The American Journal of Human Genetics, Volume *105*

Supplemental Data

A Fast and Accurate Method for Genome-wide Scale Phenome-wide G × E Analysis and Its Application to UK Biobank

Wenjian Bi, Zhangchen Zhao, Rounak Dey, Lars G. Fritsche, Bhramar Mukherjee, and Seunggeun Lee

Supplementary Methods

Section A: R codes to evaluate computation time of Wald test under different case-control ratios

```
library(rbenchmark)
set.seed(1)
N = 400000
MAF = 0.3
Data1 = data.frame(y1=rbinom(N,1,0.5),
                   y2=rbinom(N,1,0.01),
                   X=matrix(rnorm(N*5),N,5),
                   g=rbinom(N,2,MAF))
benchmark(res1<-glm(y1~X.1+X.2+X.3+X.4+X.5*g,data=Data1,family = binomial),
          res2<-glm(y2~X.1+X.2+X.3+X.4+X.5*g,data=Data1,family = binomial),
          replications = 3)
res1$iter
res2$iter
```

Section B: More details about the five environmental factors in UK Biobank data analyses

Given field ID, the environmental factors can be found via UK Biobank website. The below is a brief description:

1. smoking status (http://biobank.ndph.ox.ac.uk/showcase/field.cgi?id=20116): Encoded using 0-2: 0 for never smoker; 1 for previous smoker; and 2 for current smoker.
2. vigorous physical activity (http://biobank.ndph.ox.ac.uk/showcase/field.cgi?id=904): Number of days/week of vigorous physical activity 10+ minutes: ranging from 0 to 7.
3. moderate physical activity (http://biobank.ndph.ox.ac.uk/showcase/field.cgi?id=804): Number of days/week of moderate physical activity 10+ minutes: ranging from 0 to 7.
4. gender (http://biobank.ndph.ox.ac.uk/showcase/field.cgi?id=31): 0 for female and 1 for male.
5. alcohol intake frequency (http://biobank.ndph.ox.ac.uk/showcase/field.cgi?id=1558): 1 for Daily or almost daily; 2 for Three or four times a week; 3 for Once or twice a week; 4 for One to three times a month; 5 for Special occasions only; 6 for Never

Figure S1. Empirical type I error rates based on 10^6 simulated variants with $\beta_G \neq 0$

The variants were simulated following MAF distribution of UK Biobank. SPAGE and SPAGE-NoSPA are the proposed methods with a saddlepoint approximation and a normal approximation, respectively. RAW SPAGE and RAW SPAGE-NoSPA do not use the hybrid strategy but use the approximate statistic S to test all variants.

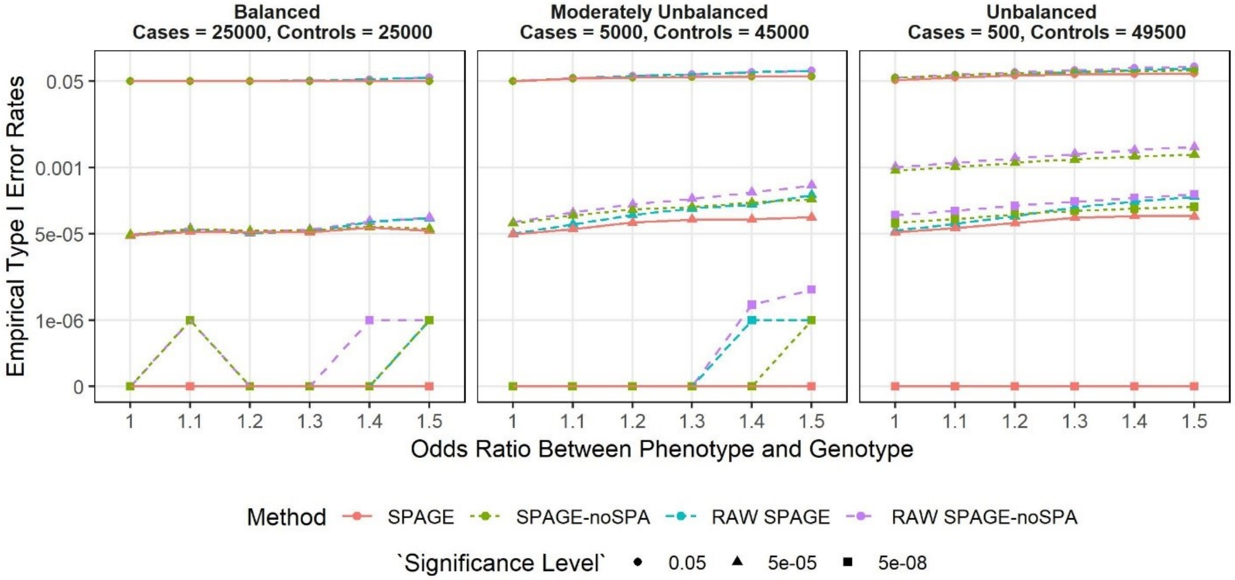


Figure S2. Power comparison of SPAGE, Wald and Firth's test when MAF=0.001

Empirical powers were estimated based on 10^5 simulated variants with a wide range of $\beta_{G\times E} \neq 0$ when MAF was fixed at 0.001. From top to bottom, the plots show empirical powers when the sample size N=50,000, 100,000 and 200,000, respectively. From left to right, the plots consider case-control ratios of 1:1 (balanced), 1:9 (moderately unbalanced), and 1:99 (unbalanced). Round points are for powers at $\alpha = 5 \times 10^{-5}$ and triangle points are for powers at $\alpha = 5 \times 10^{-8}$.

