

**Supplementary Table 1.** Characteristics of ESCC cases and controls used in the study\*

Study/phase	Controls			Cases		
	N	Age, mean (s.d.)	Sex, male (%)	N	Age, mean (s.d.)	Sex, male (%)
NCI scan	2701	57.03 (9.56)	64.20	2013	56.28 (8.74)	60.01
Henan scan	1083	47.30 (14.91)	50.09	1375	59.04 (9.60)	57.83
Beijing scan	2004	61.41 (8.51)	83.48	1958	59.79 (9.74)	79.93
Henan replication	4972	49.47 (12.67)	51.59	4850	60.53 (9.00)	61.42
Beijing replication	5086	56.39 (14.17)	76.03	4804	60.24 (9.07)	76.64

\* Nine subjects from the NCI and Henan scans were the same individuals and they were used only once in the joint analysis

**Supplementary Table 2.** Summary of SNPs prior to imputation

<b>GWAS scan</b>	<b>NCI</b>	<b>Beijing</b>	<b>Henan</b>	<b>Combined</b>
PreQC (1)	556,896	660,020	626,865	
QC excludes	95,481	7,093	155,425	
PostQC/PreImputation	461,415	652,927	471,440	
PostImputation (2)	40,497,507	40,499,458	40,497,507	
Merging (3)				40,373,742
QC excludes (4)				32,817,527
Final number of SNPs				7,556,215

Notes:

- (1) Overlap in the number of SNPs among all three GWAS scans after QC is 130,787;
- (2) Overlap in the number of SNPs after imputation is 40,497,507;
- (3) Incompatible SNPs among sets were automatically excluded;
- (4) Excluded SNPs with INFO < 0.3 or MAF < 0.01 in study control population

Supplementary Table 3. Replication data testing for 14 SNPs that passed Stage 1

SNP	CHR	LOC	GROUP	CATEGORY*	INFO	NUM_CONTROL	NUM_CASE	REFERENCE_ALLELE	EFFECT_ALLELE	EFFECT_ALLELE_FREQ_CONTROL	EFFECT_ALLELE_FREQ_CASE	OR	CI	P	P heterog.
rs7447927	chr5	138861146	3 scan analysis (Stage 1)	i,i	0.957	5786	5336	C	G	0.460	0.451	0.87	(0.82-0.92)	4.07E-06	
rs7447927	chr5	138861146	Henan Replication	g	1.000	4802	4486	C	G	0.489	0.438	0.80	(0.75-0.86)	2.70E-11	
rs7447927	chr5	138861146	Beijing Replication	g	1.000	5079	4797	C	G	0.431	0.397	0.87	(0.82-0.92)	2.92E-06	
rs7447927	chr5	138861146	Combined			15667	14619					0.85	(0.82-0.88)	7.72E-20	1.31E-01
rs1642764	chr17	7557834	3 scan analysis (Stage 1)	i,i	0.865	5786	5336	C	T	0.499	0.456	0.84	(0.79-0.89)	3.91E-08	
rs1642764	chr17	7557834	Henan Replication	g	1.000	4634	4694	C	T	0.484	0.470	0.93	(0.87-0.99)	2.67E-02	
rs1642764	chr17	7557834	Beijing Replication	g	1.000	5054	4777	C	T	0.520	0.483	0.86	(0.81-0.92)	1.55E-06	
rs1642764	chr17	7557834	Combined			15474	14807					0.88	(0.85-0.91)	3.10E-13	7.70E-02
rs35597309	chr6	32589266	3 scan analysis (Stage 1)	i,i	0.921	5787	5336	G	A	0.072	0.094	1.32	(1.18-1.47)	6.17E-07	
rs35597309	chr6	32589266	Henan Replication	g	1.000	4659	4597	G	A	0.067	0.085	1.23	(1.09-1.38)	1.00E-03	
rs35597309	chr6	32589266	Beijing Replication	g	1.000	5079	4786	G	A	0.075	0.080	1.05	(0.94-1.17)	3.59E-01	
rs35597309	chr6	32589266	Combined			15525	14719					1.19	(1.12-1.27)	1.18E-07	1.50E-02
rs61271866	chr9	21997015	3 scan analysis (Stage 1)	i,i	0.982	5786	5336	T	A	0.190	0.225	1.22	(1.13-1.31)	5.18E-08	
rs61271866	chr9	21997015	Henan Replication	g	1.000	4903	4810	T	A	0.201	0.214	1.09	(1.01-1.18)	2.36E-02	
rs61271866	chr9	21997015	Beijing Replication	g	1.000	5042	4746	T	A	0.201	0.210	1.03	(0.96-1.11)	4.50E-01	
rs61271866	chr9	21997015	Combined			15731	14892					1.11	(1.07-1.16)	7.30E-07	4.36E-03
rs7822239	chr8	133119961	3 scan analysis (Stage 1)	i,i	0.986	5787	5336	C	A	0.270	0.236	0.86	(0.81-0.92)	1.14E-05	
rs7822239	chr8	133119961	Henan Replication	g	1.000	4577	4501	C	A	0.252	0.244	0.97	(0.90-1.04)	3.82E-01	
rs7822239	chr8	133119961	Beijing Replication	g	1.000	5044	4787	C	A	0.277	0.264	0.93	(0.87-0.99)	2.42E-02	
rs7822239	chr8	133119961	Combined			15408	14624					0.91	(0.88-0.95)	8.48E-06	7.05E-02
rs4252725	chr1	204513256	3 scan analysis (Stage 1)	g,i	1.000	5787	5337	A	G	0.680	0.653	0.89	(0.83-0.94)	1.00E-04	
rs4252725	chr1	204513256	Henan Replication	g	1.000	4907	4817	A	G	0.670	0.653	0.92	(0.86-0.98)	1.44E-02	
rs4252725	chr1	204513256	Beijing Replication	g	1.000	5033	4764	A	G	0.673	0.668	0.97	(0.91-1.03)	2.86E-01	
rs4252725	chr1	204513256	Combined			15727	14918					0.92	(0.89-0.96)	1.69E-05	1.52E-01
rs9323746	chr14	84920960	3 scan analysis (Stage 1)	g,g	1.000	5787	5337	C	T	0.351	0.377	1.15	(1.09-1.22)	3.59E-06	
rs9323746	chr14	84920960	Henan Replication	g	1.000	4896	4800	C	T	0.365	0.376	1.07	(1.00-1.14)	5.85E-02	
rs9323746	chr14	84920960	Beijing Replication	g	1.000	5078	4788	C	T	0.372	0.369	1.01	(0.95-1.08)	7.04E-01	
rs9323746	chr14	84920960	Combined			15761	14925					1.08	(1.04-1.12)	5.65E-05	1.16E-02
rs7038507	chr9	122784665	3 scan analysis (Stage 1)	i,i	0.989	5787	5336	G	A	0.067	0.082	1.30	(1.16-1.45)	4.30E-06	
rs7038507	chr9	122784665	Beijing Replication	g	1.000	5083	4795	G	A	0.076	0.077	1.08	(0.96-1.20)	1.89E-01	
rs7038507	chr9	122784665	3 scan analysis (Stage 1)+Beijing Replication			10870	10131					1.18	(1.09-1.28)	2.88E-05	2.04E-02
rs1958578	chr14	34800823	3 scan analysis (Stage 1)	g,g	0.971	5787	5336	G	A	0.843	0.815	0.83	(0.77-0.90)	2.52E-06	
rs1958578	chr14	34800823	Henan Replication	g	1.000	4914	4821	G	A	0.830	0.827	0.99	(0.91-1.07)	7.49E-01	
rs1958578	chr14	34800823	Beijing Replication	g	1.000	5067	4759	G	A	0.850	0.841	0.95	(0.87-1.03)	1.87E-01	
rs1958578	chr14	34800823	Combined			15768	14916					0.91	(0.87-0.96)	1.65E-04	7.54E-03
rs27209	chr5	57625982	3 scan analysis (Stage 1)	i,i	0.979	5786	5336	G	A	0.440	0.470	1.15	(1.08-1.22)	4.33E-06	
rs27209	chr5	57623118	Beijing Replication	g	1.000	5082	4788	G	A	0.460	0.456	0.98	(0.92-1.04)	5.63E-01	
rs27209	chr5	57623118	3 scan analysis (Stage 1)+Beijing Replication			10868	10124					1.06	(1.02-1.11)	3.70E-03	3.01E-04
rs7999802	chr13	68134441	3 scan analysis (Stage 1)	g,i	0.995	5786	5337	T	C	0.872	0.893	1.26	(1.15-1.38)	6.12E-07	
rs7999802	chr13	68134441	Henan Replication	g	1.000	4814	4718	T	C	0.894	0.893	0.97	(0.87-1.07)	5.32E-01	
rs7999802	chr13	68134441	Beijing Replication	g	1.000	5063	4750	T	C	0.877	0.876	0.98	(0.89-1.07)	6.50E-01	
rs7999802	chr13	68134441	Combined			15663	14805					1.07	(1.01-1.13)	1.64E-02	5.15E-05
rs75791390	chr5	71457813	3 scan analysis (Stage 1)	i,i	0.929	5786	5336	A	G	0.613	0.651	1.15	(1.09-1.23)	3.79E-06	
rs75791390	chr5	71457813	Henan Replication	g	1.000	4875	4787	A	G	0.649	0.649	1.00	(0.93-1.07)	9.65E-01	
rs75791390	chr5	71452094	Beijing Replication	g	1.000	5081	4790	A	G	0.374	0.373	0.98	(0.92-1.04)	4.19E-01	
rs75791390	chr5	71452094	Combined			15742	14913					1.04	(1.01-1.08)	2.48E-02	2.02E-04
rs1917435	chr8	46923031	3 scan analysis (Stage 1)	i,i	0.991	5786	5336	C	T	0.687	0.674	0.88	(0.83-0.93)	2.92E-05	
rs1917435	chr8	46923031	Henan Replication	g	1.000	4907	4809	C	T	0.679	0.681	1.05	(0.98-1.12)	1.56E-01	
rs1917435	chr8	46923031	Beijing Replication	g	1.000	5069	4758	C	T	0.670	0.669	0.99	(0.93-1.05)	7.18E-01	
rs1917435	chr8	46923031	Combined			15762	14903					0.96	(0.93-1.00)	5.12E-02	3.70E-04
rs10935355	chr3	139543726	3 scan analysis (Stage 1)	g,i	0.980	5786	5336	A	T	0.230	0.202	0.85	(0.79-0.91)	5.42E-06	
rs10935355	chr3	139543726	Henan Replication	g	1.000	4902	4809	A	T	0.220	0.222	1.00	(0.93-1.08)	9.32E-01	
rs10935355	chr3	139543726	Beijing Replication	g	1.000	5080	4792	A	T	0.223	0.227	1.05	(0.98-1.13)	1.80E-01	
rs10935355	chr3	139543726	Combined			15768	14937					0.96	(0.92-1.00)	6.57E-02	7.24E-05

