687	0.9903
rs3922717	rs9467791	6	26562486	0.9858
rs3922717	rs9467798	6	26575697	0.9807
rs3922717	rs9467800	6	26578525	0.9713
rs3922717	rs9467804	6	26583129	0.9574
rs3922717	rs9986382	6	26550619	0.9878
rs13219181	rs12190473	6	27024687	0.8972
rs13219181	rs12215241	6	27023081	0.9492
rs13219181	rs12215773	6	27039233	0.9237
rs13219181	rs13191227	6	27390115	0.9842
rs13219181	rs13195040	6	27413924	0.9897
rs13219181	rs13196692	6	27379119	0.9951
rs13219181	rs13207689	6	27369704	0.9785
rs13219181	rs3922717	6	27030924	0.5664
rs13219181	rs6940638	6	27046250	0.9670
rs200968	rs13195291	6	28169241	0.9352
rs200968	rs13197574	6	28060239	0.9444
rs200968	rs13197633	6	28174757	0.9249
rs200968	rs13199649	6	27868792	0.9910
rs200968	rs13200214	6	28017250	0.9881
rs200968	rs13201308	6	28130089	0.9535
rs200968	rs13204012	6	28201531	0.8717
rs200968	rs13205211	6	28203056	0.9029
rs200968	rs13205911	6	28124114	0.9849
rs200968	rs13207689	6	27369704	0.9814
rs200968	rs13208096	6	28225311	0.8393
rs200968	rs13213152	6	28349698	0.5590
rs200968	rs13213986	6	28358009	0.3121
rs200968	rs13214023	6	28332141	0.8019
rs200968	rs13217619	6	28306671	0.9140
rs200968	rs200965	6	27866384	0.9607
rs200968	rs200968	6	27859568	0.9653
rs200968	rs200974	6	27855845	0.9737
rs200968	rs200975	6	27855625	0.9776
rs200968	rs200979	6	27852357	0.9698
rs2232426	rs13195291	6	28169241	0.9838
rs2232426	rs13197574	6	28060239	0.9879
rs2232426	rs13197633	6	28174757	0.9791
rs2232426	rs13201308	6	28130089	0.9921
rs2232426	rs13204012	6	28201531	0.9550
rs2232426	rs13205211	6	28203056	0.9691
rs2232426	rs13208096	6	28225311	0.9403
rs2232426	rs13213152	6	28349698	0.8131
rs2232426	rs13213986	6	28358009	0.7011
rs2232426	rs13214023	6	28332141	0.9233
rs2232426	rs13217619	6	28306671	0.9742
rs2232426	rs2232423	6	28366151	0.3781
rs2232426	rs2232426	6	28360659	0.1932
rs2232426	rs2232429	6	28359632	0.5595

SNPs, single nucleotide polymorphisms; CPASSOC, cross-phenotypic association; GERD, gastroesophageal reflux disease; LUSC, lung squamous cell carcinoma.

Table S6 List of SNPs in the 99% credible set identified from fine-mapping analysis for each CPASSOC-identified locus shared between GERD and SCLC

Index SNP	99% credible-set SNPs	Chromosome	Position	CumSum
rs3172494	rs13084037	3	49214066	0.9005
rs3172494	rs7617480	3	49210732	0.5461
rs3172494	rs9586	3	49213637	0.9997
rs2232423	rs13195291	6	28169241	0.9747
rs2232423	rs13197574	6	28060239	0.9875
rs2232423	rs13197633	6	28174757	0.9813
rs2232423	rs13201308	6	28130089	0.9935
rs2232423	rs13204012	6	28201531	0.9462
rs2232423	rs13205211	6	28203056	0.9596
rs2232423	rs13208096	6	28225311	0.9151
rs2232423	rs13213152	6	28349698	0.8969
rs2232423	rs13213986	6	28358009	0.6773
rs2232423	rs13214023	6	28332141	0.7902
rs2232423	rs13217619	6	28306671	0.9681
rs2232423	rs200965	6	27866384	0.9324
rs2232423	rs2232423	6	28366151	0.1908
rs2232423	rs2232426	6	28360659	0.3752
rs2232423	rs2232429	6	28359632	0.5484

SNPs, single nucleotide polymorphisms; CPASSOC, cross-phenotypic association; GERD, gastroesophageal reflux disease; SCLC, small-cell lung cancer.

Table S7 Results from colocalization analysis for each pleiotropic locus identified from CPASSOC

Index SNP	Chromosome	Position	Gastroesophageal reflux disease		Lung cancer		P _{CPASSOC}	PPH3.abf	PPH4.abf
			Beta	P value	Beta	P value			
Gastroesophageal reflux disease and lung cancer									
rs17391694	1	78623626	-0.035685568	2.54E-07	-0.106292	2.62E-08	7.94E-10	0.000	0.999
rs2782641	1	44013355	-0.027088204	4.33E-08	-0.041668	6.26E-04	5.67E-10	0.040	0.592
rs6711584	2	104421692	-0.032254466	2.66E-11	-0.044136	1.52E-04	2.13E-13	0.028	0.848
rs329122	5	133864599	0.028952886	3.05E-09	0.050511	1.69E-05	2.35E-11	0.004	0.970
rs13207689	6	27369704	0.046620595	9.32E-10	-0.139724	9.29E-11	1.35E-14	0.836	0.164
rs13220495	6	26441640	0.043286473	1.96E-08	-0.126045	7.74E-09	2.91E-12	1.000	0.000
rs17526722	6	25918855	0.032422152	5.59E-05	-0.131428	1.26E-08	1.58E-08	1.000	0.000
rs2232423	6	28366151	0.050652994	1.37E-11	-0.14533	8.04E-12	2.54E-17	0.009	0.991
rs537160	6	31916400	-0.027209424	5.08E-08	0.052519	3.98E-05	8.46E-10	0.989	0.001
rs215614	7	32347335	0.032854105	4.08E-11	0.042536	4.29E-04	1.31E-13	0.050	0.634
rs10156445	9	128617244	-0.024850116	6.33E-07	-0.040924	7.81E-04	1.51E-08	0.350	0.353
rs9328534	9	134874805	0.029341563	1.35E-08	0.043651	4.67E-04	1.25E-10	0.034	0.539
rs773109	12	56374695	0.038057215	8.71E-14	0.04369	5.14E-04	5.40E-16	0.008	0.736
rs4500831	18	53097544	0.028003873	1.21E-07	0.045982	3.42E-04	1.47E-09	0.049	0.191
Gastroesophageal reflux disease and lung adenocarcinoma									
rs6695572	1	77945635	-0.021700617	4.09E-04	-0.12281	8.34E-09	2.14E-08	0.218	0.472
rs17391694	1	78623626	-0.035685568	2.54E-07	-0.135426	3.83E-07	8.34E-09	0.000	0.999
rs6711584	2	104421692	-0.032254466	2.66E-11	-0.067323	2.89E-05	8.68E-13	0.007	0.969
rs537160	6	31916400	-0.027209424	5.08E-08	0.059983	7.89E-04	8.21E-09	0.049	0.160
Gastroesophageal reflux disease and lung squamous cell carcinoma									
rs2782641	1	44013355	-0.027088204	4.33E-08	-0.070961	2.76E-04	4.98E-09	0.077	0.879
rs329122	5	133864599	0.028952886	3.05E-09	0.079537	2.28E-05	5.12E-10	0.006	0.973
rs13191445	6	26015489	0.032472655	5.35E-05	-0.251115	1.06E-11	5.56E-11	1.000	0.000
rs9379899	6	26603015	0.042970721	1.25E-09	-0.112059	2.17E-04	1.07E-10	1.000	0.000
rs3922717	6	27030924	0.040691795	5.35E-13	-0.083107	3.75E-04	3.81E-14	0.916	0.084
rs13219181	6	27136225	0.034914578	1.32E-08	-0.106462	2.56E-05	7.00E-10	0.803	0.197
rs200968	6	27859568	0.0401529	3.94E-11	-0.105147	4.25E-05	1.62E-12	0.022	0.978
rs2232426	6	28360659	0.050647495	1.39E-11	-0.220279	1.02E-10	1.63E-14	0.013	0.987
Gastroesophageal reflux disease and small-cell lung cancer									
rs3172494	3	48731487	0.045352619	6.71E-09	0.153362	9.28E-04	5.12E-09	0.016	0.158
rs2232423	6	28366151	0.050652994	1.37E-11	-0.200395	2.14E-04	2.02E-12	0.016	0.920

CPASSOC, cross-phenotypic association; SNP, single nucleotide polymorphism.