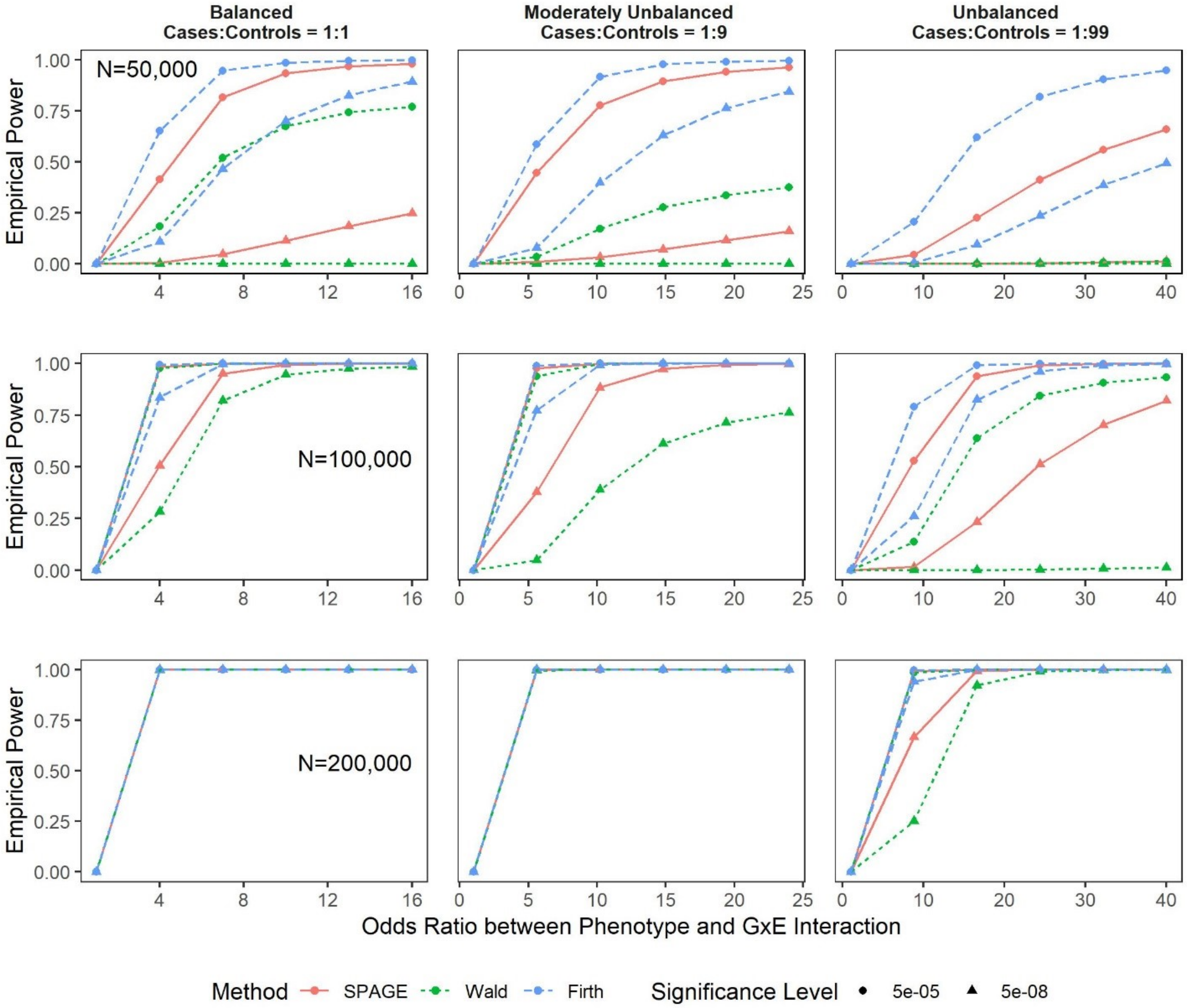


Figure S3. Power comparison of SPAGE, CML and EB when MAF=0.001

Empirical powers were estimated based on 10^5 simulated variants with a wide range of $\beta_{G\times E} \neq 0$ when MAF was fixed at 0.001. From top to bottom, the plots show empirical powers when the sample size N=50,000, 100,000 and 200,000, respectively. From left to right, the plots consider case-control ratios of 1:1 (balanced), 1:9 (moderately unbalanced), and 1:99 (unbalanced). CML (constrained maximum likelihood) and EB (empirical Bayes) were calculated via an R package CGEN. Round points are for powers at $\alpha = 5 \times 10^{-5}$ and triangle points are for powers at $\alpha = 5 \times 10^{-8}$.

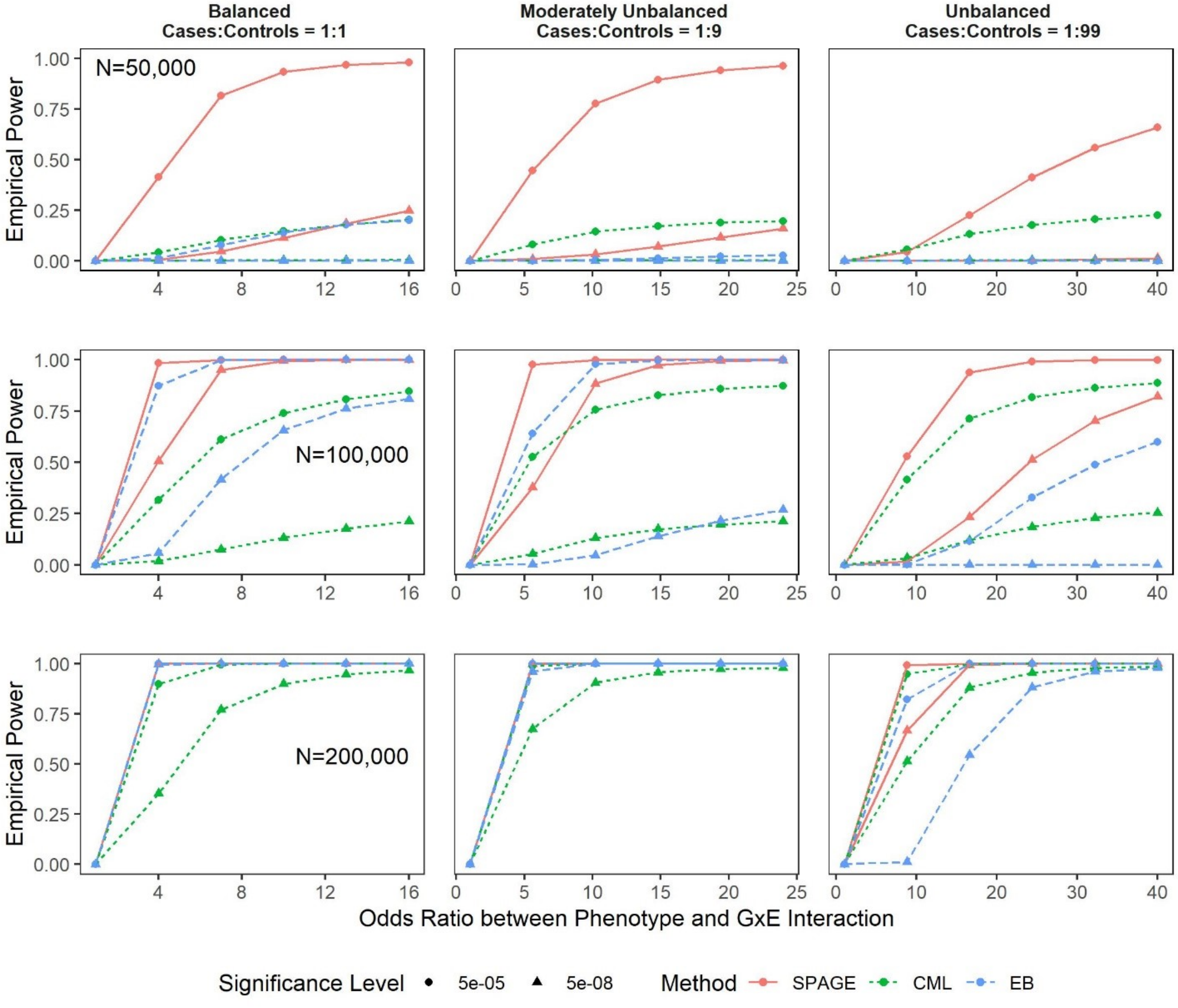


Figure S4. Empirical powers of SPAGE, CML and EB under different study designs

Empirical powers were estimated at $\alpha = 5\times10^{-8}$ based on 10,000 simulated datasets. Binary phenotype datasets were first simulated from a cohort design with $\beta_{G\times E} = \log(1.5)$ and disease prevalence=0.1, and then case-control datasets were constructed by randomly sampling 4000 cases and varying numbers of controls from 4000 to 40,000. CML (constrained maximum likelihood) and EB (empirical Bayes) were calculated via an R package CGEN.