\*Categories in Stage 1 are listed in the order Beijing, Henan, and NCI, where 'g' indicates that the SNP was genotyped on the array and 'i' indicates that the SNP was imputed

Supplementary Table 4. Individual GWAS analysis results and meta-analysis

SNP	CHR	LOC	GROUP	CATEGORY*	INFO	NUM_CONTROL	NUM_CASE	REFERENCE_ALLELE	EFFECT_ALLELE	EFFECT_ALLELE FREQ_CONTROL	EFFECT_ALLELE FREQ_CASE	OR	CI	P	P heterog.
rs7447927	chr5	138861146	nci	i	0.962	2707	2021	C	G	0.472	0.458	0.9	(0.83-0.98)	1.60E-02	
rs7447927	chr5	138861146	beijing	i	0.948	2003	1957	C	G	0.424	0.441	0.9	(0.81-1.01)	7.06E-02	
rs7447927	chr5	138861146	henan	i	0.962	1082	1374	C	G	0.500	0.454	0.77	(0.68-0.88)	7.64E-05	
rs7447927	chr5	138861146	beijing+henan+nci			5792	5352					0.87	(0.82-0.92)	6.23E-06	1.16E-01
rs1642764	chr17	7557834	nci	i	0.899	2707	2021	C	T	0.488	0.444	0.84	(0.77-0.92)	1.21E-04	
rs1642764	chr17	7557834	beijing	i	0.806	2003	1957	C	T	0.514	0.468	0.88	(0.78-0.99)	3.12E-02	
rs1642764	chr17	7557834	henan	i	0.893	1082	1374	C	T	0.498	0.457	0.84	(0.74-0.96)	1.19E-02	
rs1642764	chr17	7557834	beijing+henan+nci			5792	5352					0.85	(0.80-0.91)	4.74E-07	8.33E-01
rs35597309	chr6	32589266	nci	i	0.910	2707	2022	G	A	0.077	0.109	1.43	(1.23-1.67)	4.27E-06	
rs35597309	chr6	32589266	beijing	i	0.933	2003	1957	G	A	0.069	0.079	1.02	(0.82-1.25)	8.83E-01	
rs35597309	chr6	32589266	henan	i	0.927	1082	1374	G	A	0.063	0.093	1.55	(1.22-1.97)	3.50E-04	
rs35597309	chr6	32589266	beijing+henan+nci			5792	5353					1.32	(1.19-1.48)	5.62E-07	1.18E-02
rs61271866	chr9	21997015	nci	i	0.988	2707	2021	T	A	0.182	0.231	1.34	(1.20-1.48)	7.72E-08	
rs61271866	chr9	21997015	beijing	i	0.971	2003	1957	T	A	0.192	0.225	1.17	(1.03-1.34)	1.82E-02	
rs61271866	chr9	21997015	henan	i	0.990	1082	1374	T	A	0.208	0.218	1.03	(0.88-1.21)	6.82E-01	
rs61271866	chr9	21997015	beijing+henan+nci			5792	5352					1.21	(1.13-1.30)	1.99E-07	2.28E-02
rs7822239	chr8	133119961	nci	i	0.986	2707	2022	C	A	0.265	0.222	0.82	(0.74-0.91)	1.11E-04	
rs7822239	chr8	133119961	beijing	i	0.986	2003	1957	C	A	0.286	0.250	0.85	(0.76-0.96)	9.60E-03	
rs7822239	chr8	133119961	henan	i	0.985	1082	1375	C	A	0.252	0.237	0.93	(0.80-1.08)	3.46E-01	
rs7822239	chr8	133119961	beijing+henan+nci			5792	5354					0.85	(0.80-0.91)	5.41E-06	3.93E-01
rs4252725	chr1	204513256	nci	i	1.000	2708	2022	A	G	0.671	0.651	0.92	(0.84-1.01)	6.49E-02	
rs4252725	chr1	204513256	beijing	g	1.000	2004	1958	A	G	0.680	0.655	0.89	(0.79-0.99)	3.74E-02	
rs4252725	chr1	204513256	henan	i	0.999	1083	1375	A	G	0.702	0.654	0.8	(0.70-0.92)	1.17E-03	
rs4252725	chr1	204513256	beijing+henan+nci			5795	5355					0.88	(0.83-0.94)	8.38E-05	2.44E-01
rs9323746	chr14	84920960	nci	g	1.000	2708	2022	C	T	0.352	0.369	1.11	(1.01-1.21)	2.74E-02	
rs9323746	chr14	84920960	beijing	g	1.000	2004	1958	C	T	0.351	0.374	1.16	(1.04-1.30)	6.64E-03	
rs9323746	chr14	84920960	henan	g	1.000	1083	1375	C	T	0.350	0.392	1.26	(1.10-1.44)	7.08E-04	
rs9323746	chr14	84920960	beijing+henan+nci			5795	5355					1.15	(1.09-1.23)	4.33E-06	2.77E-01
rs7038507	chr9	122784665	nci	i	0.988	2707	2022	G	A	0.072	0.086	1.31	(1.12-1.54)	9.48E-04	
rs7038507	chr9	122784665	beijing	i	0.991	2003	1957	G	A	0.061	0.078	1.3	(1.06-1.59)	1.35E-02	
rs7038507	chr9	122784665	henan	i	0.987	1082	1374	G	A	0.064	0.081	1.08	(0.85-1.38)	5.09E-01	
rs7038507	chr9	122784665	beijing+henan+nci			5792	5353					1.26	(1.12-1.40)	7.54E-05	4.07E-01
rs1958578	chr14	34800823	nci	g	1.000	2708	2022	G	A	0.840	0.819	0.87	(0.77-0.97)	1.36E-02	
rs1958578	chr14	34800823	beijing	i	0.918	2004	1957	G	A	0.848	0.810	0.79	(0.68-0.91)	1.50E-03	
rs1958578	chr14	34800823	henan	g	1.000	1083	1375	G	A	0.844	0.815	0.83	(0.71-0.98)	2.99E-02	
rs1958578	chr14	34800823	beijing+henan+nci			5795	5354					0.84	(0.77-0.90)	8.29E-06	6.03E-01
rs27209	chr5	57625982	nci	i	0.985	2707	2021	G	A	0.446	0.468	1.09	(1.00-1.19)	4.19E-02	
rs27209	chr5	57625982	beijing	i	0.969	2003	1957	G	A	0.438	0.462	1.18	(1.06-1.32)	2.64E-03	
rs27209	chr5	57625982	henan	i	0.986	1083	1374	G	A	0.430	0.484	1.25	(1.10-1.42)	5.51E-04	
rs27209	chr5	57625982	beijing+henan+nci			5793	5352					1.15	(1.09-1.22)	2.94E-06	1.96E-01
rs7999802	chr13	68134441	nci	i	0.992	2708	2022	T	C	0.873	0.899	1.3	(1.13-1.48)	1.44E-04	
rs7999802	chr13	68134441	beijing	g	1.000	2004	1958	T	C	0.870	0.889	1.19	(1.01-1.41)	3.68E-02	
rs7999802	chr13	68134441	henan	i	0.992	1082	1375	T	C	0.872	0.889	1.14	(0.93-1.40)	1.97E-01	
rs7999802	chr13	68134441	beijing+henan+nci			5794	5355					1.23	(1.12-1.35)	1.17E-05	5.31E-01
rs75791390	chr5	71457813	nci	i	0.952	2707	2021	A	G	0.602	0.647	1.19	(1.09-1.30)	1.62E-04	
rs75791390	chr5	71457813	beijing	i	0.888	2003	1957	A	G	0.623	0.663	1.13	(1.01-1.27)	3.85E-02	
rs75791390	chr5	71457813	henan	i	0.948	1082	1374	A	G	0.621	0.640	1.08	(0.95-1.24)	2.39E-01	
rs75791390	chr5	71457813	beijing+henan+nci			5792	5352					1.15	(1.08-1.22)	1.62E-05	5.15E-01
rs1917435	chr8	46923031	nci	i	0.993	2707	2021	C	T	0.689	0.681	0.92	(0.84-1.01)	8.18E-02	
rs1917435	chr8	46923031	beijing	i	0.989	2003	1957	C	T	0.679	0.666	0.86	(0.77-0.96)	8.64E-03	
rs1917435	chr8	46923031	henan	i	0.990	1082	1374	C	T	0.698	0.674	0.83	(0.73-0.95)	8.50E-03	
rs1917435	chr8	46923031	beijing+henan+nci			5792	5352					0.88	(0.83-0.94)	1.06E-04	4.02E-01
rs10935355	chr3	139543726	nci	i	0.970	2708	2021	A	T	0.227	0.199	0.83	(0.75-0.93)	7.94E-04	
rs10935355	chr3	139543726	beijing	g	1.000	2004	1958	A	T	0.235	0.206	0.87	(0.76-0.98)	2.77E-02	
rs10935355	chr3	139543726	henan	i	0.967	1082	1374	A	T	0.227	0.203	0.84	(0.72-0.98)	2.86E-02	
rs10935355	chr3	139543726	beijing+henan+nci			5794	5353					0.85	(0.79-0.91)	5.47E-06	8.96E-01