Table S8 TWAS-identified shared gene-tissue pairs between GERD and LC

Gene	Tissue type	CHR	SNP Num	Gastroesophageal reflux disease				Lung cancer			
				BEST.GWAS.ID	BEST.GWAS.Z	TWAS.P	FDR	BEST.GWAS.ID	BEST.GWAS.Z	TWAS.P	FDR
<i>FUBP1</i>	Adipose subcutaneous	1	332	rs17391694	5.16	2.54E-07	4.50E-05	rs17391694	5.57	2.62E-08	2.48E-05
<i>ERAP1</i>	Adipose subcutaneous	5	494	rs28129	-4.45	1.08E-04	1.04E-02	rs27039	3.68	5.43E-04	4.47E-02
<i>MAPKAP1</i>	Adipose visceral omentum	9	355	rs12352375	-4.95	2.20E-03	2.96E-02	rs13291556	4.24	2.27E-04	3.45E-02
<i>FUBP1</i>	Adipose visceral omentum	1	332	rs17391694	5.16	2.91E-05	2.52E-03	rs17391694	5.57	3.59E-07	2.63E-04
<i>CEP57</i>	Adipose visceral omentum	11	617	rs568668	-4.58	8.39E-06	1.03E-03	rs10831447	-3.95	1.72E-04	4.01E-02
<i>PBX3</i>	Adipose visceral omentum	9	377	rs12352375	-4.93	4.24E-07	1.16E-04	rs13291556	4.24	4.73E-04	3.45E-02
<i>MTMR2</i>	Artery aorta	11	602	rs568668	-4.58	9.51E-05	8.52E-03	rs10831447	-3.95	3.94E-04	4.39E-02
<i>YIPF4</i>	Artery aorta	2	314	rs176403	3.61	8.05E-04	2.91E-02	rs458628	4.16	2.69E-05	6.16E-03
<i>ZDHHC5</i>	Artery aorta	11	393	rs12790660	4.83	4.72E-06	2.11E-03	rs11229042	-4.88	4.78E-04	4.39E-02
<i>MTMR2</i>	Artery tibial	11	604	rs568668	-4.58	1.45E-04	7.24E-03	rs10831447	-3.95	4.79E-04	3.78E-02
<i>MEGF9</i>	Artery tibial	9	341	rs12377227	-3.40	2.69E-03	3.66E-02	rs1060817	-3.78	3.24E-04	3.95E-02
<i>PTPRF</i>	Artery tibial	1	444	rs2782641	-5.48	7.05E-07	1.52E-04	rs4660740	-3.69	1.22E-04	2.78E-02
<i>FUBP1</i>	Artery tibial	1	332	rs17391694	5.16	2.54E-07	7.28E-05	rs17391694	5.57	2.62E-08	2.39E-05
<i>CEP57</i>	Artery tibial	11	613	rs568668	-4.58	3.89E-04	1.19E-02	rs10831447	-3.95	1.04E-03	4.78E-02
<i>ERAP1</i>	Brain amygdala	5	498	rs28129	-4.45	1.16E-03	4.52E-02	rs27039	3.68	3.53E-04	2.11E-02
<i>MAP2K5</i>	Brain caudate basal ganglia	15	408	rs8025889	4.74	1.47E-03	4.04E-02	rs1001870	-3.65	2.66E-04	5.73E-03
<i>ERAP1</i>	Brain caudate basal ganglia	5	497	rs28129	-4.45	6.90E-04	4.17E-02	rs27039	3.68	2.84E-04	4.17E-02
<i>ENSG00000276517</i>	Brain cerebellar hemisphere	2	378	rs176403	3.61	2.03E-03	4.38E-02	rs458628	4.16	1.08E-04	2.15E-02
<i>FUBP1</i>	Brain cerebellum	1	332	rs17391694	5.16	2.54E-07	8.50E-05	rs17391694	5.57	2.62E-08	1.87E-05
<i>ERAP1</i>	Brain cortex	5	496	rs28129	-4.45	1.25E-03	3.91E-02	rs27039	3.68	3.62E-04	3.18E-02
<i>ENSG00000276334</i>	Brain frontal cortex BA9	2	375	rs176403	3.61	1.10E-03	2.60E-02	rs458628	4.16	6.81E-05	2.13E-02
<i>ERAP1</i>	Brain nucleus accumbens basal ganglia	5	499	rs28129	-4.45	1.18E-03	3.42E-02	rs27039	3.68	3.18E-04	3.14E-02
<i>VPS33B-DT</i>	Brain nucleus accumbens basal ganglia	15	487	rs11073964	3.53	1.01E-03	2.86E-02	rs7601	-3.50	1.76E-04	4.97E-03
<i>MAP2K5</i>	Brain putamen basal ganglia	15	408	rs8025889	4.74	3.66E-07	3.31E-05	rs1001870	-3.65	5.85E-03	4.87E-02
<i>ERAP1</i>	Brain putamen basal ganglia	5	499	rs28129	-4.45	8.01E-04	4.03E-02	rs27039	3.68	2.74E-04	3.64E-02
<i>DISP2</i>	Brain spinal cord cervical c-1	15	396	rs11070293	-4.18	1.92E-03	4.02E-02	rs1992272	-3.99	7.38E-05	2.34E-03
<i>ERAP1</i>	Brain substantia nigra	5	500	rs28129	-4.45	1.17E-03	2.66E-02	rs27039	3.68	1.47E-04	1.41E-02
<i>FUBP1</i>	Breast mammary tissue	1	332	rs17391694	5.16	2.54E-07	1.46E-04	rs17391694	5.57	2.62E-08	1.61E-05
<i>CEP57</i>	Breast mammary tissue	11	613	rs568668	-4.58	1.57E-05	1.50E-03	rs10831447	-3.95	1.02E-04	1.96E-02
<i>TIE1</i>	Cells cultured fibroblasts	1	460	rs2782641	-5.48	3.92E-05	7.10E-03	rs4660740	-3.69	1.35E-04	3.28E-02
<i>MEPCE</i>	Cells cultured fibroblasts	7	311	rs12532238	3.52	7.58E-04	3.63E-02	rs314370	3.32	1.56E-05	8.38E-03
<i>PBX3</i>	Cells cultured fibroblasts	9	377	rs12352375	-4.93	2.02E-06	7.27E-04	rs13291556	4.24	2.51E-05	9.71E-03
<i>ERAP1</i>	Cells EBV-transformed lymphocytes	5	490	rs28129	-4.45	2.70E-04	2.50E-02	rs27039	3.68	1.70E-04	1.10E-02
<i>CEP57</i>	Cells EBV-transformed lymphocytes	11	614	rs568668	-4.58	8.25E-06	1.25E-03	rs10831447	-3.95	2.06E-04	1.95E-02

Table S8 (continued)

Table S8 (continued)

Gene	Tissue type	CHR	SNP Num	Gastroesophageal reflux disease				Lung cancer			
				BEST.GWAS. ID	BEST. GWAS.Z	TWAS.P	FDR	BEST.GWAS. ID	BEST. GWAS.Z	TWAS.P	FDR
<i>PBX3</i>	Cells EBV-transformed lymphocytes	9	378	rs12352375	-4.93	3.47E-04	6.71E-03	rs13291556	4.24	1.83E-05	1.67E-03
<i>FUBP1</i>	Colon sigmoid	1	331	rs17391694	5.16	1.58E-08	9.07E-06	rs17391694	5.57	1.36E-08	8.24E-06
<i>ERAP1</i>	Colon sigmoid	5	493	rs28129	-4.45	3.96E-04	2.27E-02	rs27039	3.68	2.69E-04	2.04E-02
<i>CEP57</i>	Colon sigmoid	11	614	rs568668	-4.58	9.41E-06	8.42E-04	rs10831447	-3.95	1.32E-04	2.37E-02
<i>PBX3</i>	Colon sigmoid	9	377	rs12352375	-4.93	9.37E-07	1.06E-04	rs13291556	4.24	1.79E-05	4.31E-03
<i>ENSG00000272109</i>	Colon sigmoid	5	493	rs28129	-4.45	7.56E-04	2.81E-02	rs27039	3.68	9.91E-05	1.00E-02
<i>ERAP1</i>	Colon transverse	5	496	rs28129	-4.45	4.08E-05	5.76E-03	rs27039	3.68	2.77E-05	8.37E-03
<i>PBX3</i>	Colon transverse	9	375	rs12352375	-4.93	1.58E-07	3.73E-05	rs13291556	4.24	1.13E-04	1.50E-02
<i>FUBP1</i>	Esophagus gastroesophageal junction	1	331	rs17391694	5.16	2.54E-07	5.02E-05	rs17391694	5.57	2.62E-08	1.65E-05
<i>FUBP1</i>	Esophagus mucosa	1	332	rs17391694	5.16	2.54E-07	5.55E-05	rs17391694	5.57	2.62E-08	2.41E-05
<i>ERAP1</i>	Esophagus mucosa	5	493	rs28129	-4.45	1.50E-04	9.75E-03	rs27039	3.68	7.76E-05	7.95E-03
<i>ENSG00000272109</i>	Esophagus mucosa	5	493	rs28129	-4.45	1.48E-03	4.96E-02	rs27039	3.68	3.94E-04	3.23E-02
<i>FUBP1</i>	Esophagus muscularis	1	332	rs17391694	5.16	5.47E-07	1.54E-04	rs17391694	5.57	8.49E-10	7.52E-07
<i>CEP57</i>	Esophagus muscularis	11	613	rs568668	-4.58	1.30E-05	1.68E-03	rs10831447	-3.95	1.92E-04	3.99E-02
<i>ZDHHC5</i>	Heart atrial appendage	11	393	rs12790660	4.83	2.08E-06	3.92E-04	rs11229042	-4.88	1.82E-04	3.46E-02
<i>MED19</i>	Heart atrial appendage	11	386	rs12790660	4.83	6.09E-06	5.74E-04	rs11229042	-4.88	6.28E-04	4.77E-02
<i>FUBP1</i>	Heart atrial appendage	1	332	rs17391694	5.16	2.84E-08	8.89E-06	rs17391694	5.57	1.15E-08	7.59E-06
<i>CEP57</i>	Heart atrial appendage	11	613	rs568668	-4.58	3.22E-04	1.01E-02	rs10831447	-3.95	4.64E-04	4.41E-02
<i>PBX3</i>	Heart atrial appendage	9	375	rs12352375	-4.93	1.11E-06	2.79E-04	rs13291556	4.24	2.79E-04	3.79E-02
<i>SKOR1</i>	Heart atrial appendage	15	350	rs8025889	4.98	5.39E-04	2.07E-02	rs1001870	-3.65	9.09E-04	2.08E-02
<i>MTMR2</i>	Heart left ventricle	11	603	rs568668	-4.58	1.13E-03	2.84E-02	rs10831447	-3.95	8.81E-04	3.22E-02
<i>ZDHHC5</i>	Heart left ventricle	11	393	rs12790660	4.83	4.72E-06	5.13E-04	rs11229042	-4.88	4.78E-04	2.62E-02
<i>MED19</i>	Heart left ventricle	11	386	rs12790660	4.83	4.02E-06	5.13E-04	rs11229042	-4.88	7.02E-04	3.15E-02
<i>ERAP1</i>	Heart left ventricle	5	492	rs28129	-4.45	7.55E-04	2.82E-02	rs27039	3.68	6.56E-05	1.66E-02
<i>CEP57</i>	Heart left ventricle	11	612	rs568668	-4.58	8.02E-06	5.25E-04	rs10831447	-3.95	1.69E-04	1.39E-02
<i>FAM76B</i>	Liver	11	614	rs568668	-4.58	8.26E-06	9.09E-04	rs10831447	-3.95	1.64E-04	1.21E-02
<i>ERAP1</i>	Liver	5	495	rs28129	-4.45	6.56E-04	2.38E-02	rs27039	3.68	3.51E-04	2.71E-02
<i>MTMR2</i>	Lung	11	602	rs568668	-4.58	1.89E-05	1.55E-03	rs10831447	-3.95	1.47E-04	2.04E-02
<i>MAPKAP1</i>	Lung	9	355	rs12352375	-4.95	1.43E-03	2.48E-02	rs13291556	4.24	1.15E-04	3.78E-02
<i>FUBP1</i>	Lung	1	332	rs17391694	5.16	2.54E-07	6.68E-05	rs17391694	5.57	2.62E-08	2.20E-05
<i>ERAP1</i>	Lung	5	495	rs28129	-4.45	2.71E-04	2.70E-02	rs27039	3.68	1.35E-04	1.88E-02
<i>CEP57</i>	Lung	11	613	rs568668	-4.58	9.16E-06	1.20E-03	rs10831447	-3.95	1.65E-04	2.04E-02
<i>DISP2</i>	Minor salivary gland	15	392	rs11070293	-4.18	1.10E-03	2.57E-02	rs1992272	-3.99	1.30E-04	3.80E-03
<i>ERAP1</i>	Minor salivary gland	5	491	rs28129	-4.45	2.15E-04	1.15E-02	rs27039	3.68	8.89E-04	3.44E-02
<i>TRIM38</i>	Muscle skeletal	6	666	rs1614887	7.05	1.24E-05	6.57E-04	rs2393592	6.48	4.63E-05	5.73E-03
<i>FUBP1</i>	Muscle skeletal	1	332	rs17391694	5.16	2.54E-07	6.71E-05	rs17391694	5.57	2.62E-08	2.19E-05
<i>HYKK</i>	Muscle skeletal	15	422	rs34016249	3.31	4.58E-04	1.54E-02	rs12914385	21.45	3.12E-26	5.19E-24
<i>FUBP1</i>	Nerve tibial	1	332	rs17391694	5.16	5.26E-07	1.78E-04	rs17391694	5.57	1.58E-09	1.71E-06
<i>CEP57</i>	Nerve tibial	11	616	rs568668	-4.58	3.40E-05	3.62E-03	rs10831447	-3.95	1.97E-04	2.53E-02
<i>TMX2</i>	Nerve tibial	11	386	rs12790660	4.83	1.09E-05	1.39E-03	rs11229042	-4.88	1.49E-04	2.53E-02
<i>MTMR2</i>	Ovary	11	604	rs568668	-4.58	1.22E-05	2.07E-03	rs10831447	-3.95	1.44E-04	2.46E-02
<i>TRIM38</i>	Pancreas	6	661	rs1614887	7.04	5.71E-04	1.99E-02	rs2393592	6.48	9.69E-04	3.97E-02
<i>FUBP1</i>	Pancreas	1	332	rs17391694	5.16	3.11E-06	3.09E-04	rs17391694	5.57	3.88E-10	2.06E-07
<i>ERAP1</i>	Pancreas	5	492	rs28129	-4.45	2.24E-04	8.19E-03	rs27039	3.68	1.23E-04	1.64E-02
<i>LINC02609</i>	Pituitary	1	415	rs12089815	4.60	9.98E-04	4.30E-02	rs1342780	-4.28	1.84E-05	1.03E-02