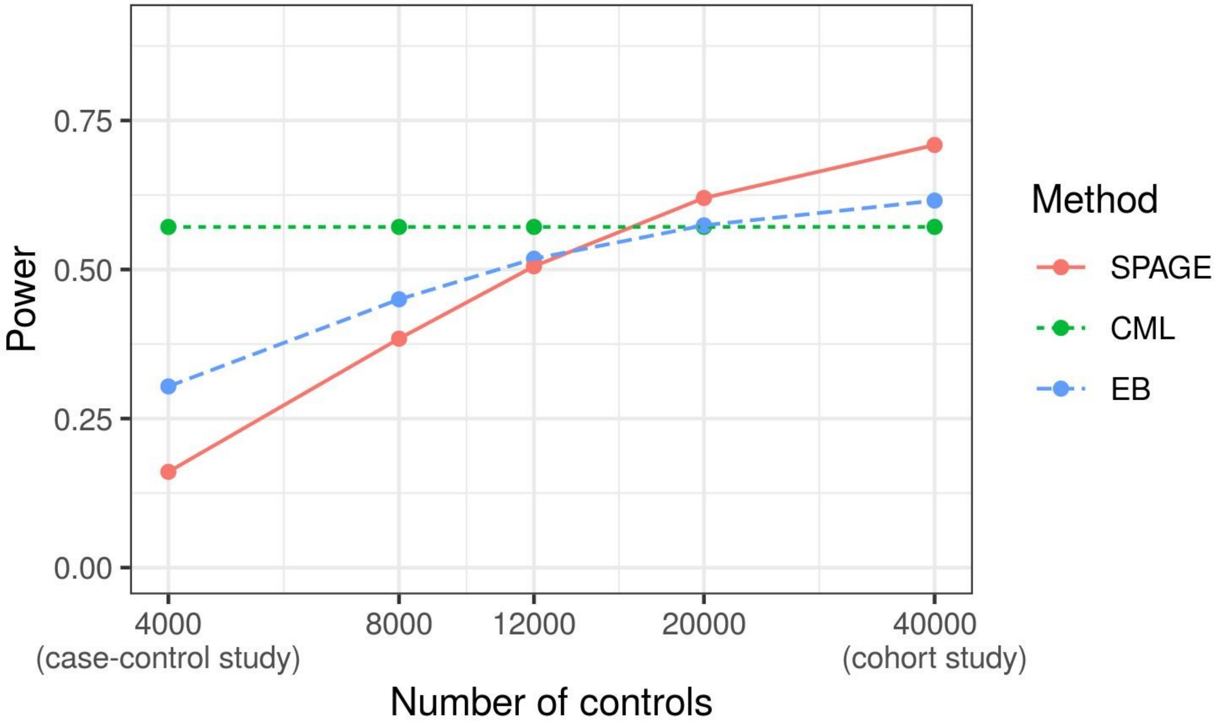


Figure S5. Failure rate of CO

Plots shows the empirical failure rates based on 10^4 simulated variants with $\beta_G = 0$ and $\beta_{G\times E} \neq 0$. The failure rate is defined as the proportion of "NA" (not a p value) outputted by the CO method in GxEScan (version: 0.5.0). From top to bottom, the plots consider MAFs of 0.01, 0.05, and 0.3. From left to right, the plots consider case-control ratios of 25,000:25,000 (balanced), 5,000:45,000 (moderately unbalanced), and 500:49,500 (unbalanced).

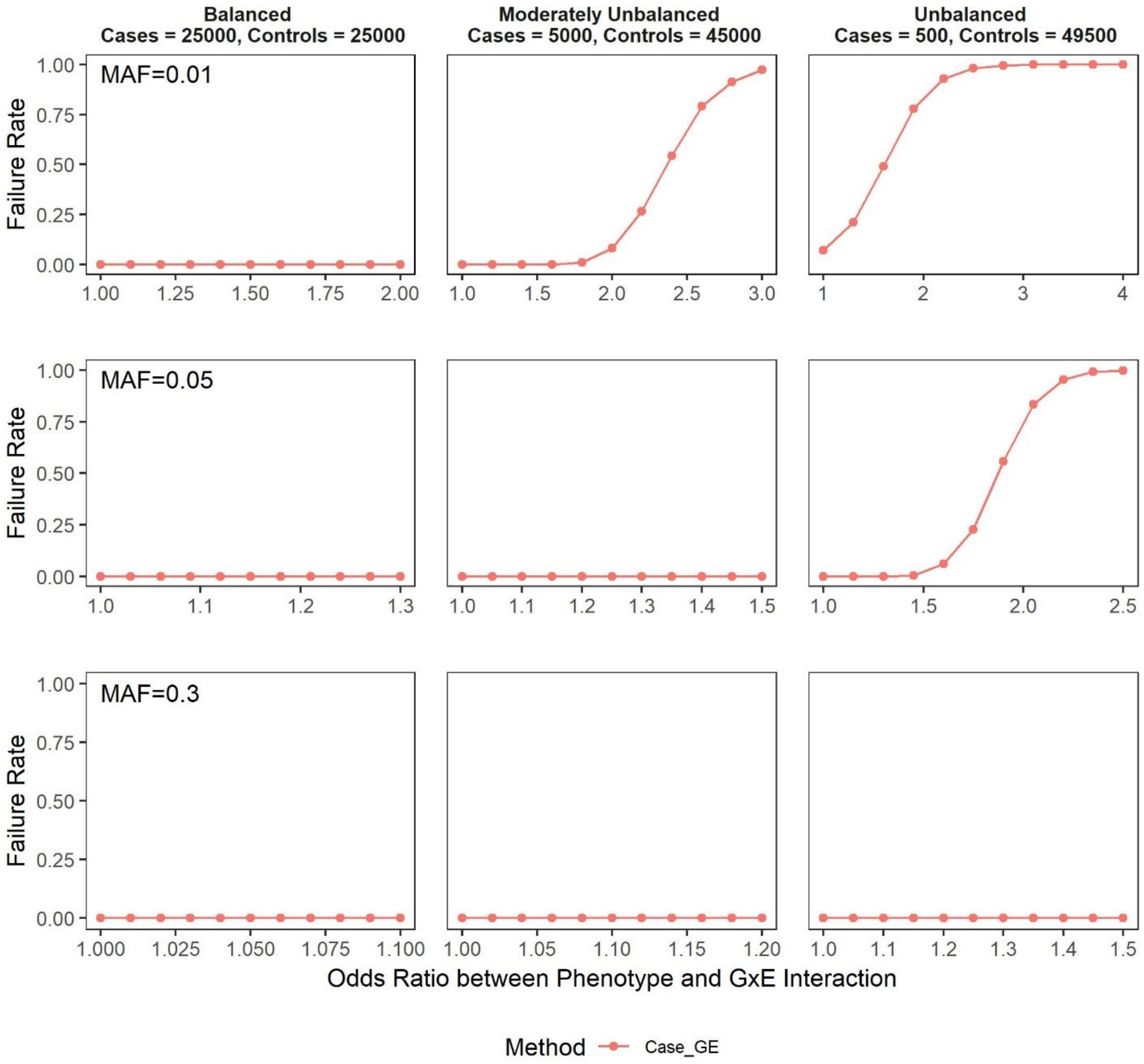
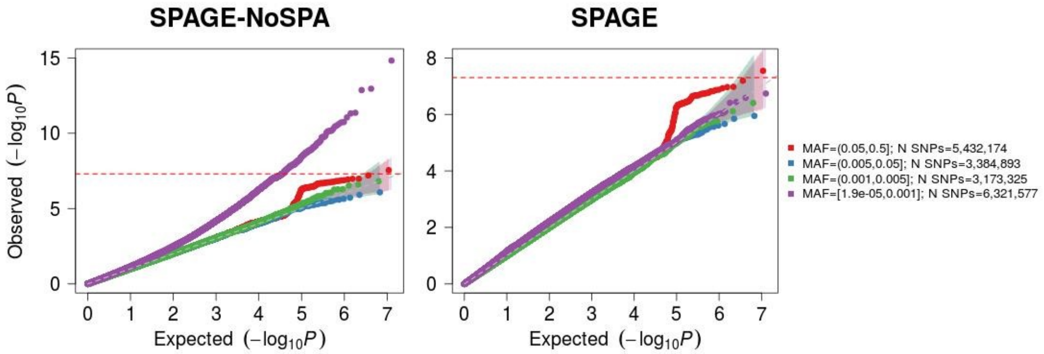