\* 'g' indicates that the SNP was genotyped on the array and 'i' indicates that the SNP was imputed

**Supplementary Table 5.** Association results for top 4 SNPs stratified by study group and alcohol status

Group	SNP	CHR	LOC	GROUP	CATEGORY*	INFO	NUM_CONTROL	NUM_CASE	REFERENCE_ALLELE	EFFECT_ALLELE	EFFECT_ALLELE FREQ_CONTROL	EFFECT_ALLELE FREQ_CASE	OR	CI	P	P heterog.
Beijing	rs7447927	chr5	138861146	nondrinker	i	0.948	1113	864	C	G	0.413	0.443	0.95	(0.81-1.11)	4.92E-01	
Beijing	rs7447927	chr5	138861146	drinker	i	0.948	889	1092	C	G	0.437	0.439	0.87	(0.74-1.02)	7.99E-02	
Beijing	rs7447927	chr5	138861146	drinker+nondrinker			2002	1956					0.91	(0.81-1.01)	8.56E-02	4.46E-01
Henan	rs7447927	chr5	138861146	nondrinker	i	0.961	129	927	C	G	0.505	0.442	0.78	(0.60-1.01)	5.75E-02	
Henan	rs7447927	chr5	138861146	drinker	i	0.969	38	170	C	G	0.512	0.479	0.84	(0.51-1.40)	5.04E-01	
Henan	rs7447927	chr5	138861146	drinker+nondrinker			167	1097					0.79	(0.63-1.00)	4.61E-02	7.88E-01
NCI	rs7447927	chr5	138861146	nondrinker	i	0.962	1808	1622	C	G	0.490	0.465	0.91	(0.83-1.00)	5.33E-02	
NCI	rs7447927	chr5	138861146	drinker	i	0.96	295	303	C	G	0.478	0.430	0.81	(0.64-1.03)	7.95E-02	
NCI	rs7447927	chr5	138861146	drinker+nondrinker			2103	1925					0.89	(0.82-0.98)	1.43E-02	3.69E-01
Beijing	rs1642764	chr17	7557834	nondrinker	i	0.806	1113	864	C	T	0.513	0.460	0.82	(0.69-0.97)	2.02E-02	
Beijing	rs1642764	chr17	7557834	drinker	i	0.807	889	1092	C	T	0.515	0.474	0.93	(0.79-1.11)	4.41E-01	
Beijing	rs1642764	chr17	7557834	drinker+nondrinker			2002	1956					0.87	(0.77-0.99)	2.80E-02	2.81E-01
Henan	rs1642764	chr17	7557834	nondrinker	i	0.888	129	927	C	T	0.529	0.469	0.76	(0.58-1.00)	5.31E-02	
Henan	rs1642764	chr17	7557834	drinker	i	0.890	38	170	C	T	0.510	0.468	0.84	(0.50-1.41)	5.10E-01	
Henan	rs1642764	chr17	7557834	drinker+nondrinker			167	1097					0.78	(0.61-0.99)	4.38E-02	7.38E-01
NCI	rs1642764	chr17	7557834	nondrinker	i	0.899	1808	1622	C	T	0.478	0.443	0.84	(0.76-0.93)	5.36E-04	
NCI	rs1642764	chr17	7557834	drinker	i	0.900	295	303	C	T	0.483	0.444	0.84	(0.66-1.08)	1.70E-01	
NCI	rs1642764	chr17	7557834	drinker+nondrinker			2103	1925					0.84	(0.76-0.92)	1.97E-04	9.41E-01
Beijing	rs35597309	chr6	32589266	nondrinker	i	0.936	1113	864	G	A	0.067	0.090	1.08	(0.81-1.43)	6.05E-01	
Beijing	rs35597309	chr6	32589266	drinker	i	0.930	889	1092	G	A	0.071	0.071	0.96	(0.70-1.30)	7.72E-01	
Beijing	rs35597309	chr6	32589266	drinker+nondrinker			2002	1956					1.02	(0.83-1.26)	8.53E-01	5.74E-01
Henan	rs35597309	chr6	32589266	nondrinker	i	0.925	129	927	G	A	0.064	0.102	1.64	(1.03-2.60)	3.77E-02	
Henan	rs35597309	chr6	32589266	drinker	i	0.927	39	170	G	A	0.108	0.085	0.72	(0.29-1.78)	4.75E-01	
Henan	rs35597309	chr6	32589266	drinker+nondrinker			168	1097					1.38	(0.91-2.09)	1.28E-01	1.13E-01
NCI	rs35597309	chr6	32589266	nondrinker	i	0.906	1809	1622	G	A	0.079	0.112	1.54	(1.29-1.83)	1.04E-06	
NCI	rs35597309	chr6	32589266	drinker	i	0.921	295	303	G	A	0.106	0.111	1.05	(0.72-1.54)	7.89E-01	
NCI	rs35597309	chr6	32589266	drinker+nondrinker			2104	1925					1.44	(1.23-1.69)	5.13E-06	7.74E-02
Beijing	rs61271866	chr9	21997015	nondrinker	i	0.970	1113	864	T	A	0.194	0.230	1.12	(0.93-1.35)	2.13E-01	
Beijing	rs61271866	chr9	21997015	drinker	i	0.971	889	1092	T	A	0.189	0.220	1.22	(1.01-1.48)	4.23E-02	
Beijing	rs61271866	chr9	21997015	drinker+nondrinker			2002	1956					1.17	(1.02-1.34)	2.12E-02	5.47E-01
Henan	rs61271866	chr9	21997015	nondrinker	i	0.990	129	927	T	A	0.215	0.214	1.00	(0.72-1.38)	9.98E-01	
Henan	rs61271866	chr9	21997015	drinker	i	0.995	38	170	T	A	0.255	0.222	0.75	(0.41-1.38)	3.52E-01	
Henan	rs61271866	chr9	21997015	drinker+nondrinker			167	1097					0.94	(0.70-1.25)	6.59E-01	4.12E-01
NCI	rs61271866	chr9	21997015	nondrinker	i	0.989	1809	1622	T	A	0.187	0.230	1.32	(1.17-1.49)	4.06E-06	
NCI	rs61271866	chr9	21997015	drinker	i	0.987	295	303	T	A	0.188	0.242	1.42	(1.07-1.87)	1.45E-02	
NCI	rs61271866	chr9	21997015	drinker+nondrinker			2104	1925					1.34	(1.20-1.49)	2.04E-07	6.64E-01

\* 'g' indicates that the SNP was genotyped on the array and 'i' indicates that the SNP was imputed