Table S8 (continued)

Table S8 (continued)

Gene	Tissue type	CHR	SNP Num	Gastroesophageal reflux disease				Lung cancer			
				BEST.GWAS. ID	BEST. GWAS.Z	TWAS.P	FDR	BEST.GWAS. ID	BEST. GWAS.Z	TWAS.P	FDR
<i>ERAP1</i>	Prostate	5	495	rs28129	-4.45	1.30E-03	3.75E-02	rs27039	3.68	1.67E-05	3.11E-03
<i>CEP57</i>	Prostate	11	616	rs568668	-4.58	4.41E-05	5.36E-03	rs10831447	-3.95	7.85E-05	1.92E-02
<i>ENSG00000272109</i>	Prostate	5	495	rs28129	-4.45	2.31E-04	1.78E-02	rs27039	3.68	5.41E-04	2.81E-02
<i>ENSG00000276334</i>	Prostate	2	375	rs176403	3.61	7.00E-04	2.94E-02	rs458628	4.16	5.81E-05	1.91E-02
<i>FAM76B</i>	Skin not sun exposed suprapubic	11	618	rs568668	-4.58	6.64E-06	1.74E-03	rs10831447	-3.95	2.78E-04	2.75E-02
<i>PRPF6</i>	Skin not sun exposed suprapubic	20	371	rs6011118	-4.50	1.53E-04	9.75E-03	rs7264220	-4.71	6.25E-05	1.61E-02
<i>FUBP1</i>	Skin not sun exposed suprapubic	1	332	rs17391694	5.16	2.54E-07	7.50E-05	rs17391694	5.57	2.62E-08	2.45E-05
<i>CEP57</i>	Skin not sun exposed suprapubic	11	617	rs568668	-4.58	2.54E-04	1.33E-02	rs10831447	-3.95	3.83E-04	2.88E-02
<i>FUBP1</i>	Skin sun exposed lower leg	1	332	rs17391694	5.16	7.73E-11	7.58E-08	rs17391694	5.57	5.28E-10	5.46E-07
<i>CEP57</i>	Skin sun exposed lower leg	11	617	rs568668	-4.58	1.00E-04	6.01E-03	rs10831447	-3.95	1.88E-04	2.85E-02
<i>VPS33B-DT</i>	Skin sun exposed lower leg	15	485	rs11073964	3.53	1.13E-03	2.78E-02	rs7601	-3.50	1.55E-03	2.83E-02
<i>ERAP1</i>	Small intestine terminal ileum	5	490	rs28129	-4.45	1.41E-04	2.06E-02	rs27039	3.68	2.20E-04	8.31E-03
<i>ZDHHC5</i>	Spleen	11	393	rs12790660	4.83	1.86E-06	6.21E-04	rs11229042	-4.88	6.48E-04	4.62E-02
<i>CEP57</i>	Spleen	11	613	rs568668	-4.58	6.92E-06	6.81E-04	rs10831447	-3.95	2.72E-04	4.58E-02
<i>ENSG00000272109</i>	Spleen	5	497	rs28129	-4.45	1.06E-03	3.91E-02	rs27039	3.68	1.68E-04	1.09E-02
<i>DISP2</i>	Stomach	15	398	rs11070293	-4.18	1.10E-03	1.67E-02	rs1992272	-3.99	1.30E-04	4.78E-03
<i>ERAP1</i>	Stomach	5	492	rs28129	-4.45	1.05E-04	8.12E-03	rs27039	3.68	3.94E-05	3.15E-03
<i>CEP57</i>	Stomach	11	612	rs568668	-4.58	8.50E-06	1.21E-03	rs10831447	-3.95	1.65E-04	1.58E-02
<i>SEMA6D</i>	Testis	15	426	rs8034783	4.88	7.16E-05	7.93E-03	rs7165678	5.43	9.18E-05	3.16E-03
<i>DISP2</i>	Testis	15	398	rs11070293	-4.18	1.80E-03	4.98E-02	rs1992272	-3.99	1.23E-04	3.93E-03
<i>ERAP1</i>	Testis	5	494	rs28129	-4.45	1.37E-04	8.74E-03	rs27039	3.68	3.33E-04	3.25E-02
<i>FAM76B</i>	Thyroid	11	616	rs568668	-4.58	9.56E-06	1.18E-03	rs10831447	-3.95	2.98E-04	3.08E-02
<i>SERPING1</i>	Thyroid	11	386	rs12790660	4.83	8.08E-05	4.96E-03	rs11229042	-4.88	1.59E-04	2.47E-02
<i>FUBP1</i>	Thyroid	1	332	rs17391694	5.16	2.54E-07	8.56E-05	rs17391694	5.57	2.62E-08	2.82E-05
<i>CEP57</i>	Thyroid	11	615	rs568668	-4.58	5.50E-06	1.18E-03	rs10831447	-3.95	1.50E-04	2.47E-02
<i>ENSG00000254602</i>	Thyroid	11	397	rs12790660	4.83	1.09E-05	1.18E-03	rs11229042	-4.88	1.24E-04	2.47E-02
<i>N4BP2L2-IT2</i>	Uterus	13	469	rs7988462	-4.49	7.45E-04	1.19E-02	rs9943888	-4.77	6.90E-04	3.31E-02
<i>ENSG00000272109</i>	Vagina	5	492	rs28129	-4.45	2.33E-03	3.65E-02	rs27039	3.68	1.77E-03	3.51E-02
<i>FAM76B</i>	Whole blood	11	618	rs568668	-4.58	6.64E-06	6.10E-04	rs10831447	-3.95	2.78E-04	2.57E-02
<i>SERPING1</i>	Whole blood	11	386	rs12790660	4.83	1.30E-06	2.07E-04	rs11229042	-4.88	1.87E-04	2.16E-02

TWAS, transcriptome-wide association study; GERD, gastroesophageal reflux disease; LC, lung cancer; CHR, chromosome; SNP, single nucleotide polymorphism; GWAS, genome-wide association study; FDR, false discovery rate.

Table S9 TWAS-identified shared gene-tissue pairs between GERD and LUAD

Gene	Tissue type	CHR	SNP Num	Gastroesophageal reflux disease				Lung adenocarcinoma			
				BEST.GWAS.ID	BEST.GWAS.Z	TWAS.P	FDR	BEST.GWAS.ID	BEST.GWAS.Z	TWAS.P	FDR
<i>FUBP1</i>	Adipose subcutaneous	1	332	rs17391694	5.16	2.54E-07	4.50E-05	rs6695572	5.76	3.83E-07	3.63E-04
<i>FUBP1</i>	Adipose visceral omentum	1	332	rs17391694	5.16	2.91E-05	2.52E-03	rs6695572	5.76	1.55E-08	1.14E-05
<i>FUBP1</i>	Artery tibial	1	332	rs17391694	5.16	2.54E-07	7.28E-05	rs6695572	5.76	3.83E-07	3.50E-04
<i>CEP192</i>	Brain amygdala	18	398	rs1786263	-2.92	5.81E-03	4.18E-02	rs1981354	3.45	1.90E-03	3.41E-02
<i>FUBP1</i>	Brain cerebellum	1	332	rs17391694	5.16	2.54E-07	8.50E-05	rs6695572	5.76	3.83E-07	2.73E-04
<i>FUBP1</i>	Breast mammary tissue	1	332	rs17391694	5.16	2.54E-07	1.46E-04	rs6695572	5.76	3.83E-07	2.36E-04
<i>MEPCE</i>	Cells cultured fibroblasts	7	311	rs12532238	3.52	7.58E-04	3.63E-02	rs314311	3.41	4.44E-05	2.38E-02
<i>FUBP1</i>	Colon sigmoid	1	331	rs17391694	5.16	1.58E-08	9.07E-06	rs6695572	5.76	5.48E-07	3.32E-04
<i>FUBP1</i>	Esophagus gastroesophageal junction	1	331	rs17391694	5.16	2.54E-07	5.02E-05	rs6695572	5.76	3.83E-07	2.43E-04
<i>FAM227B</i>	Esophagus gastroesophageal junction	15	364	rs769136	2.74	7.30E-04	1.86E-02	rs10519226	-6.20	2.12E-04	1.10E-02
<i>FUBP1</i>	Esophagus mucosa	1	332	rs17391694	5.16	2.54E-07	5.55E-05	rs6695572	5.76	3.83E-07	3.54E-04
<i>ERAP1</i>	Esophagus mucosa	5	493	rs28129	-4.45	1.50E-04	9.75E-03	rs3853202	2.81	4.78E-04	4.90E-02
<i>FUBP1</i>	Esophagus muscularis	1	332	rs17391694	5.16	5.47E-07	1.54E-04	rs6695572	5.76	1.49E-10	1.32E-07
<i>FUBP1</i>	Heart atrial appendage	1	332	rs17391694	5.16	2.84E-08	8.89E-06	rs6695572	5.76	4.37E-08	2.89E-05
<i>FUBP1</i>	Lung	1	332	rs17391694	5.16	2.54E-07	6.68E-05	rs6695572	5.76	3.83E-07	3.23E-04
<i>FUBP1</i>	Muscle skeletal	1	332	rs17391694	5.16	2.54E-07	6.71E-05	rs6695572	5.76	3.83E-07	3.21E-04
<i>HYKK</i>	Muscle skeletal	15	422	rs34016249	3.31	4.58E-04	1.54E-02	rs1051730	14.48	5.88E-12	9.79E-10
<i>FUBP1</i>	Nerve tibial	1	332	rs17391694	5.16	5.26E-07	1.78E-04	rs6695572	5.76	5.59E-09	6.04E-06
<i>FUBP1</i>	Pancreas	1	332	rs17391694	5.16	3.11E-06	3.09E-04	rs6695572	5.76	1.73E-07	9.17E-05
<i>ERAP1</i>	Prostate	5	495	rs28129	-4.45	1.30E-03	3.75E-02	rs3853202	2.81	1.25E-04	1.31E-02
<i>PRPF6</i>	Skin not sun exposed suprapubic	20	371	rs6011118	-4.50	1.53E-04	9.75E-03	rs3761121	5.78	1.16E-04	2.98E-02
<i>FUBP1</i>	Skin not sun exposed suprapubic	1	332	rs17391694	5.16	2.54E-07	7.50E-05	rs6695572	5.76	3.83E-07	3.58E-04
<i>FUBP1</i>	Skin sun exposed lower leg	1	332	rs17391694	5.16	7.73E-11	7.58E-08	rs6695572	5.76	1.67E-07	1.73E-04
<i>TNFRSF6B</i>	Skin sun exposed lower leg	20	429	rs6011118	-4.50	2.85E-05	3.16E-03	rs3761121	5.78	1.00E-05	1.40E-03
<i>SLC6A3</i>	Stomach	5	527	rs2550948	-3.22	1.30E-03	3.51E-02	rs2853677	11.75	2.10E-04	1.23E-02
<i>ERAP1</i>	Stomach	5	492	rs28129	-4.45	1.05E-04	8.12E-03	rs3853202	2.82	9.38E-04	3.77E-02
<i>DISP2</i>	Testis	15	398	rs11070293	-4.18	1.80E-03	4.98E-02	rs679882	3.37	1.23E-03	3.93E-02
<i>FUBP1</i>	Thyroid	1	332	rs17391694	5.16	2.54E-07	8.56E-05	rs6695572	5.76	3.83E-07	4.12E-04