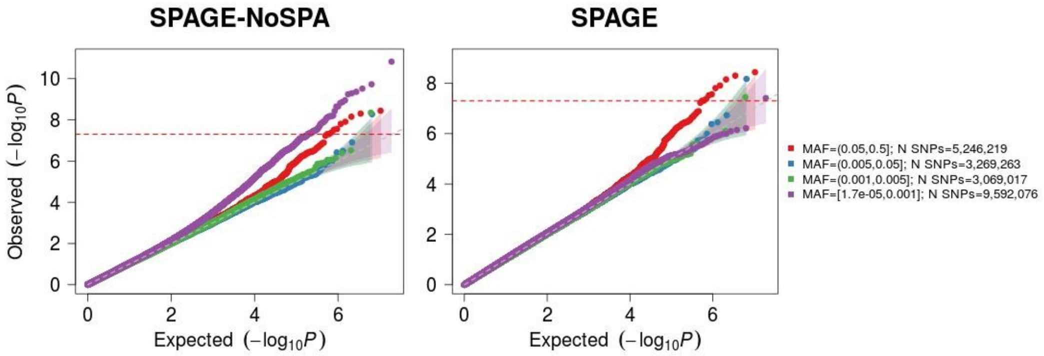
Figure S6. QQ-plots for three combinations of environmental factors and phenotypes from UK Biobank

The left panels show QQ-plots based on SPAGE-NoSPA and the right panels show QQ-plots based on SPAGE. The red line represents the genome-wide significance level $\alpha = 5 \times 10^{-8}$.

a. *Smoking Status* vs *Chronic Airway Obstruction (8,701 cases and 314,750 controls)*



b. *Vigorous Physical Activity* vs *Hyperlipidemia (27,622 cases and 299,859 controls)*



c. *Gender* vs *Cardiac Dysrhythmias (20,754 cases and 320,152 controls)*

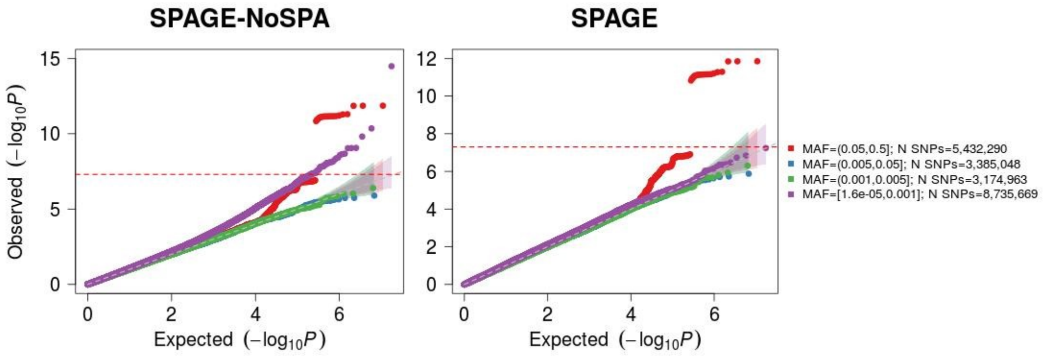


Figure S7. Associations between phenotypes and environmental factors under different genotypes

Definitions of the abbreviations of phenotypes and environmental factors can be seen in Figure 6. P values and ORs (with 99% confidence interval) were calculated from the Firth's bias correction. SMK: odds ratio > 1 means smoking increases the disease risk; Sex: odds ratio < 1 means female risk is lower than male risk; VPA: odds ratio < 1 means physical activities can reduce the disease rate. Note that p=0 means the Firth's test $p < 1\times10^{-100}$.