**Supplementary Table 6.** Association results for top 4 SNPs stratified by study group and tobacco status

Group	SNP	CHR	LOC	GROUP	CATEGORY*	INFO	NUM_CONTROL	NUM_CASE	REFERENCE_ALLELE	EFFECT_ALLELE	EFFECT_ALLELE	EFFECT_ALLELE	OR	CI	P	P heterog.
Beijing	rs7447927	chr5	138861146	nonsmoker	i	0.95	877	679	C	G	0.412	0.442	0.98	(0.82-1.16)	7.79E-01	
Beijing	rs7447927	chr5	138861146	smoker	i	0.95	1125	1277	C	G	0.433	0.440	0.86	(0.74-0.99)	4.09E-02	
Beijing	rs7447927	chr5	138861146	nonsmoker+smoker			2002	1956					0.91	(0.81-1.01)	8.22E-02	2.66E-01
Henan	rs7447927	chr5	138861146	nonsmoker	i	0.96	135	809	C	G	0.508	0.441	0.76	(0.59-0.98)	3.24E-02	
Henan	rs7447927	chr5	138861146	smoker	i	0.96	32	288	C	G	0.501	0.468	0.91	(0.54-1.53)	7.22E-01	
Henan	rs7447927	chr5	138861146	nonsmoker+smoker			167	1097					0.78	(0.62-0.99)	3.78E-02	5.33E-01
NCI	rs7447927	chr5	138861146	nonsmoker	i	0.96	881	922	C	G	0.485	0.450	0.86	(0.76-0.99)	3.30E-02	
NCI	rs7447927	chr5	138861146	smoker	i	0.96	1222	1003	C	G	0.491	0.469	0.92	(0.81-1.03)	1.50E-01	
NCI	rs7447927	chr5	138861146	nonsmoker+smoker			2103	1925					0.89	(0.82-0.98)	1.26E-02	5.32E-01
Beijing	rs1642764	chr17	7557834	nonsmoker	i	0.805	877	679	C	T	0.518	0.471	0.88	(0.74-1.06)	1.77E-01	
Beijing	rs1642764	chr17	7557834	smoker	i	0.807	1125	1277	C	T	0.511	0.466	0.88	(0.75-1.03)	1.15E-01	
Beijing	rs1642764	chr17	7557834	nonsmoker+smoker			2002	1956					0.88	(0.78-0.99)	3.80E-02	9.70E-01
Henan	rs1642764	chr17	7557834	nonsmoker	i	0.886	135	809	C	T	0.515	0.467	0.80	(0.61-1.05)	1.11E-01	
Henan	rs1642764	chr17	7557834	smoker	i	0.895	32	288	C	T	0.565	0.473	0.65	(0.38-1.12)	1.22E-01	
Henan	rs1642764	chr17	7557834	nonsmoker+smoker			167	1097					0.77	(0.60-0.98)	3.37E-02	5.10E-01
NCI	rs1642764	chr17	7557834	nonsmoker	i	0.896	881	922	C	T	0.499	0.450	0.80	(0.69-0.91)	1.13E-03	
NCI	rs1642764	chr17	7557834	smoker	i	0.901	1222	1003	C	T	0.464	0.436	0.89	(0.78-1.01)	7.44E-02	
NCI	rs1642764	chr17	7557834	nonsmoker+smoker			2103	1925					0.85	(0.77-0.93)	4.29E-04	2.38E-01
Beijing	rs35597309	chr6	32589266	nonsmoker	i	0.943	877	679	G	A	0.072	0.090	0.97	(0.71-1.31)	8.27E-01	
Beijing	rs35597309	chr6	32589266	smoker	i	0.926	1125	1278	G	A	0.066	0.074	1.06	(0.79-1.43)	6.78E-01	
Beijing	rs35597309	chr6	32589266	nonsmoker+smoker			2002	1957					1.02	(0.82-1.25)	8.84E-01	6.56E-01
Henan	rs35597309	chr6	32589266	nonsmoker	i	0.923	136	809	G	A	0.074	0.103	1.39	(0.88-2.20)	1.61E-01	
Henan	rs35597309	chr6	32589266	smoker	i	0.932	33	288	G	A	0.075	0.088	1.13	(0.42-3.02)	8.11E-01	
Henan	rs35597309	chr6	32589266	nonsmoker+smoker			169	1097					1.34	(0.88-2.03)	1.71E-01	7.08E-01
NCI	rs35597309	chr6	32589266	nonsmoker	i	0.909	881	922	G	A	0.073	0.123	1.91	(1.51-2.40)	5.84E-08	
NCI	rs35597309	chr6	32589266	smoker	i	0.908	1222	1003	G	A	0.090	0.101	1.15	(0.93-1.43)	1.86E-01	
NCI	rs35597309	chr6	32589266	nonsmoker+smoker			2103	1925					1.45	(1.24-1.69)	3.64E-06	1.81E-03
Beijing	rs61271866	chr9	21997015	nonsmoker	i	0.971	877	679	T	A	0.192	0.239	1.24	(1.01-1.52)	3.90E-02	
Beijing	rs61271866	chr9	21997015	smoker	i	0.970	1125	1277	T	A	0.192	0.217	1.15	(0.97-1.38)	1.12E-01	
Beijing	rs61271866	chr9	21997015	nonsmoker+smoker			2002	1956					1.19	(1.04-1.36)	1.07E-02	6.01E-01
Henan	rs61271866	chr9	21997015	nonsmoker	i	0.990	135	809	T	A	0.210	0.216	1.05	(0.76-1.45)	7.55E-01	
Henan	rs61271866	chr9	21997015	smoker	i	0.994	32	288	T	A	0.284	0.213	0.65	(0.35-1.22)	1.82E-01	
Henan	rs61271866	chr9	21997015	nonsmoker+smoker			167	1097					0.95	(0.72-1.27)	7.47E-01	1.83E-01
NCI	rs61271866	chr9	21997015	nonsmoker	i	0.990	881	922	T	A	0.191	0.229	1.29	(1.10-1.52)	2.04E-03	
NCI	rs61271866	chr9	21997015	smoker	i	0.987	1222	1003	T	A	0.185	0.235	1.36	(1.17-1.57)	4.26E-05	
NCI	rs61271866	chr9	21997015	nonsmoker+smoker			2103	1925					1.33	(1.19-1.48)	3.28E-07	6.62E-01

\* 'g' indicates that the SNP was genotyped on the array and 'i' indicates that the SNP was imputed