TWAS, transcriptome-wide association study; GERD, gastroesophageal reflux disease; LUAD, lung adenocarcinoma; CHR, chromosome; SNP, single nucleotide polymorphism; GWAS, genome-wide association study; FDR, false discovery rate.

Table S10 TWAS-identified shared gene-tissue pairs between GERD and LUSC

Gene	Tissue type	CHR	SNP.Num	Gastroesophageal reflux disease				Lung squamous cell carcinoma			
				BEST. GWAS.ID	BEST. GWAS.Z	TWAS.P	FDR	BEST. GWAS.ID	BEST. GWAS.Z	TWAS.P	FDR
<i>PBX3</i>	Adipose subcutaneous	9	377	rs12352375	-4.93	1.86E-06	6.05E-04	rs6478712	-4.38	4.72E-05	1.64E-02
<i>PBX3</i>	Adipose visceral omentum	9	377	rs12352375	-4.93	4.24E-07	1.16E-04	rs6478712	-4.38	2.61E-05	7.70E-03
<i>PBX3</i>	Artery aorta	9	377	rs12352375	-4.93	9.87E-07	2.87E-04	rs6478712	-4.38	2.97E-05	9.33E-03
<i>PTPRF</i>	Artery tibial	1	444	rs2782641	-5.48	7.05E-07	1.52E-04	rs4660740	-4.57	9.98E-06	7.78E-03
<i>PBX3</i>	Artery tibial	9	377	rs12352375	-4.93	1.07E-06	1.82E-04	rs6478712	-4.38	2.97E-05	1.09E-02
<i>MAP2K5</i>	Brain caudate basal ganglia	15	408	rs8025889	4.74	1.47E-03	4.04E-02	rs12905397	4.03	1.41E-03	2.74E-02
<i>SZT2</i>	Brain hypothalamus	1	455	rs2782641	-5.48	1.08E-07	3.43E-05	rs4660740	-4.57	1.25E-04	1.42E-02
<i>TMEM125</i>	Brain putamen basal ganglia	1	452	rs2782641	-5.48	1.53E-05	3.64E-03	rs4660740	-4.57	1.83E-05	7.89E-03
<i>PBX3</i>	Breast mammary tissue	9	377	rs12352375	-4.93	2.26E-06	5.18E-04	rs6478712	-4.38	1.39E-04	1.70E-02
<i>TIE1</i>	Cells cultured fibroblasts	1	460	rs2782641	-5.48	3.92E-05	7.10E-03	rs4660740	-4.57	4.75E-05	4.16E-02
<i>PBX3</i>	Cells cultured fibroblasts	9	377	rs12352375	-4.93	2.02E-06	7.27E-04	rs6478712	-4.38	1.90E-05	7.39E-03
<i>PBX3</i>	Cells EBV-transformed lymphocytes	9	378	rs12352375	-4.93	3.47E-04	6.71E-03	rs6478712	-4.38	1.73E-04	1.59E-02
<i>NA</i>	Cells EBV-transformed lymphocytes	1	420	rs596522	-5.48	1.63E-05	1.24E-03	rs4660740	-4.57	1.07E-04	2.59E-02
<i>PBX3</i>	Colon sigmoid	9	377	rs12352375	-4.93	9.37E-07	1.06E-04	rs6478712	-4.38	5.58E-06	1.36E-03
<i>PBX3</i>	Colon transverse	9	375	rs12352375	-4.93	1.58E-07	3.73E-05	rs6478712	-4.38	2.42E-05	6.41E-03
<i>PBX3</i>	Esophagus gastroesophageal junction	9	377	rs12352375	-4.93	1.84E-06	3.64E-04	rs6478712	-4.38	6.57E-05	1.70E-02
<i>SKOR1</i>	Esophagus mucosa	15	341	rs8025889	4.98	3.47E-04	1.47E-02	rs12905397	4.03	3.31E-04	1.26E-02
<i>PBX3</i>	Esophagus muscularis	9	377	rs12352375	-4.93	2.21E-06	6.76E-04	rs6478712	-4.38	9.63E-06	3.20E-03
<i>PBX3</i>	Heart atrial appendage	9	375	rs12352375	-4.93	1.11E-06	2.79E-04	rs6478712	-4.38	7.00E-06	1.90E-03
<i>SKOR1</i>	Heart atrial appendage	15	350	rs8025889	4.98	5.39E-04	2.07E-02	rs12905397	4.03	2.57E-04	1.77E-02
<i>PBX3</i>	Heart left ventricle	9	375	rs12352375	-4.93	2.27E-06	5.02E-04	rs6478712	-4.38	2.18E-05	5.23E-03
<i>PBX3</i>	Lung	9	377	rs12352375	-4.93	2.05E-06	6.40E-04	rs6478712	-4.38	3.28E-05	1.09E-02
<i>HYKK</i>	Muscle skeletal	15	422	rs34016249	3.31	4.58E-04	1.54E-02	rs8040868	13.47	1.46E-12	2.43E-10
<i>TRIM38</i>	Pancreas	6	661	rs1614887	7.04	5.71E-04	1.99E-02	rs13212534	6.62	2.77E-05	6.81E-03
<i>FUBP1</i>	Pancreas	1	332	rs17391694	5.16	3.11E-06	3.09E-04	rs17101224	-3.37	2.74E-05	1.46E-02
<i>PBX3</i>	Pancreas	9	378	rs12352375	-4.93	3.26E-06	6.55E-04	rs6478712	-4.38	1.19E-05	2.75E-03
<i>SKOR1</i>	Pancreas	15	351	rs8025889	4.98	9.68E-04	4.63E-02	rs12905397	4.03	2.82E-04	1.09E-02
<i>SORCS3</i>	Pituitary	10	488	rs1021362	6.17	4.94E-06	1.20E-03	rs4532962	3.68	3.21E-04	4.11E-02
<i>PBX3</i>	Skin not sun exposed suprapubic	9	376	rs12352375	-4.93	2.27E-06	2.40E-04	rs6478712	-4.38	2.18E-05	7.63E-03
<i>SKOR1</i>	Skin not sun exposed suprapubic	15	341	rs8025889	4.98	7.45E-04	2.18E-02	rs12905397	4.03	3.89E-04	2.33E-02
<i>PBX3</i>	Testis	9	377	rs12352375	-4.93	9.63E-07	1.88E-04	rs6478712	-4.38	9.19E-05	3.83E-02

TWAS, transcriptome-wide association study; GERD, gastroesophageal reflux disease; LUSC, lung squamous cell carcinoma; CHR, chromosome; SNP, single nucleotide polymorphism; GWAS, genome-wide association study; FDR, false discovery rate.

Table S11 TWAS-identified shared gene-tissue pairs between GERD and SCLC

Gene	Tissue type	CHR	SNP Num	Gastroesophageal reflux				Small-cell lung cancer			
				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	rs12524934	-4.56	1.62E-05	1.51E-03	rs12524934	3.88	3.71E-04	3.89E-02
<i>ASCC3</i>	Artery coronary	6	299	rs12524934	-4.56	7.10E-05	2.07E-03	rs12524934	3.88	2.26E-04	3.96E-02
<i>ENSG00000265055</i>	Artery tibial	17	320	rs6504573	4.80	9.50E-05	5.00E-03	rs11867618	4.28	7.83E-05	4.49E-02
<i>C6orf163</i>	Brain frontal cortex BA9	6	409	rs2268992	4.39	2.07E-03	2.99E-02	rs12663587	3.50	2.57E-04	4.86E-02
<i>ENSG00000237854</i>	Brain frontal cortex BA9	17	318	rs6504573	4.80	1.18E-04	3.91E-03	rs11867618	4.28	8.59E-05	1.98E-02
<i>NBN</i>	Brain putamen basal ganglia	8	375	rs40457	3.33	2.34E-03	3.98E-02	rs16902897	4.28	3.93E-05	6.01E-03
<i>ENSG00000278730</i>	Colon sigmoid	17	321	rs6504573	4.71	7.11E-04	1.72E-02	rs11867618	4.34	2.54E-04	3.51E-02
<i>BPTF</i>	Heart atrial appendage	17	318	rs6504573	4.51	7.11E-05	3.73E-03	rs7216064	4.10	6.74E-05	1.91E-02
<i>ENSG00000265055</i>	Heart atrial appendage	17	320	rs6504573	4.80	6.63E-05	3.73E-03	rs11867618	4.28	9.19E-05	1.91E-02
<i>GMPPB</i>	Minor salivary gland	3	313	rs2526743	-9.82	3.70E-14	2.78E-12	rs11130208	3.69	2.22E-04	3.31E-02
<i>HYKK</i>	Muscle skeletal	15	422	rs34016249	3.31	4.58E-04	1.54E-02	rs2036527	9.35	2.48E-07	4.13E-05
<i>C17orf58</i>	Pituitary	17	329	rs6504573	4.66	1.02E-04	5.20E-03	rs7216064	4.10	1.00E-04	2.81E-02
<i>ENSG00000265055</i>	Prostate	17	319	rs6504573	4.80	3.41E-04	7.65E-03	rs11867618	4.31	6.72E-05	1.88E-02
<i>ENSG00000267708</i>	Testis	17	320	rs6504573	4.35	2.42E-04	1.23E-02	rs11867618	4.40	6.64E-05	2.20E-02
<i>ENSG00000274712</i>	Uterus	17	343	rs6504573	4.32	5.66E-04	1.43E-02	rs11867618	4.46	2.16E-04	3.24E-02

GERD, gastroesophageal reflux disease; SCLC, small-cell lung cancer; CHR, chromosome; SNP, single nucleotide polymorphism; GWAS, genome-wide association study; FDR, false discovery rate.