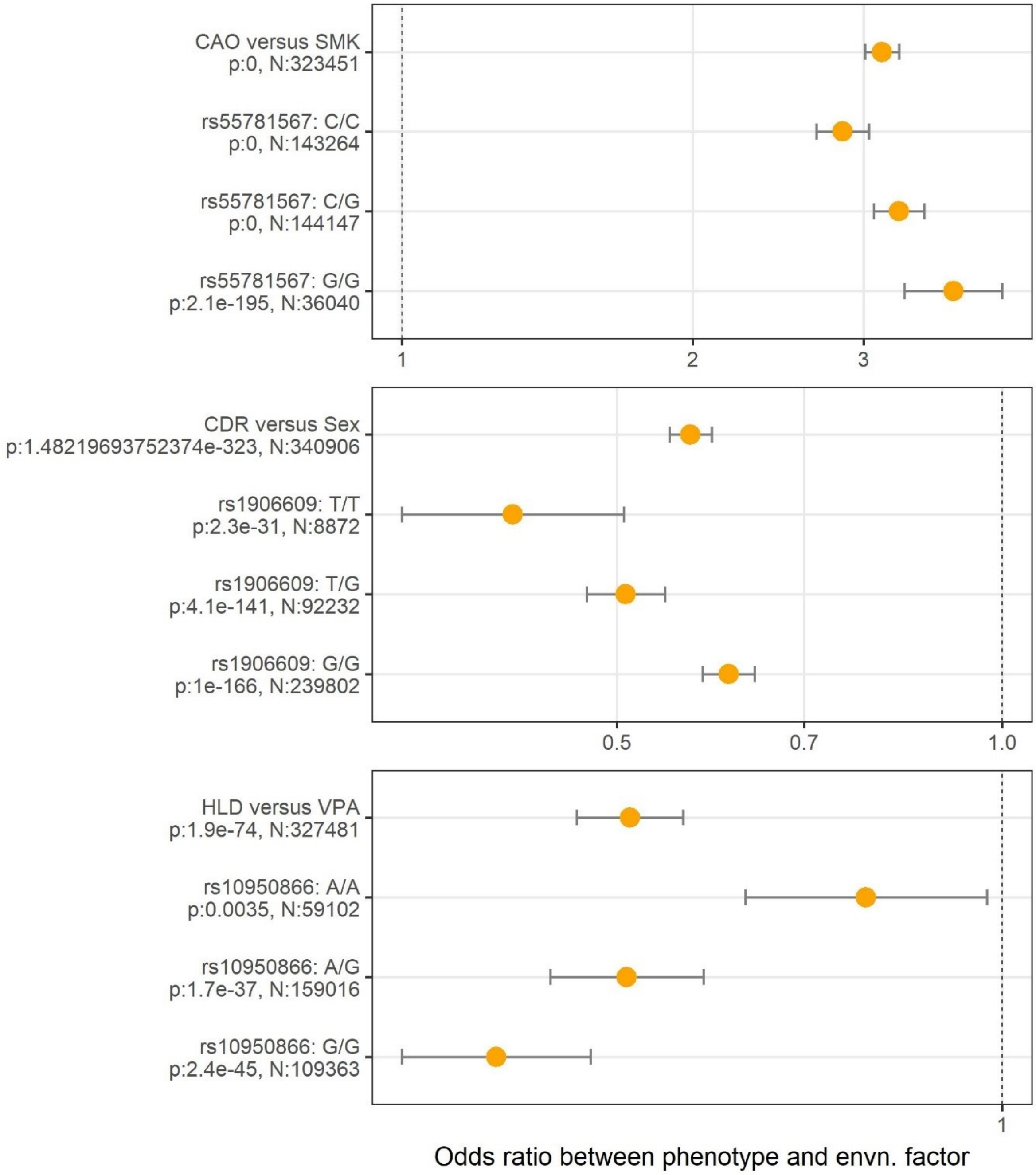


Figure S8. QQ plots and Manhattan plots of hybrid-version Wald and Firth's test for Alcohol × Colorectal Cancer

Left panels show analysis results from the hybrid-version of Firth's test and right panels show the analysis results from the hybrid-version of Wald test. Hybrid-version Wald (Firth's test) is to use SPAGE to calculate p values first, and then calculate p values of Wald test (Firth's test) if the SPAGE p values $< 5 \times 10^{-3}$. The red line represents the genome-wide significance level $\alpha = 5 \times 10^{-8}$.

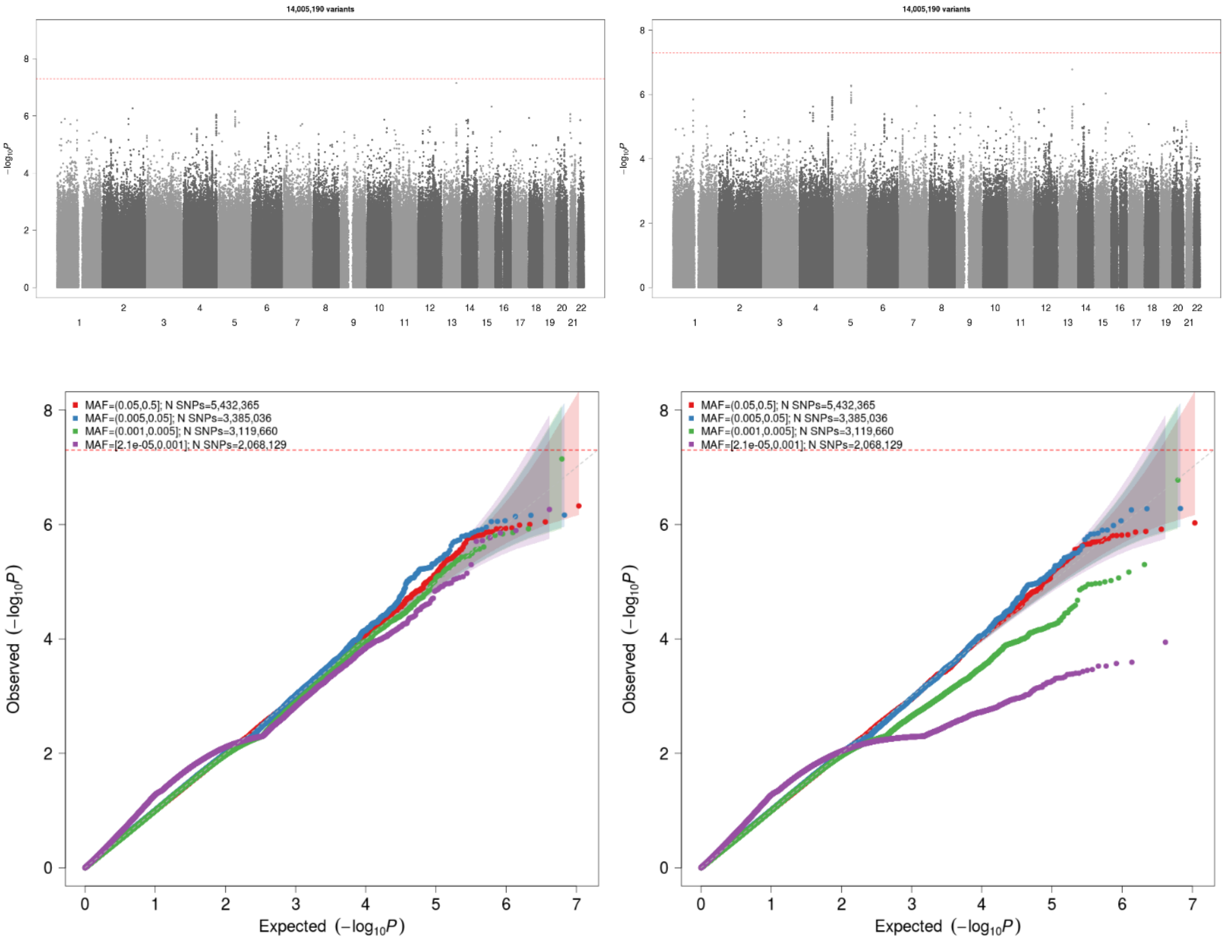


Table S1(a). Projected computation time (CPU years) for testing 1,500 phenotypes across 20 million variants by different methods. Total sample size was 400k.