Supplementary Table 7. Summary of genomic annotation by HaploReg v2 and RegulomeDB

chr	pos(hg19)	LD	variant	Ref	Alt	Alternative allele frequency				Conservation	Histone marks	DNase	Proteins bound	eQTL tissues	Motifs changed	GENCODE genes	RefSeq genes	dbSNP func annot	RegulomeDB score <sup>†</sup>
						AFR	AMR	ASN	EUR										
6	32589266	hit	rs35597309	G	A	0.08	0.03	0.08	0.05			GM12878	4 bound proteins		6.7kb 5' of HLA-DQA1	16kb 5' of HLA-DQA1		5	
6	32588201	1	rs35945734	A	G	0.1	0.04	0.07	0.06					Pou2f2	7.8kb 5' of HLA-DQA1	17kb 5' of HLA-DQA1		7	
6	32587820	1	rs71542418	G	A,C	0.1	0.04	0.08	0.06						8.1kb 5' of HLA-DQA1	17kb 5' of HLA-DQA1		6	
6	32589700	1	rs77875016	C	T	0.08	0.03	0.07	0.05			GM12878		MAZR,p300	6.3kb 5' of HLA-DQA1	15kb 5' of HLA-DQA1		7	
6	32588432	1	rs34697429	A	T	0.1	0.04	0.07	0.06					Arid3a,Foxp1	7.5kb 5' of HLA-DQA1	17kb 5' of HLA-DQA1		6	
6	32590315	1	rs71542421	C	T	0.09	0.03	0.07	0.05			GM12878, HMEC	12 cell types		5.6kb 5' of HLA-DQA1	15kb 5' of HLA-DQA1		4	
6	32588939	1	rs28699237	A	T	0.08	0.03	0.08	0.05			GM12878		ERalpha-a	7kb 5' of HLA-DQA1	16kb 5' of HLA-DQA1		7	
6	32588272	1	rs28644259	C	G	0.09	0.03	0.08	0.05					NF-AT	7.7kb 5' of HLA-DQA1	17kb 5' of HLA-DQA1		7	
6	32588460	1	rs28592295	G	A	0.11	0.04	0.08	0.06					AP-1,Irf	7.5kb 5' of HLA-DQA1	17kb 5' of HLA-DQA1		7	
6	32611647	1	rs28566533	G	C	0.09	0.03	0.07	0.05					PU.1,Pbx3,SP2	HLA-DQA1	217bp 3' of HLA-DQA1		5	
6	32587384	1	rs28411161	C	G	0.08	0.03	0.08	0.05					HES1	8.6kb 5' of HLA-DQA1	18kb 5' of HLA-DQA1		7	
6	32587390	1	rs28391139	T	C	0.08	0.03	0.08	0.05					HES1	8.6kb 5' of HLA-DQA1	18kb 5' of HLA-DQA1		7	
6	32605309	1	rs12722042	A	C,G,T	0.08	0.03	0.07	0.05			GM12878	FibroP		HLA-DQA1	HLA-DQA1	missense	4	
6	32605284	1	rs12722039	G	A	0.08	0.03	0.07	0.05			GM12878	FibroP		HLA-DQA1	HLA-DQA1	missense	4	
6	32591151	1	rs35765065	C	T	0.08	0.03	0.07	0.05					NRSF	HLA-DQA1	HLA-DQA1		4	
6	32581157	1	rs75765164	G	A	0.08	0.03	0.07	0.05			NHEK, GM12878, HMEC	GM19238,Urothelia	RFX5,TBP	4.8kb 5' of HLA-DQA1	14kb 5' of HLA-DQA1		3a	
6	32600468	1	rs116499104	G	A	0.08	0.03	0.06	0.04					8 altered motifs	15kb 5' of HLA-DQA1	24kb 5' of HLA-DRB1		7	
6	32585681	1	rs13217507	A	T	0.08	0.03	0.08	0.05					STAT,TCF4	HLA-DQA1	4.7kb 5' of HLA-DQA1		7	
6	32588216	1	rs71542420	A	G	0.08	0.03	0.07	0.05					AP-1,PRDM1,PU.1	10kb 5' of HLA-DQA1	20kb 5' of HLA-DQA1		6	
6	32574108	1	rs34107399	G	A	0.08	0.03	0.07	0.05					5 altered motifs	10kb 5' of HLA-DQA1	20kb 5' of HLA-DQA1		5	
6	32572742	1	rs115673262	C	G	0.08	0.03	0.07	0.05					4 altered motifs	7.7kb 5' of HLA-DQA1	17kb 5' of HLA-DQA1		6	
6	32585052	1	rs13213778	C	A	0.09	0.03	0.07	0.05			GM12878		LXR,Znf143	16kb 5' of HLA-DRB1	17kb 5' of HLA-DRB1	intronic	7	
6	32589495	1	rs35990832	G	A	0.08	0.04	0.07	0.05			GM12878		TAL1	15kb 5' of HLA-DRB1	15kb 5' of HLA-DRB1	intronic	7	
6	32589101	1	rs34846487	T	G	0.08	0.03	0.07	0.05			GM12878	CD20+	4 altered motifs	11kb 5' of HLA-DQA1	20kb 5' of HLA-DQA1		6	
6	32589095	1	rs28669773	A	G	0.1	0.04	0.07	0.06			GM12878		Foxm1,Pou2f2	6.5kb 5' of HLA-DQA1	16kb 5' of HLA-DQA1		5	
6	32586157	1	rs70993900	AC	A	0.09	0.03	0.07	0.05			GM12878		Sox,TAL1	6.9kb 5' of HLA-DQA1	16kb 5' of HLA-DQA1		6	
6	32588080	1	rs35372933	T	C	0.09	0.03	0.07	0.05					SIX5,Sox	6.9kb 5' of HLA-DQA1	16kb 5' of HLA-DQA1		6	
6	32599904	1	rs34680078	G	A	0.08	0.03	0.07	0.05					4 altered motifs	9.8kb 5' of HLA-DQA1	19kb 5' of HLA-DQA1		6	
6	32586961	1	rs114812135	A	T	0.08	0.03	0.07	0.05					LBP-1,Nanog,TEF-1	7.9kb 5' of HLA-DQA1	17kb 5' of HLA-DQA1		7	
6	32597341	1	rs114798579	G	A	0.08	0.03	0.07	0.05					Ets,Foxp3	HLA-DQA1	5.3kb 5' of HLA-DQA1		7	
6	32585696	1	rs13217512	A	C	0.08	0.03	0.08	0.05					4 altered motifs	9kb 5' of HLA-DQA1	18kb 5' of HLA-DQA1		7	
6	32589372	1	rs28664035	T	A	0.1	0.05	0.08	0.06					SETDB1	HLA-DQA1	7.8kb 5' of HLA-DQA1		7	
6	32591360	1	rs114480004	G	C	0.08	0.03	0.07	0.05			GM12878		5 bound proteins	10kb 5' of HLA-DQA1	19kb 5' of HLA-DQA1		5	