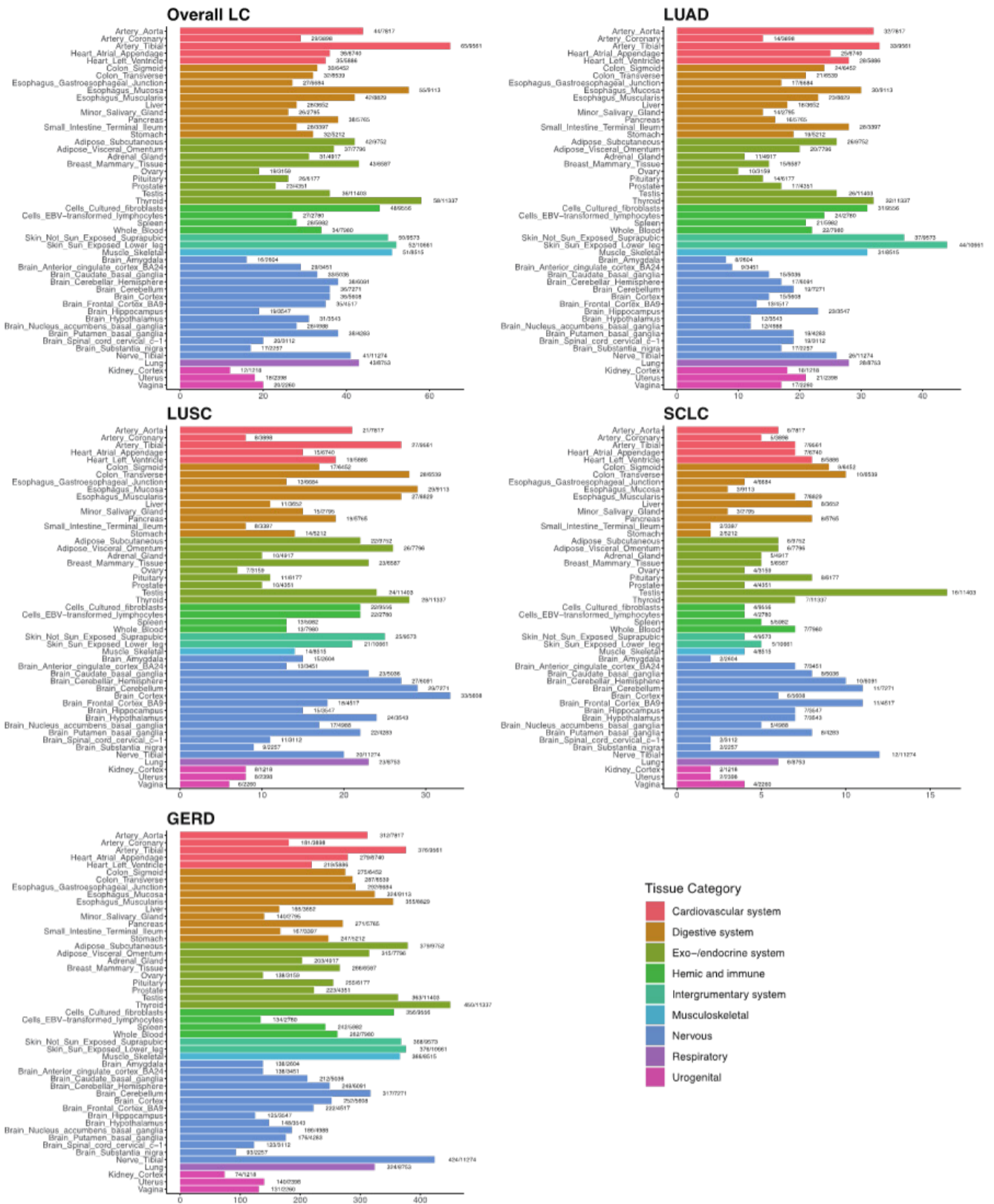


Figure S2 Number of TWAS significant genes for GERD and LC across 49 GTEx tissues (version 8). The X axis showcases the count of genes from GTEx tissues that meet the significance thresholds for multiple testing for each trait. The Y axis lists the respective GTEx tissues. Different tissue categories are indicated by distinct colors. The null hypothesis of TWAS assumes no expression-trait association, implying no genetic correlation between expression and a trait, under the condition of the observed GWAS statistics at the corresponding locus. In total, there are approximately 290,000 TWAS gene-tissue pairs undergoing testing across these 49 GTEx tissues. TWAS, transcriptome-wide association study; GERD, gastroesophageal reflux disease; LC, lung cancer; LUAD, lung adenocarcinoma; LUSC, lung squamous cell carcinoma; SCLC, small-cell lung cancer.

Table S12 Details of instrumental variables selected for GERD

SNP	Chromosome	Position	Effect allele	Other allele	Effect allele frequency	Beta	Standard error	Sample size	P value	R ²	F-statistic	Pleiotropic traits
rs12357321	10	21790476	G	A	0.6889	-0.0317	0.0052	367411	1.33E-09	4.31E-04	158.48	
rs1021363	10	106610839	A	G	0.3580	0.0312	0.0050	367411	5.10E-10	4.48E-04	164.66	
rs761777	10	134938075	A	G	0.7460	-0.0345	0.0055	367411	4.71E-10	4.52E-04	166.14	
rs10837002	11	38565727	C	G	0.6488	-0.0276	0.0050	367411	4.03E-08	3.48E-04	128.05	
rs7942368	11	76465362	C	T	0.7853	0.0340	0.0059	367411	9.54E-09	3.89E-04	142.99	
rs7104724	11	112837559	T	A	0.8833	-0.0416	0.0075	367411	3.01E-08	3.57E-04	131.39	Past tobacco smoking
rs2734839	11	113286490	C	T	0.3933	0.0283	0.0049	367411	8.79E-09	3.84E-04	140.96	
rs1479405	12	15387519	C	T	0.6783	-0.0315	0.0052	367411	9.85E-10	4.33E-04	159.01	
rs773109	12	56374695	G	A	0.6647	0.0381	0.0051	367411	8.71E-14	6.46E-04	237.34	
rs324769	12	83969240	C	T	0.5508	0.0268	0.0048	367411	3.05E-08	3.55E-04	130.33	
rs1716171	12	123716376	C	T	0.2100	-0.0384	0.0059	367411	7.82E-11	4.89E-04	179.81	
rs9542729	13	31833578	C	G	0.7976	0.0363	0.0060	367411	1.41E-09	4.26E-04	156.57	
rs1334297	13	58335375	G	A	0.2658	0.0388	0.0055	367411	1.14E-12	5.87E-04	215.96	
rs9540720	13	66922705	A	G	0.5211	-0.0267	0.0048	367411	3.01E-08	3.56E-04	130.77	
rs9517313	13	99105892	G	C	0.6168	-0.0331	0.0049	367411	2.05E-11	5.18E-04	190.55	
rs957345	14	75276079	C	G	0.4598	-0.0291	0.0048	367411	1.72E-09	4.19E-04	154.12	
rs17701934	14	89394474	T	C	0.5629	0.0265	0.0048	367411	4.60E-08	3.45E-04	126.91	
rs942065	14	94032065	G	A	0.3660	-0.0307	0.0050	367411	8.45E-10	4.38E-04	161.17	
rs10133111	14	103377321	G	A	0.8370	-0.0418	0.0065	367411	1.35E-10	4.76E-04	175.14	
rs11645288	16	51172677	G	A	0.8087	-0.0339	0.0061	367411	2.78E-08	3.56E-04	130.93	
rs9940128	16	53800754	G	A	0.5782	-0.0333	0.0049	367411	8.06E-12	5.39E-04	198.25	Type II diabetes
rs12598916	16	60658751	C	G	0.7252	0.0333	0.0054	367411	6.87E-10	4.41E-04	162.08	
rs7206608	16	82872628	C	G	0.6771	-0.0292	0.0051	367411	1.46E-08	3.72E-04	136.61	
rs12453010	17	50316131	C	T	0.6052	-0.0297	0.0049	367411	1.75E-09	4.21E-04	154.90	
rs12967855	18	35138245	A	G	0.3296	0.0365	0.0051	367411	1.09E-12	5.90E-04	216.97	
rs1431196	18	50832102	A	G	0.5716	-0.0324	0.0049	367411	2.65E-11	5.15E-04	189.22	
rs1942262	18	52873317	G	A	0.7086	-0.0315	0.0053	367411	2.60E-09	4.10E-04	150.64	
rs7241572	18	77580712	G	A	0.7909	-0.0366	0.0060	367411	9.49E-10	4.42E-04	162.42	
rs9636202	19	18449238	G	A	0.7334	0.0350	0.0055	367411	1.51E-10	4.80E-04	176.54	
rs2023878	19	18834124	C	T	0.8076	0.0363	0.0061	367411	3.04E-09	4.09E-04	150.37	
rs569356	1	29136686	A	G	0.8592	0.0379	0.0069	367411	4.07E-08	3.48E-04	127.89	
rs3766823	1	32197257	G	A	0.8285	-0.0394	0.0064	367411	7.09E-10	4.40E-04	161.80	
rs2782641	1	44013355	G	A	0.3873	-0.0271	0.0049	367411	4.33E-08	3.48E-04	128.00	
rs1937450	1	66478840	T	G	0.4623	-0.0316	0.0048	367411	7.07E-11	4.96E-04	182.31	
rs2815749	1	72814783	A	G	0.1990	-0.0389	0.0060	367411	1.07E-10	4.82E-04	177.13	Whole body fat mass
rs17379561	1	98340139	A	T	0.8556	-0.0531	0.0069	367411	1.08E-14	6.96E-04	255.87	
rs861575	1	184725099	T	C	0.5759	-0.0276	0.0049	367411	1.63E-08	3.73E-04	136.94	
rs7527682	1	189172684	A	G	0.4628	0.0267	0.0048	367411	3.13E-08	3.54E-04	130.12	
rs7541875	1	190957589	A	G	0.5739	-0.0274	0.0048	367411	1.61E-08	3.67E-04	134.92	
rs903678	1	201809918	G	A	0.6606	-0.0277	0.0051	367411	4.89E-08	3.45E-04	126.80	Whole body fat mass
rs1883842	20	41223062	T	G	0.7207	-0.0308	0.0054	367411	9.27E-09	3.83E-04	140.66	
rs2834005	21	34291708	T	C	0.6850	-0.0297	0.0052	367411	9.42E-09	3.81E-04	139.91	
rs2183588	21	42626882	A	G	0.3506	-0.0288	0.0051	367411	1.22E-08	3.79E-04	139.28	
rs2838771	21	46501576	G	C	0.3533	0.0281	0.0051	367411	2.91E-08	3.61E-04	132.60	
rs9615905	22	48875699	C	T	0.5418	-0.0276	0.0048	367411	1.21E-08	3.77E-04	138.67	
rs4300861	2	22549441	C	T	0.6179	-0.0307	0.0049	367411	5.43E-10	4.45E-04	163.72	
rs12997558	2	41704580	G	A	0.6412	-0.0278	0.0050	367411	3.04E-08	3.56E-04	130.86	
rs1011407	2	60665768	A	G	0.8784	0.0421	0.0074	367411	1.09E-08	3.78E-04	138.94	
rs4851239	2	100489966	C	T	0.6204	0.0329	0.0050	367411	3.24E-11	5.08E-04	186.88	
rs6722661	2	100806588	G	A	0.6353	0.0323	0.0050	367411	1.15E-10	4.82E-04	177.20	
rs6711584	2	104421692	G	A	0.5480	-0.0323	0.0048	367411	2.66E-11	5.15E-04	189.45	Whole body fat mass