Number of covariates	CPU time (Years)					
	SPAGE	SPAGE-NoSPA	Wald	Firth's test	CML	CO
Unbalanced: Cases = 4k, Controls = 396k						
5	33.60	27.58	1808.95	4056.78	2866.16	25.14
10	41.22	35.68	2360.20	7688.51	3619.76	32.80
15	48.68	43.36	3010.14	12548.06	4392.09	44.75
20	57.32	51.88	3830.10	18256.50	4939.77	50.49
25	65.69	59.93	4794.46	24893.76	5858.55	70.56
30	73.60	67.82	5790.57	32391.50	6731.22	80.47
Moderately Unbalanced: Cases = 40k, Controls = 360k						
5	32.32	27.15	1249.63	3090.29	4785.18	94.73
10	40.43	35.49	1581.89	5864.45	5433.71	120.77
15	47.57	42.89	1982.25	9540.05	5943.39	149.17
20	56.08	51.47	2529.88	13954.00	6903.87	189.81
25	64.42	59.47	3117.80	18901.81	7837.37	242.42
30	72.57	67.51	3762.15	24638.23	8782.24	316.61
Balanced: Cases = 20k, Controls = 20k						
5	31.44	26.90	1127.26	2285.45	8219.98	193.49
10	39.67	35.25	1406.31	4328.11	9321.18	335.47
15	47.08	42.51	1739.04	7029.65	9809.76	464.30
20	55.79	51.24	2171.09	10124.53	10761.05	627.03
25	63.99	59.48	2647.43	13735.33	11597.75	996.46
30	72.12	67.30	3194.51	17832.00	12908.09	1387.74

Table S1(b). Projected computation time (CPU years) for testing 1,500 phenotypes across 20 million variants by different methods. The number of covariates was 15.

Total sample size	CPU time (Years)					
	SPAGE	SPAGE-NoSPA	Wald	Firth's test	CML	CO
Unbalanced: Cases = 1%, Controls = 99%						
10k	1.27	0.99	82.83	266.05	167.83	1.24
20k	2.26	1.95	158.23	465.31	321.61	2.37
40k	4.43	3.81	301.81	947.23	689.46	4.52
100k	10.90	9.56	735.91	2741.12	1155.24	11.03
200k	22.90	20.06	1486.52	6153.09	1954.26	22.28
400k	48.68	43.36	3010.14	13031.65	4517.15	40.91
Moderately Unbalanced: Cases = 10%, Controls = 90%						
10k	1.18	0.98	51.69	177.00	212.65	5.60
20k	2.07	1.81	94.71	344.18	420.91	10.87
40k	4.22	3.68	177.61	720.76	1039.32	17.87
100k	10.41	9.27	450.17	2062.28	1833.37	46.50
200k	21.97	19.65	950.03	4636.29	3767.90	95.08
400k	47.57	42.89	1982.25	9884.51	5227.76	166.34
Balanced: Cases = 50%, Controls = 50%						
10k	1.14	0.94	37.07	138.38	267.59	17.08
20k	2.06	1.82	74.17	263.44	709.83	32.28
40k	4.11	3.65	149.81	530.44	1221.45	57.00
100k	10.25	9.19	394.43	1535.77	3310.66	141.78
200k	21.94	19.99	834.71	3428.65	5996.31	273.11
400k	47.08	42.51	1739.04	7242.01	8477.31	536.19

Table S2. Empirical type I error rates based on 10^9 simulated variants, of which 99.9% had no marginal genetic effect and 0.1% had marginal genetic effects with odds ratio of 1.4.

Significance Levels	MAF	Empirical type I error rates			
		SPAGE	SPAGE-NoSPA	Wald	Firth's test
Unbalanced: Cases = 500, Controls = 49,500					
0.05	0.001	0.052	0.07	0.051	0.052
	0.01	0.052	0.052	0.052	0.052
	0.05	0.05	0.05	0.05	0.05
	0.3	0.05	0.05	0.05	0.05
5E-5	0.001	2.90E-05	0.002	2.00E-09	4.70E-06
	0.01	4.50E-05	0.00019	2.00E-05	4.50E-05
	0.05	4.70E-05	7.40E-05	5.00E-05	5.00E-05
	0.3	4.70E-05	5.30E-05	5.70E-05	5.00E-05
5E-8	0.001	1.00E-09	0.00015	0	1.00E-09
	0.01	4.80E-08	1.80E-06	8.00E-09	4.00E-08
	0.05	3.70E-08	1.70E-07	4.30E-08	4.40E-08
	0.3	4.20E-08	6.20E-08	8.00E-08	5.20E-08
Moderately Unbalanced: Cases = 5,000, Controls = 45,000					
0.05	0.001	0.051	0.051	0.051	0.051
	0.01	0.05	0.05	0.05	0.05
	0.05	0.05	0.05	0.05	0.05
	0.3	0.05	0.05	0.05	0.05
5E-5	0.001	4.80E-05	0.00013	3.70E-06	3.90E-05
	0.01	5.00E-05	5.70E-05	4.00E-05	4.90E-05
	0.05	5.00E-05	5.10E-05	4.80E-05	5.00E-05
	0.3	5.00E-05	5.00E-05	5.00E-05	5.00E-05
5E-8	0.001	2.60E-08	1.10E-06	0	3.10E-08
	0.01	5.10E-08	1.00E-07	3.80E-08	5.10E-08
	0.05	4.90E-08	5.20E-08	4.10E-08	4.40E-08
	0.3	4.10E-08	4.30E-08	4.30E-08	4.20E-08
Balanced: Cases = 25,000, Controls = 25,000					
0.05	0.001	0.049	0.049	0.049	0.049
	0.01	0.05	0.05	0.05	0.05
	0.05	0.05	0.05	0.05	0.05
	0.3	0.05	0.05	0.05	0.05
5E-5	0.001	5.00E-05	5.60E-05	1.60E-05	4.50E-05
	0.01	5.00E-05	5.10E-05	4.50E-05	5.00E-05
	0.05	5.00E-05	5.00E-05	4.90E-05	5.00E-05
	0.3	5.00E-05	5.00E-05	5.00E-05	5.00E-05
5E-8	0.001	4.20E-08	9.80E-08	1.00E-09	4.20E-08
	0.01	5.10E-08	6.20E-08	4.20E-08	5.00E-08