6	32590529	1	rs35407883	A	G	0.08	0.03	0.07	0.05			NHEK, GM12878, HMEC		7 altered motifs	6.6kb 5' of HLA-DQA1	16kb 5' of HLA-DQA1		5	
6	32584237	1	rs6930731	C	T	0.08	0.03	0.07	0.05			GM12878, HMEC, NHEK	14 cell types	GATA,HNF1,Nkx3	4.6kb 5' of HLA-DQA1	14kb 5' of HLA-DQA1		7	
6	32607513	0.932	rs71542422	C	T	0.09	0.03	0.09	0.06			GM12878		Pou5f1,TBX5	5.4kb 5' of HLA-DQA1	15kb 5' of HLA-DQA1		4	
6	32615346	0.932	rs28609302	C	G	0.09	0.04	0.08	0.05					Pax-5,RREB-1,Znf143	12kb 5' of HLA-DQA1	21kb 5' of HLA-DQA1		7	
6	32585128	0.932	rs67265013	T	TC	0.09	0.04	0.08	0.06			GM12878		ATF3,E2F,XBP-1	HLA-DQA1	HLA-DQA1	intronic	5	
6	32573025	0.928	rs144453041	A	G	0.07	0.03	0.07	0.05			GM12878		5 altered motifs	506bp 3' of HLA-DQA1	3.9kb 3' of HLA-DQA1		6	
6	32604588	0.928	rs28619112	C	G	0.09	0.03	0.07	0.05			GM12878	H9ES,Myometr,RPTEC	13 altered motifs	11kb 5' of HLA-DQA1	20kb 5' of HLA-DQA1		6	
6	32586432	0.928	rs13191494	G	C	0.09	0.03	0.07	0.05					8 altered motifs	15kb 5' of HLA-DRB1	15kb 5' of HLA-DRB1	intronic	6	
6	32586465	0.928	rs34598287	A	T	0.08	0.03	0.07	0.05					7 altered motifs	HLA-DQA1	593bp 5' of HLA-DQA1		3a	
6	32575610	0.928	rs34356392	T	G	0.08	0.03	0.07	0.04			GM12878	5 cell types	Ets,Znf143,p300	9.5kb 5' of HLA-DQA1	19kb 5' of HLA-DQA1		7	
6	32618187	0.872	rs138279058	T	C	0.11	0.05	0.1	0.08					Maf,STAT	9.5kb 5' of HLA-DQA1	19kb 5' of HLA-DQA1		7	
6	32588449	0.872	rs28456694	G	T	0.1	0.04	0.08	0.06					Pou2f2	18kb 5' of HLA-DRB1	18kb 5' of HLA-DRB1		4	
6	32619285	0.86	rs28418633	C	T	0.11	0.06	0.09	0.08					6 altered motifs	3.3kb 3' of HLA-DQA1	6.8kb 3' of HLA-DQA1		6	
6	32601204	0.856	rs114549185	C	G	0.07	0.03	0.06	0.05					5 altered motifs	7.5kb 5' of HLA-DQA1	17kb 5' of HLA-DQA1		7	
6	32596247	0.856	rs117418599	G	T	0.07	0.03	0.07	0.05			GM12878		5 altered motifs	4.4kb 3' of HLA-DQA1	7.9kb 3' of HLA-DQA1		7	
6	32614938	0.818	rs28546328	G	A	0.09	0.05	0.09	0.06			GM12878	GM06990	5 altered motifs	HLA-DQA1	4kb 5' of HLA-DQA1		6	
6	32587835	0.818	rs71542419	C	A	0.14	0.08	0.08	0.11					8 altered motifs	HLA-DQA1	8.9kb 5' of HLA-DQA1		5	
5	138861146	hit	rs7447927	C	G	0.11	0.52	0.38	0.69			H5MM	6 cell types	TCF12	TMEM173	TMEM173	synonymous	5	
5	138852369	0.978	rs13153461	G	A	0.09	0.59	0.38	0.69				Huvec, H1	4 altered motifs	2.7kb 3' of TMEM173	2.7kb 3' of TMEM173		1f	
5	138862744	0.978	rs13166214	A	G	0.14	0.52	0.38	0.68				8 cell types	BATF,Irf	223bp 5' of TMEM173	400bp 5' of TMEM173		7	
5	138850905	0.956	rs13181561	G	A	0.39	0.61	0.38	0.69				H1	CEBPB	4.2kb 3' of TMEM173	4.2kb 3' of TMEM173		1f	
5	138842818	0.934	rs9716069	T	A	0.34	0.61	0.39	0.68				Huvec	Hoxd10	489bp 5' of ECSCR	497bp 5' of ECSCR		7	
17	7557834	hit	rs1642764	C	T	0.25	0.48	0.55	0.52				Th1,Hepatocytes,Osteobl	5 altered motifs	ATP1B2	ATP1B2	intronic	5	
17	7557419	0.734	rs1642763	A	G	0.92	0.8	0.63	0.78				Adult_CD4_Th0	AP-2,EBF,NRSF	ATP1B2	ATP1B2		1f	
17	7559462	0.662	rs1641512	G	A,C,T	0.68	0.78	0.61	0.77				H1		ATP1B2	ATP1B2	3'-UTR	7	
17	7559677	0.662	rs1641511	G	A	0.58	0.77	0.61	0.77				H1		ATP1B2	ATP1B2		7	
17	7560835	0.575	rs1050541	T	G	0.59	0.4	0.36	0.51				8 cell types	12 altered motifs	ATP1B2	ATP1B2	3'-UTR	1b	
17	7554772	0.567	rs1642762	C	T	0.07	0.6	0.44	0.56			H1	6 cell types	9 altered motifs	ATP1B2	ATP1B2	5'-UTR	5	
17	7549681	0.567	rs1641523	C	T	0.25	0.58	0.44	0.58				K562		263bp 5' of ATP1B2	4.6kb 5' of ATP1B2		1f	
17	7553743	0.567	rs1624085	G	C	0.16	0.6	0.44	0.57				7 cell types	6 altered motifs	ATP1B2	509bp 5' of ATP1B2		2b	
17	7563354	0.542	rs2908807	T	C	0.18	0.5	0.61	0.26					9 altered motifs	ATP1B2	1.7kb 3' of TP53	2.3kb 3' of ATP1B2		6
17	7455707	0.521	rs78608249	C	T	0.18	0.26	0.41	0.28			GM12878		6 altered motifs	ATP1B2	509bp 5' of ATP1B2		2b	
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Supplementary Table 8. Independent and joint analysis of 12 previously reported loci associated with risk of ESCC