Table S12 (continued)

Table S12 (continued)

SNP	Chromosome	Position	Effect allele	Other allele	Effect allele frequency	Beta	Standard error	Sample size	P value	R ²	F-statistic	Pleiotropic traits
rs13409451	2	144257639	A	G	0.6076	0.0277	0.0049	367411	1.93E-08	3.66E-04	134.56	
rs2358016	2	162007430	C	G	0.5019	-0.0283	0.0048	367411	4.17E-09	4.00E-04	146.88	
rs1596747	2	193802478	A	G	0.5059	-0.0311	0.0048	367411	1.00E-10	4.83E-04	177.59	
rs7600261	2	212622818	C	T	0.6936	-0.0338	0.0052	367411	9.47E-11	4.86E-04	178.53	
rs7612999	3	35678337	G	A	0.7547	-0.0305	0.0056	367411	4.90E-08	3.45E-04	126.80	
rs6441814	3	44049114	G	A	0.5294	0.0284	0.0048	367411	3.86E-09	4.03E-04	147.97	
rs3172494	3	48731487	G	T	0.8930	0.0454	0.0078	367411	6.71E-09	3.93E-04	144.51	
rs2240326	3	50128386	G	A	0.5262	0.0472	0.0048	367411	1.13E-22	1.11E-03	408.04	
rs2016933	3	65653157	C	G	0.2699	0.0310	0.0054	367411	1.04E-08	3.79E-04	139.45	
rs6780459	3	104624105	A	T	0.2534	-0.0306	0.0055	367411	3.14E-08	3.53E-04	129.79	
rs7685686	4	3207142	A	G	0.5776	0.0279	0.0049	367411	1.14E-08	3.80E-04	139.82	
rs2164300	4	67813017	C	T	0.4767	0.0265	0.0048	367411	4.13E-08	3.50E-04	128.53	
rs7675588	4	80734978	C	A	0.2054	0.0335	0.0060	367411	1.80E-08	3.67E-04	134.81	
rs13107325	4	103188709	C	T	0.9256	-0.0701	0.0092	367411	2.20E-14	6.78E-04	249.29	Body mass index
rs1510719	4	140938116	T	C	0.6166	0.0389	0.0049	367411	3.84E-15	7.15E-04	262.85	
rs10010963	4	159839313	C	T	0.3836	0.0270	0.0049	367411	4.92E-08	3.44E-04	126.52	
rs1592757	5	103889998	G	C	0.6442	-0.0311	0.0050	367411	6.00E-10	4.44E-04	163.02	
rs11953061	5	120144025	C	T	0.6611	-0.0282	0.0051	367411	3.10E-08	3.55E-04	130.60	
rs329122	5	133864599	G	A	0.5804	0.0290	0.0049	367411	3.05E-09	4.08E-04	150.08	Type 2 diabetes
rs4461735	6	16946758	A	G	0.7620	0.0346	0.0056	367411	8.78E-10	4.35E-04	159.82	
rs9358901	6	26024436	G	T	0.3067	0.0327	0.0052	367411	3.68E-10	4.54E-04	166.77	
rs2145318	6	26496603	T	A	0.5134	-0.0353	0.0048	367411	2.03E-13	6.24E-04	229.45	
rs3828917	6	31465917	G	T	0.9582	-0.0671	0.0120	367411	2.27E-08	3.61E-04	132.68	
rs4713692	6	33807638	C	T	0.6322	0.0276	0.0050	367411	3.07E-08	3.55E-04	130.32	
rs205262	6	34563164	A	G	0.7328	-0.0348	0.0054	367411	1.38E-10	4.75E-04	174.47	Trunk predicted mass
rs9372625	6	98344031	G	A	0.6170	0.0377	0.0050	367411	2.62E-14	6.73E-04	247.33	
rs9373363	6	143150043	A	G	0.7464	0.0327	0.0056	367411	4.13E-09	4.04E-04	148.65	
rs12204714	6	152235339	C	T	0.3678	0.0288	0.0050	367411	7.92E-09	3.86E-04	141.94	
rs11762636	7	2061111	C	A	0.8197	0.0515	0.0063	367411	1.88E-16	7.83E-04	288.04	
rs10242223	7	3521573	A	G	0.3302	0.0282	0.0051	367411	3.79E-08	3.52E-04	129.48	Past tobacco smoking
rs2043539	7	12253880	G	A	0.5813	-0.0272	0.0049	367411	2.24E-08	3.60E-04	132.42	
rs215614	7	32347335	G	A	0.3703	0.0329	0.0050	367411	4.08E-11	5.03E-04	185.03	Whole body fat mass
rs2396133	7	109197067	A	G	0.5247	-0.0294	0.0048	367411	1.11E-09	4.30E-04	157.98	
rs2396766	7	114318071	G	A	0.5269	-0.0322	0.0048	367411	2.33E-11	5.17E-04	190.09	
rs2106353	7	126506598	G	T	0.7685	-0.0367	0.0057	367411	1.37E-10	4.80E-04	176.61	
rs3863241	8	73890335	C	T	0.4730	-0.0325	0.0048	367411	1.49E-11	5.27E-04	193.55	
rs903959	8	142630782	T	A	0.6007	-0.0292	0.0049	367411	2.99E-09	4.08E-04	149.96	
rs3793577	9	23737627	A	G	0.4617	-0.0270	0.0048	367411	2.49E-08	3.63E-04	133.49	
rs7032155	9	122672771	C	A	0.4082	-0.0278	0.0049	367411	1.63E-08	3.72E-04	136.74	
rs4382592	9	134870755	T	G	0.3005	0.0303	0.0053	367411	8.20E-09	3.85E-04	141.55	

F-statistic was calculated using the following formulas: $R^2=2 \times \beta^2 \times EAF \times (1 - EAF)$ 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 is the effect allele frequency. SNP, single nucleotide polymorphism; GERD, gastroesophageal reflux disease.

Table S13 Causal Analysis Using Summary Effect estimates (CAUSE) results for GERD on LC

Exposure	Outcome	Model 1	Model 2	Delta_ ELPD	se_delta_ ELPD	z score	γ (95% CI)	η (95% CI)	q (95% CI)	P value
GERD	LC	Null	Sharing	-19.0	5.2	-3.6	NA	0.49 (0.32, 0.75)	0.41 (0.22, 0.63)	1.30E-04
GERD	LC	Null	Causal	-24.0	6.6	-3.6	0.26 (0.17, 0.35)	0.02 (-1.11, 1.21)	0.04 (0, 0.26)	1.80E-04
GERD	LC	Sharing	Causal	-4.5	1.8	-2.5	NA	NA	NA	6.10E-03
GERD	LUAD	Null	Sharing	-4.6	2.4	-1.9	NA	0.53 (0.21, 1.19)	0.21 (0.03, 0.47)	2.60E-02
GERD	LUAD	Null	Causal	-8.0	4.0	-2.0	0.19 (0.09, 0.30)	0.04 (-1.52, 1.96)	0.03 (0, 0.25)	2.30E-02
GERD	LUAD	Sharing	Causal	-3.4	1.8	-1.9	NA	NA	NA	3.00E-02
GERD	LUSC	Null	Sharing	-13.0	4.4	-3.0	NA	0.73 (0.42, 1.25)	0.33 (0.14, 0.56)	1.40E-03
GERD	LUSC	Null	Causal	-17.0	5.6	-3.0	0.32 (0.19, 0.45)	0.07 (-1.77, 2.08)	0.04 (0, 0.25)	1.40E-03
GERD	LUSC	Sharing	Causal	-3.8	1.7	-2.3	NA	NA	NA	1.10E-02
GERD	SCLC	Null	Sharing	-13.0	4.4	-2.9	NA	1.14 (0.66, 1.87)	0.32 (0.14, 0.55)	1.60E-03
GERD	SCLC	Null	Causal	-16.0	5.7	-2.8	0.49 (0.28, 0.70)	-0.01 (-2.92, 2.73)	0.04 (0, 0.26)	2.50E-03
GERD	SCLC	Sharing	Causal	-3.1	1.7	-1.8	NA	NA	NA	3.90E-02

Model 1 and model 2 represent the models being compared (null, sharing, or causal). The fit of the models is assessed by examining the change in Expected Log Pointwise Posterior Density (ELPD), denoted as Delta_ELPD; negative values of z indicate that model 2 fits the data better. Delta_ELPD, estimated difference in ELPD; se_delta_ELPD, estimated standard error of delta_ELPD; z, delta_ELPD/se_delta_ELPD; GERD, gastroesophageal reflux disease; LC, lung cancer; LUAD, lung adenocarcinoma; LUSC, lung squamous cell carcinoma; SCLC, small-cell lung cancer; γ (gamma), estimate of causal effect if causal model is correct; η (eta), estimate of correlated pleiotropy; q, proportion of effect due to correlated pleiotropy; CI, confidence interval; NA, not applicable.

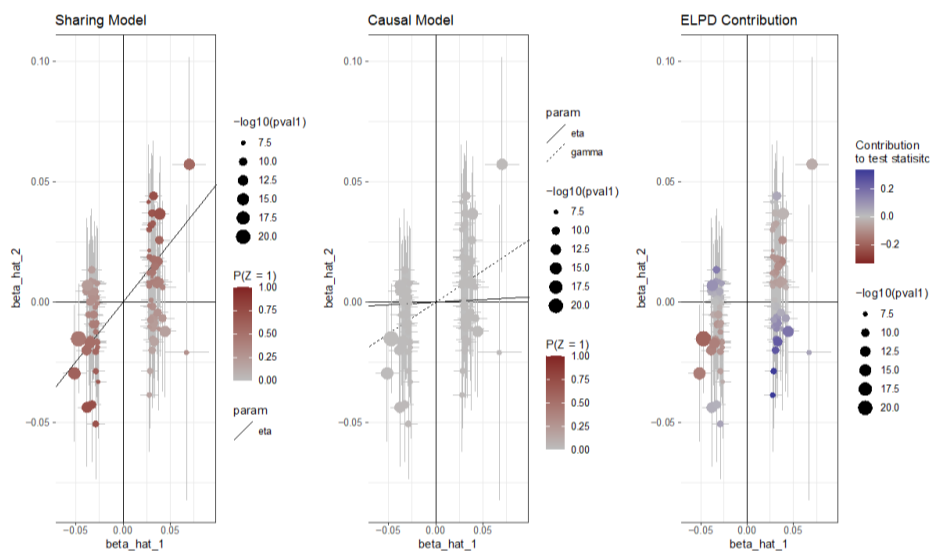


Figure S3 Causal Analysis Using Summary Effect estimates (CAUSE) results for GERD on overall LC. Plots illustrate the sharing, causal and expected log pointwise posterior density (ELPD) models for GERD on LC. CAUSE shows that there is significant evidence supporting both the sharing (correlated pleiotropy) and causal models compared to the null (no effect) model. Comparing both shared and causal models, there is significant evidence indicating that the causal model fits the data better than the sharing model, indicating that correlated pleiotropy could be discounted. Gamma represents the estimate of causal effect if causal model is correct, while Eta represents the estimate of correlated pleiotropy. GERD, gastroesophageal reflux disease; LC, lung cancer.