0.05	4.90E-08	5.50E-08	4.80E-08	5.90E-08
0.3	5.70E-08	5.70E-08	5.70E-08	5.60E-08

Table S3. Complete list of 79 UK-Biobank G×E analyses

Environmental factor	PheCode	Phenotype name
Smoking Status	153.2	Colon cancer
	165.1	Cancer of bronchus; lung
	250.2	Type 2 diabetes
	415	Pulmonary heart disease
	480	Pneumonia
	495	Asthma
	496	Chronic airway obstruction
	496.2	Chronic bronchitis
	512.7	Shortness of breath
	740.1	Osteoarthritis; localized
Vigorous Physical Activity	153	Colorectal cancer
	153.2	Colon cancer
	174.1	Breast cancer [female]
	272.1	Hyperlipidemia
	278.1	Obesity
	401	Hypertension
	411.4	Coronary atherosclerosis
	495	Asthma
	740.1	Osteoarthritis; localized
Moderate Physical Activity	153	Colorectal cancer
	153.2	Colon cancer
	174.1	Breast cancer [female]
	272.1	Hyperlipidemia
	278.1	Obesity
	411.4	Coronary atherosclerosis
	495	Asthma
	740.1	Osteoarthritis; localized
Gender	153	Colorectal cancer
	153.2	Colon cancer
	174	Breast cancer
	208	Benign neoplasm of colon
	250.1	Type 1 diabetes
	250.2	Type 2 diabetes
	272.1	Hyperlipidemia
	278.1	Obesity
	366	Cataract
	401	Hypertension
	411.4	Coronary atherosclerosis
	427	Cardiac dysrhythmias

	455	Hemorrhoids
	495	Asthma
	530.1	Esophagitis, GERD and related diseases
	550.2	Diaphragmatic hernia
	562.1	Diverticulosis
	740.1	Osteoarthritis; localized
Alcohol Intake Frequency	151	Cancer of stomach
	153	Colorectal cancer
	153.2	Colon cancer
	155	Cancer of liver and intrahepatic bile duct
	174.1	Breast cancer [female]
	180	Cervical cancer and dysplasia
	185	Cancer of prostate
	189	Cancer of urinary organs (incl. kidney and bladder)
	198.4	Secondary malignant neoplasm of liver
	242.1	Graves' disease
	250.2	Type 2 diabetes
	272.1	Hyperlipidemia
	296.2	Depression
	317.11	Alcoholic liver damage
	335	Multiple sclerosis
	345	Epilepsy, recurrent seizures, convulsions
	357	Inflammatory and toxic neuropathy
	401.1	Essential hypertension
	411.4	Coronary atherosclerosis
	535	Gastritis and duodenitis
	555	Inflammatory bowel disease and other gastroenteritis and colitis
	571	Chronic liver disease and cirrhosis
	571.8	Liver abscess and sequelae of chronic liver disease
	573.7	Abnormal results of function study of liver
	580	Nephritis; nephrosis; renal sclerosis
	601	Inflammatory diseases of prostate
	613.1	Inflammatory disease of breast
	614	Inflammatory diseases of female pelvic organs
	614.5	Inflammatory disease of cervix, vagina, and vulva
	696.4	Psoriasis
	714	Rheumatoid arthritis and other inflammatory polyarthropathies
	714.1	Rheumatoid arthritis
	740	Osteoarthrosis
	740.1	Osteoarthritis; localized

Table S4. Complete list of SNPs identified with GxE p-values less than 5×10^{-8} for all 79 combinations. Only the most significant SNP is displayed for each gene.

Environ. factor	Phenotype	RSID	POS	Imputation Info Score	MAF	P value (G effect)	P value (SPAGE)	P value (Wald)	P value (Firth)	Func.refGene	Gene.refGene
Smoking Status	Pulmonary heart disease	rs7110737	chr11:35221862_T/A	0.97	0.411128	0.398979	3.57E-08	3.57E-08	3.80E-08	intronic	*CD44*
	Pneumonia	rs143536717	chr3:191177346_A/G	0.97	0.007473	0.01789	4.93E-08	5.54E-07	4.57E-07	ncRNA_intronic	*LINCR-0002*
	Chronic airway obstruction	rs55781567	chr15:78857986_C/G	1.00	0.33425	7.76E-12	2.87E-08	2.64E-08	2.55E-08	UTR5	*CHRNA5*
	Osteoarthritis; localized	rs78340654	chr7:1532370_G/A	0.89	0.000163451	0.010843181	4.50E-08	1.57E-04	1.76E-06		
Vigorous Physical Activity	Colon cancer	rs79671386	chr5:99062643_T/C	0.99	0.05274	0.459981	3.36E-08	2.69E-08	7.11E-08	intergenic	*LINC02113; LOC100133050*
	Breast cancer [female]	rs184243882	chr4:20512383_A/G	0.66	0.00072	0.201173	1.80E-08	1.35E-06	6.17E-08	intronic	*SLIT2*
	Hyperlipidemia	rs10950866	chr7:21691020_A/G	0.99	0.422983	0.256812	3.64E-09	3.75E-09	3.82E-09	intronic	*DNAH11*
		rs72766601	chr16:4487228_T/C	0.94	0.02624	0.237775	6.76E-09	4.01E-09	1.47E-09	intronic	*DNAJA3*
		rs148392361	chr5:134774969_G/C	0.77	0.001389	0.695679	3.58E-08	4.04E-08	5.83E-08	intergenic	*H2AFY; DCANP1*
		rs751416555	chr12:5324708_A/T	0.68	0.000211	0.15628	3.89E-08	1.93E-06	1.90E-07	intergenic	*KCNA5; LINC02443*
	Obesity	rs573332928	chr6:134079709_G/A	0.74	0.000271	0.025765	1.35E-08	6.74E-05	1.36E-07	ncRNA_intronic	*TARID*
	Hypertension	rs544654680	chr7:126380856_C/T	0.55	8.94E-05	0.163684	4.11E-08	2.99E-04	2.69E-07	intronic	*GRM8*
	Coronary atherosclerosis	rs187091750	chr2:13326086_A/G	0.68	0.001044	0.027349	2.35E-08	3.72E-07	3.80E-07	intergenic	*LOC100506474; LINC00276*
		rs560526713	chr19:28773859_C/T	0.81	0.0014	0.101384	3.81E-08	2.26E-07	2.60E-07	intergenic	*LOC101927151; LOC100420587*
	Osteoarthritis; localized	rs777378934	chr4:7851958_G/A	0.86	0.000189	0.00968	4.85E-08	5.09E-05	1.96E-06	intronic	*AFAP1*
Moderate Physical Activity	Breast cancer [female]	rs749311254	chr12:62966647_G/A	0.47	0.000182	0.00183	1.80E-08	7.10E-04	2.79E-06	intronic	*MON2*
		rs773484956	chr7:97812510_C/T	0.49	0.000117	0.007363	2.75E-08	8.93E-03	1.46E-07	intronic	*LMTK2*
		12:63024809_C_T	chr12:63024809_C/T	0.52	0.000228	0.002734	3.49E-08	4.57E-04	4.38E-06	intergenic	*MIRLET7I; PPM1H*
	Hyperlipidemia	rs575180110	chr1:166580616_A/T	0.93	0.000877	0.561031	7.61E-09	4.74E-08	2.34E-10	ncRNA_intronic	*FMO9P*
		rs566421195	chr1:166618041_G/A	0.91	0.000872	0.544749	4.39E-08	1.40E-07	2.10E-09	intergenic	*FMO9P; POGK*
	Coronary atherosclerosis	6:4226163_A_G	chr6:4226163_A/G	0.69	0.000146	0.045534	4.95E-08	2.84E-04	1.95E-07	intergenic	*LOC102724096; MIR7641-2*
Gender	Breast cancer	rs187684970	chr16:22882559_C/G	0.64	0.000426	0.019957	4.08E-08	5.32E-11	1.92E-07	intronic	*HS3ST2*