Loci	Gene	rsID	Ref_Allele	Effect_Allele	NCI					Henan					Beijing					Combined				
					Effect_Allele	Effect_Allele	P_value	OR	95% CI	Effect_Allele	Effect_Allele	P_value	OR	95% CI	Effect_Allele	Effect_Allele	P_value	OR	95% CI	Effect_Allele	Effect_Allele	P_value	OR	95% CI
					Freq_Control	Freq_Case				Freq_Control	Freq_Case				Freq_Control	Freq_Case				Freq_Control	Freq_Case			
10q23.33	PLCE1,KIAA1516	rs2274223	A	G	0.210	0.260	3.47E-09	1.36	(1.23-1.50)	0.213	0.271	1.80E-05	1.38	(1.19-1.59)	0.207	0.263	1.12E-05	1.32	(1.17-1.50)	0.209	0.264	3.65E-18	1.35	(1.26-1.45)
2q33.1	CASP8,ALS2CR12	rs13016963	A	G	0.728	0.687	1.16E-06	0.79	(0.72-0.87)	0.739	0.686	6.94E-05	0.75	(0.65-0.87)	0.690	0.659	4.47E-04	0.82	(0.73-0.91)	0.717	0.676	4.29E-13	0.79	(0.75-0.84)
21q22.12	RUNX1	rs2014300	A	G	0.865	0.866	7.64E-01	1.02	(0.90-1.16)	0.854	0.872	2.88E-02	1.23	(1.02-1.49)	0.808	0.876	8.42E-13	1.68	(1.46-1.94)	0.843	0.871	7.91E-09	1.28	(1.18-1.39)
22q12.1	CHEK2,CCDC117,XBP1	rs2239815	T	C	0.609	0.562	2.19E-05	0.83	(0.76-0.91)	0.599	0.573	1.06E-01	0.90	(0.79-1.02)	0.627	0.568	2.39E-02	0.88	(0.79-0.98)	0.613	0.567	4.09E-07	0.86	(0.81-0.91)
5q11.2	PDE4D,PDE4DN2	rs10052657	C	A	0.149	0.148	4.12E-01	0.95	(0.85-1.07)	0.161	0.150	1.69E-01	0.88	(0.74-1.05)	0.060	0.019	1.32E-16	0.34	(0.26-0.44)	0.120	0.101	1.15E-06	0.80	(0.73-0.87)
16q12.1	HEATR3	rs4785204	C	T	0.274	0.285	3.99E-01	1.04	(0.95-1.15)	0.263	0.300	4.60E-04	1.29	(1.12-1.48)	0.253	0.307	9.06E-05	1.26	(1.12-1.42)	0.265	0.297	1.83E-05	1.15	(1.08-1.23)
3q27.3	ST6GAL1	rs2239612	G	A	0.188	0.206	5.19E-02	1.11	(1.00-1.23)	0.189	0.198	9.32E-01	1.01	(0.86-1.18)	0.168	0.212	5.17E-03	1.21	(1.06-1.39)	0.182	0.206	2.82E-03	1.12	(1.04-1.20)
6p21.1		rs10484761	T	C	0.112	0.101	9.04E-02	0.89	(0.77-1.02)	0.104	0.098	9.70E-01	1.00	(0.81-1.24)	0.058	0.111	2.39E-12	1.84	(1.55-2.18)	0.092	0.104	4.62E-03	1.14	(1.04-1.26)
17q21.2	JUP,HAP1	rs6503659	A	T	0.853	0.850	7.29E-01	1.02	(0.90-1.15)	0.843	0.839	8.76E-01	1.01	(0.85-1.21)	0.881	0.842	8.49E-03	0.81	(0.70-0.95)	0.861	0.844	1.67E-01	0.94	(0.87-1.02)
17p13.3	SMG6	rs17761864	C	A	0.175	0.182	5.05E-01	0.96	(0.86-1.08)	0.174	0.193	2.03E-01	1.11	(0.94-1.31)	0.137	0.179	1.12E-01	1.12	(0.97-1.29)	0.162	0.183	2.71E-01	1.04	(0.97-1.12)
20p13	C20orf54	rs13042395	C	T	0.302	0.255	3.04E-01	0.95	(0.86-1.05)	0.287	0.249	9.12E-02	0.88	(0.76-1.02)	0.375	0.339	3.34E-01	1.07	(0.93-1.23)	0.324	0.284	3.02E-01	0.96	(0.90-1.03)
18p11.21	PTPN2	rs2847281	A	G	0.191	0.192	2.86E-01	0.94	(0.85-1.05)	0.189	0.204	2.72E-01	1.10	(0.93-1.29)	0.156	0.196	2.47E-01	1.08	(0.95-1.24)	0.178	0.196	5.75E-01	1.02	(0.95-1.10)