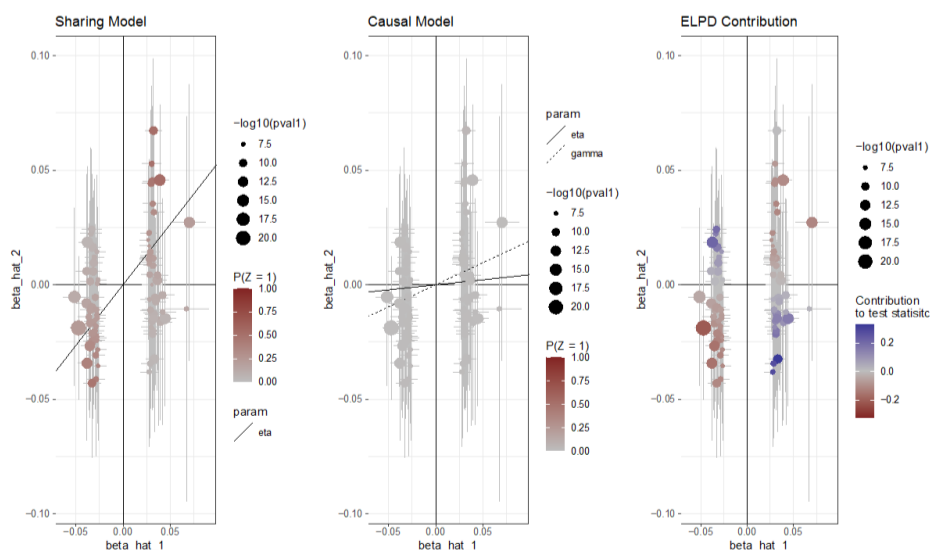


Figure S4 Causal Analysis Using Summary Effect estimates (CAUSE) results for GERD on LUAD. Plots illustrate the sharing, causal and expected log pointwise posterior density (ELPD) models for GERD on LUAD. CAUSE shows that there is significant evidence supporting both the sharing (correlated pleiotropy) and causal models compared to the null (no effect) model. Comparing both shared and causal models, there is significant evidence indicating that the causal model fits the data better than the sharing model, indicating that correlated pleiotropy could be discounted. Gamma represents the estimate of causal effect if causal model is correct, while Eta represents the estimate of correlated pleiotropy. GERD, gastroesophageal reflux disease; LUAD, lung adenocarcinoma.

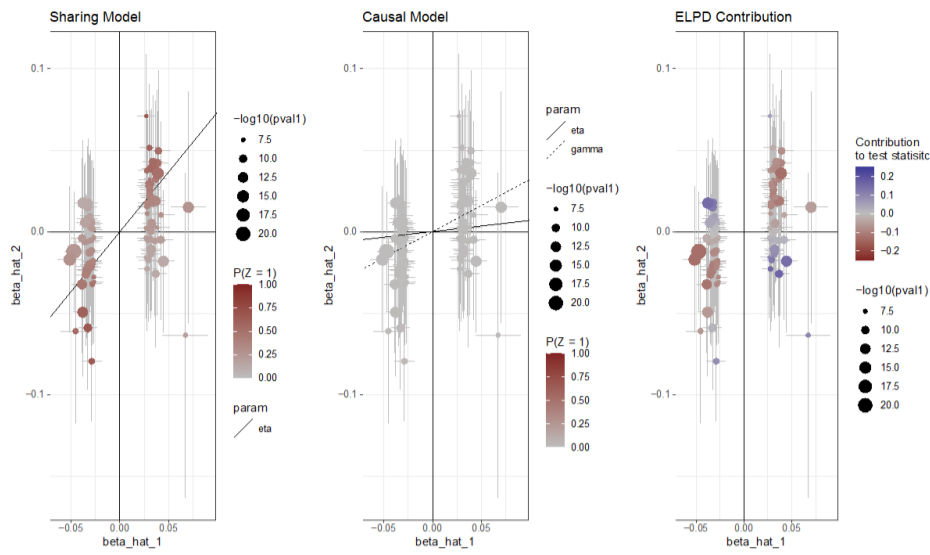


Figure S5 Causal Analysis Using Summary Effect estimates (CAUSE) results for GERD on LUSC. Plots illustrate the sharing, causal and expected log pointwise posterior density (ELPD) models for GERD on LUSC. CAUSE shows that there is significant evidence supporting both the sharing (correlated pleiotropy) and causal models compared to the null (no effect) model. Comparing both shared and causal models, there is significant evidence indicating that the causal model fits the data better than the sharing model, indicating that correlated pleiotropy could be discounted. Gamma represents the estimate of causal effect if causal model is correct, while eta represents the estimate of correlated pleiotropy. GERD, gastroesophageal reflux disease; LUSC, lung squamous cell carcinoma.

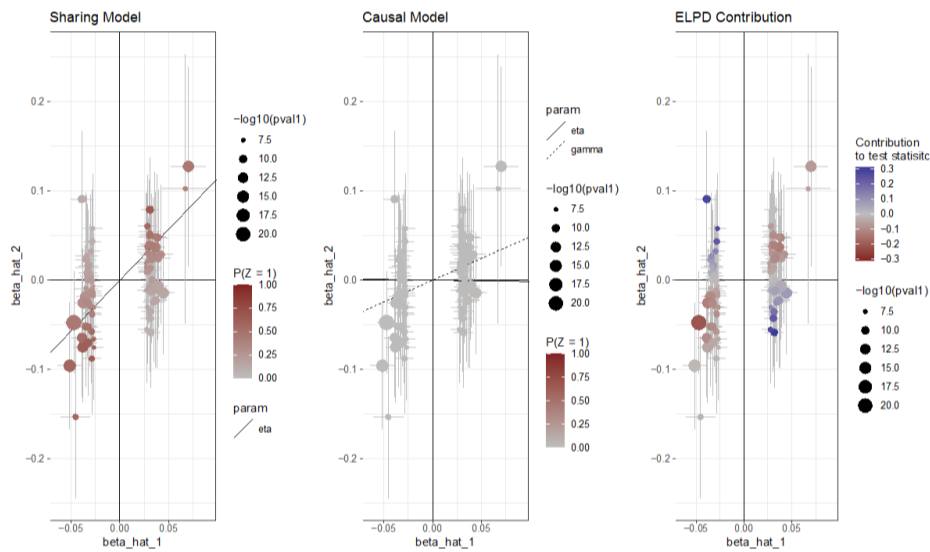


Figure S6 Causal Analysis Using Summary Effect estimates (CAUSE) results for GERD on SCLC. Plots illustrate the sharing, causal and expected log pointwise posterior density (ELPD) models for GERD on SCLC. CAUSE shows that there is significant evidence supporting both the sharing (correlated pleiotropy) and causal models compared to the null (no effect) model. Comparing both shared and causal models, there is significant evidence indicating that the causal model fits the data better than the sharing model, indicating that correlated pleiotropy could be discounted. Gamma represents the estimate of causal effect if causal model is correct, while eta represents the estimate of correlated pleiotropy. GERD, gastroesophageal reflux disease; SCLC, small-cell lung cancer.

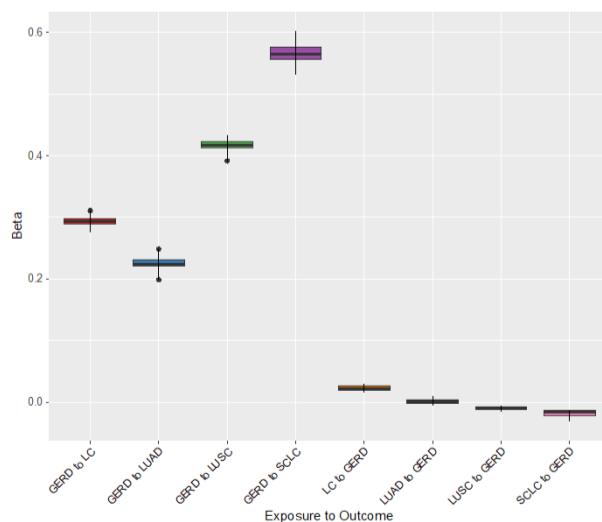


Figure S7 Box plot of the leave-one-out analysis. Each SNP was systematically removed at a time, and inverse-variance weighted analysis was performed using the remaining SNPs. Beta, effect allele beta coefficient; GERD, gastroesophageal reflux disease; LC, lung cancer; LUAD, lung adenocarcinoma; LUSC, lung squamous cell carcinoma; SCLC, small-cell lung cancer.

Table S14 Power of mendelian randomization analysis of GERD on LC

Exposure	Outcome	Power
Gastroesophageal reflux disease	Lung cancer	100%
	Lung adenocarcinoma	100%
	Lung squamous cell carcinoma	100%
	Small-cell lung cancer	100%

The power of MR analyses was calculated based on an online calculator (<https://shiny.cnsngenomics.com/mRnd/>). The calculation incorporated the type I error of 0.05, sample size, proportion of cases (Table S1), explained genetic variation (Table S12), and odds ratios from IVW analyses (Figure 4). GERD, gastroesophageal reflux disease; LC, lung cancer; MR, Mendelian randomization; IVW, inverse variance-weighted.

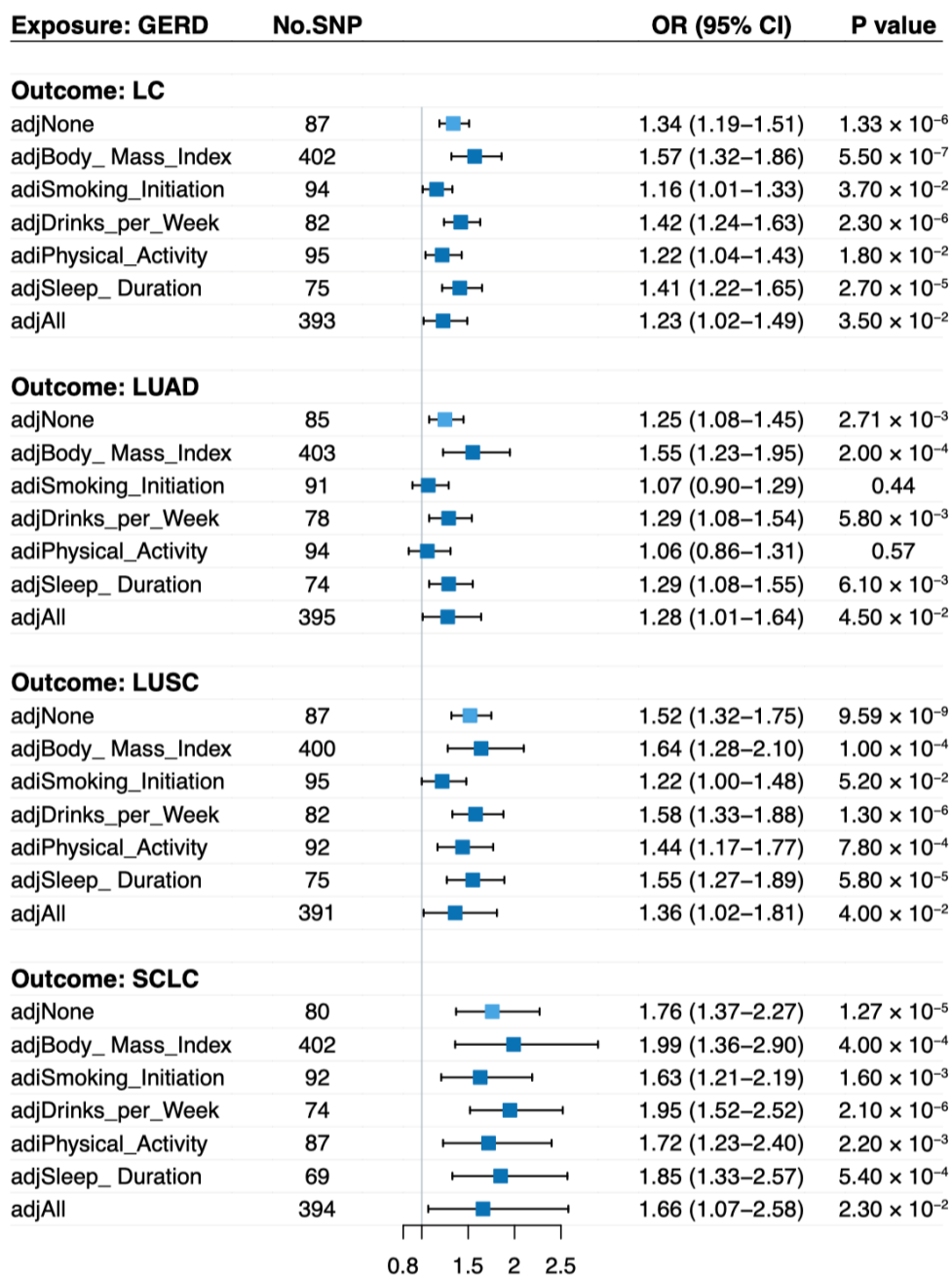


Figure S8 Multivariable Mendelian randomization of genetically predicted GERD on LC. The estimated effect sizes were adjusted for each potential confounder separately and combined. The x-axis indicates the genetically predicted confounder for which adjustment was made. The boxes represent the point estimates of the causal effects of genetically predicted GERD on LC, with error bars representing the 95% confidence intervals. “adjNone” refers to the point estimates of the causal effects of genetically predicted GERD on LC using univariable Mendelian randomization. GERD, gastroesophageal reflux disease; LC, lung cancer; LUAD, lung adenocarcinoma; LUSC, lung squamous cell carcinoma; SCLC, small-cell lung cancer; SNP, single nucleotide polymorphism; OR, odds ratio; CI, confidence interval.

Table S15 Details of instrumental variables selected for lung cancer

Phenotype	SNP	Chromosome	Position	Effect allele	Other allele	Effect allele frequency	Beta	Standard error	Sample size	P value	R ²	F-statistic
Lung cancer	rs10265693	7	130720805	G	A	0.0930	0.0861	0.0197	85716	1.87E-06	1.25E-03	107.45
Lung cancer	rs1039766	2	65520145	T	C	0.1544	0.1541	0.0163	85716	2.05E-06	6.20E-03	534.80
Lung cancer	rs10904377	10	4978419	T	G	0.0380	0.0491	0.0284	85716	2.24E-06	1.76E-04	15.11
Lung cancer	rs11780471	8	27344719	A	G	0.0638	0.0596	0.0250	85716	1.69E-08	4.25E-04	36.40
Lung cancer	rs12081674	1	90337025	G	A	0.1810	0.1841	0.0154	85716	4.14E-06	1.00E-02	869.67
Lung cancer	rs150211	21	19415773	C	T	0.0411	0.0383	0.0326	85716	3.59E-06	1.16E-04	10.00
Lung cancer	rs17181550	17	70299958	G	T	0.4170	0.4265	0.0119	85716	1.98E-07	8.84E-02	8316.61
Lung cancer	rs17775239	8	128897079	A	T	0.2609	0.2615	0.0135	85716	2.78E-06	2.64E-02	2322.19
Lung cancer	rs1991625	2	153831482	G	A	0.3056	0.3221	0.0125	85716	3.99E-06	4.40E-02	3948.86
Lung cancer	rs239935	6	167411788	G	A	0.4816	0.4785	0.0118	85716	1.29E-08	1.14E-01	11062.39
Lung cancer	rs380286	5	1320247	A	G	0.4371	0.4226	0.0119	85716	1.51E-32	8.79E-02	8260.00
Lung cancer	rs631644	18	2280388	G	A	0.3878	0.4040	0.0139	85716	3.06E-06	7.75E-02	7200.82
Lung cancer	rs7805022	7	9825541	A	T	0.3398	0.3256	0.0125	85716	1.92E-06	4.76E-02	4281.52
Lung cancer	rs9869622	3	16671821	T	C	0.1863	0.1808	0.0152	85716	1.73E-06	9.91E-03	857.92
Lung adenocarcinoma	rs1039766	2	65520145	T	C	0.1539	0.1054	0.0224	66756	2.60E-06	2.89E-03	193.78
Lung adenocarcinoma	rs10445262	17	4943176	G	A	0.2437	0.0852	0.0186	66756	4.76E-06	2.68E-03	179.20
Lung adenocarcinoma	rs1056562	11	118125625	T	C	0.4731	0.1021	0.0162	66756	2.76E-10	5.20E-03	349.01
Lung adenocarcinoma	rs11591710	10	105687632	C	A	0.1368	0.1506	0.0230	66756	6.30E-11	5.35E-03	359.20
Lung adenocarcinoma	rs11848063	14	47235445	G	A	0.4083	-0.0777	0.0167	66756	3.31E-06	2.91E-03	195.05
Lung adenocarcinoma	rs11855650	15	70431773	T	G	0.3825	0.0829	0.0166	66756	5.60E-07	3.25E-03	217.65
Lung adenocarcinoma	rs12369136	12	20576874	G	A	0.0400	0.2042	0.0438	66756	3.21E-06	3.20E-03	214.32
Lung adenocarcinoma	rs1512829	11	9951257	G	A	0.2384	0.0915	0.0191	66756	1.66E-06	3.04E-03	203.69
Lung adenocarcinoma	rs17181550	17	70299958	G	T	0.4263	-0.0767	0.0165	66756	3.21E-06	2.88E-03	192.64
Lung adenocarcinoma	rs2320614	4	164070122	C	T	0.4002	0.0846	0.0164	66756	2.48E-07	3.44E-03	230.38
Lung adenocarcinoma	rs2608029	8	129170126	G	C	0.3510	0.0810	0.0168	66756	1.44E-06	2.99E-03	199.96
Lung adenocarcinoma	rs421629	5	1320136	A	G	0.4267	-0.1566	0.0163	66756	9.75E-22	1.20E-02	810.54
Lung adenocarcinoma	rs4236709	8	32410110	G	A	0.2178	0.1243	0.0193	66756	1.28E-10	5.27E-03	353.34
Lung adenocarcinoma	rs8108034	19	39813853	G	T	0.0988	0.1302	0.0281	66756	3.50E-06	3.02E-03	201.96
Lung adenocarcinoma	rs885518	9	21830157	G	A	0.1011	0.1545	0.0253	66756	9.96E-10	4.34E-03	291.05
Lung squamous cell carcinoma	rs1108581	9	136505241	G	A	0.2034	-0.1154	0.0235	63053	9.09E-07	4.31E-03	273.09
Lung squamous cell carcinoma	rs13031455	2	17784157	C	T	0.4048	-0.0899	0.0190	63053	2.23E-06	3.89E-03	246.29
Lung squamous cell carcinoma	rs1333040	9	22083404	C	T	0.4579	0.0936	0.0189	63053	7.02E-07	4.35E-03	275.62
Lung squamous cell carcinoma	rs1534979	20	2331513	T	C	0.3242	0.0908	0.0199	63053	4.90E-06	3.61E-03	228.56
Lung squamous cell carcinoma	rs2674946	17	13066819	T	A	0.2791	0.0978	0.0211	63053	3.74E-06	3.85E-03	243.67
Lung squamous cell carcinoma	rs3754287	1	41952597	T	C	0.1426	0.1299	0.0271	63053	1.66E-06	4.13E-03	261.18
Lung squamous cell carcinoma	rs4453114	10	4961021	C	T	0.0508	0.2072	0.0436	63053	2.04E-06	4.14E-03	262.27
Lung squamous cell carcinoma	rs467095	5	1336221	C	T	0.4269	-0.1788	0.0191	63053	6.73E-21	1.56E-02	1002.37
Lung squamous cell carcinoma	rs6957511	7	130668618	C	T	0.3978	0.0951	0.0194	63053	9.78E-07	4.33E-03	274.23
Lung squamous cell carcinoma	rs7591446	2	45834076	T	C	0.1903	-0.1075	0.0235	63053	4.73E-06	3.56E-03	225.23
Lung squamous cell carcinoma	rs7658584	4	89096641	A	G	0.1546	0.1194	0.0253	63053	2.41E-06	3.73E-03	235.95
Lung squamous cell carcinoma	rs8040868	15	78911181	C	T	0.4135	0.2550	0.0189	63053	2.50E-41	3.15E-02	2053.12
Lung squamous cell carcinoma	rs9602270	13	84281063	T	A	0.0486	0.2385	0.0467	63053	3.28E-07	5.26E-03	333.56
Small-cell lung cancer	rs1703426	5	133185535	T	C	0.1749	-0.1861	0.0388	24108	1.59E-06	1.00E-02	243.55
Small-cell lung cancer	rs17185553	9	17934120	C	G	0.0810	0.2575	0.0524	24108	8.94E-07	9.88E-03	240.45
Small-cell lung cancer	rs3134425	11	122709178	T	C	0.3810	-0.1497	0.0311	24108	1.47E-06	1.06E-02	257.62
Small-cell lung cancer	rs6463739	7	7906724	C	G	0.4033	-0.1445	0.0304	24108	1.94E-06	1.01E-02	244.84

F-statistic was calculated using the following formulas: $R^2=2 \times \beta^2 \times EAF \times (1 - EAF)$ 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 is the effect allele frequency. SNP, single nucleotide polymorphism.