**Supplementary Table 9.** Associations in individual GWAS for top 4 SNPs before and after PC adjustment

SNP	Beijing			
	Before PC Adjustment		After PC Adjustment	
	OR (95% CI)	P	OR (95% CI)	P
<b>rs7447927</b>	1.11 (1.01-1.22)	2.72E-02	0.90 (0.81-1.01)	5.60E-02
<b>rs1642764</b>	0.80 (0.73-0.89)	2.50E-05	0.88 (0.78-0.99)	3.12E-02
<b>rs35597309</b>	1.14 (0.96-1.37)	1.38E-01	1.02 (0.82-1.25)	8.83E-01
<b>rs61271866</b>	1.23 (1.10-1.38)	2.57E-04	1.17 (1.03-1.34)	1.82E-02

  

	NCI			
	Before PC Adjustment		After PC Adjustment	
	OR (95% CI)	P	OR (95% CI)	P
<b>rs7447927</b>	0.90 (0.83-0.98)	1.78E-02	0.90 (0.83-0.98)	1.60E-02
<b>rs1642764</b>	0.84 (0.77-0.92)	1.28E-04	0.84 (0.77-0.92)	1.21E-04
<b>rs35597309</b>	1.44(1.23-1.67)	3.76E-06	1.43 (1.23-1.67)	4.27E-06
<b>rs61271866</b>	1.34 (1.20-1.49)	6.84E-08	1.34 (1.20-1.48)	7.72E-08

  

	Henan			
	Before PC Adjustment		After PC Adjustment*	
	OR (95% CI)	P	OR (95% CI)	P
<b>rs7447927</b>	0.77 (0.68-0.88)	7.64E-05		
<b>rs1642764</b>	0.84 (0.74-0.96)	1.19E-02		
<b>rs35597309</b>	1.55 (1.22-1.97)	3.50E-04		
<b>rs61271866</b>	1.03 (0.88-1.21)	6.82E-01		

\*Baseline risk model indicated no need for PC adjustment (lambda value before PC adjustment 1.02)