	Obesity	rs111916547	chr5:100752821_G/C	0.93	0.024807	0.658796	2.71E-08	2.58E-08	1.89E-08	intergenic	*ST8SIA4; SLCO4C1*
	Hypertension	rs536096974	chr12:68684330_T/G	0.85	0.000273	0.407587	4.04E-08	1.63E-06	9.72E-08	intergenic	*IL22;MDM1*
	Cardiac dysrhythmias	rs1906609	chr4:111666451_T/G	0.99	0.161169	3.06E-68	1.42E-12	1.11E-12	9.12E-13	intergenic	*PITX2;C4orf32*
	Osteoarthritis; localized	rs764592273	chr6:147505792_G/T	0.55	0.000228	0.002254	1.32E-08	3.04E-03	2.01E-06	ncRNA_intronic	*STXBP5-AS1*
Alcohol Intake Frequency	Colorectal cancer	rs182738346	chr13:46910214_G/A	0.97	0.004272	0.23162	2.20E-08	1.67E-07	7.15E-08	intergenic	*LINC00563; RUBCNL*
	Cancer of liver and intrahepatic bile duct	rs142741673	chr1:121333234_A/G	0.66	0.038023	0.066781	3.28E-08	1.05E-06	2.31E-07	intergenic	*EMBP1; NONE*
	Hyperlipidemia	rs11590266	chr1:4668423_A/G	0.98	0.448755	0.123365	1.70E-08	1.68E-08	1.68E-08	intergenic	*LINC01646; AJAP1*
	Coronary atherosclerosis	rs117925601	chr7:54226938_C/A	0.75	0.001869	0.095424	2.18E-09	3.12E-08	1.75E-08	intergenic	*LINC01446; HPVC1*
	Gastritis and duodenitis	rs2980819	chr8:40030619_A/G	0.92	0.000196	0.027399	9.07E-09	8.92E-05	2.01E-07	intergenic	*C8orf4; ZMAT4*
	Inflammatory bowel disease and other gastroenteritis and colitis	rs112987403	chr1:222211061_C/T	0.98	0.032692	0.737616	1.11E-08	1.45E-08	1.53E-08	intergenic	*LINC01655; HHIPL2*
		rs531476607	chr2:151185194_T/G	0.80	0.001605	0.004403	2.42E-08	1.17E-05	1.87E-06	intergenic	*LINC01817; RND3*
		rs188807449	chr22:23942723_C/T	0.76	0.000567	0.018596	5.00E-08	5.81E-04	5.28E-07	intergenic	*IGLL1; DRICH1*

Table S5. Complete list of SNPs identified with GxE p-values less than 5×10^{-8} for the highlighted three combinations.

Environ. factor	Phenotype	RSID	POS	Imputation Info Score	MAF	P-value (G effect)	P-value (SPAGE)	P-value (Firth)	P-value (Wald)	Func.refGene	Gene.refGene
Smoking Status	Chronic Airway Obstruction	rs55781567	chr15:78857986_C/G	1	0.3343	7.76E-12	2.87E-08	2.55E-08	2.64E-08	UTR5	*CHRNA5*
Gender	Cardiac Dysrhythmias	rs1906609	chr4:111666451_T/G	0.99	0.1612	3.06E-68	1.42E-12	9.12E-13	1.11E-12	intergenic	*PITX2; C4orf32*
		rs2634073	chr4:111665783_T/C	0.99	0.1613	3.53E-68	1.43E-12	9.19E-13	1.12E-12	intergenic	*PITX2; C4orf32*
		rs2634071	chr4:111669220_T/C	0.99	0.1613	3.23E-68	1.44E-12	9.29E-13	1.13E-12	intergenic	*PITX2; C4orf32*
		rs1906599	chr4:111712686_T/C	0.99	0.1935	6.03E-77	5.16E-12	3.40E-12	3.94E-12	intergenic	*PITX2; C4orf32*
		rs2129977	chr4:111712432_A/G	0.99	0.1933	5.65E-77	5.37E-12	3.54E-12	4.10E-12	intergenic	*PITX2; C4orf32*
		rs2129983	chr4:111704080_G/A	0.99	0.1935	1.22E-76	6.29E-12	4.17E-12	4.82E-12	intergenic	*PITX2; C4orf32*
		rs6854111	chr4:111704536_A/T	0.99	0.1930	8.38E-77	6.89E-12	4.57E-12	5.28E-12	intergenic	*PITX2; C4orf32*
		rs2129982	chr4:111704143_A/G	0.99	0.1930	1.06E-76	7.00E-12	4.65E-12	5.37E-12	intergenic	*PITX2; C4orf32*
		rs7689774	chr4:111703510_G/T	0.99	0.1932	1.27E-76	7.05E-12	4.68E-12	5.41E-12	intergenic	*PITX2; C4orf32*
		rs13143308	chr4:111714419_T/G	1.00	0.1937	3.98E-77	7.11E-12	4.71E-12	5.45E-12	intergenic	*PITX2; C4orf32*
		rs67249485	chr4:111699685_A/T	0.99	0.1930	1.04E-76	7.21E-12	4.79E-12	5.53E-12	intergenic	*PITX2; C4orf32*
		rs6820568	chr4:111699831_C/T	0.99	0.1932	1.39E-76	7.26E-12	4.83E-12	5.58E-12	intergenic	*PITX2; C4orf32*
		rs6837901	chr4:111698108_T/C	0.99	0.1931	1.58E-76	7.36E-12	4.89E-12	5.65E-12	intergenic	*PITX2; C4orf32*

		rs1906616	chr4:111697568_A/G	0.99	0.1931	1.53E-76	7.47E-12	4.97E-12	5.74E-12	intergenic	*PITX2; C4orf32*
		rs1906615	chr4:111701798_G/T	0.99	0.1930	1.10E-76	7.83E-12	5.21E-12	6.02E-12	intergenic	*PITX2; C4orf32*
		rs6843082	chr4:111718067_G/A	1.00	0.1932	2.07E-78	8.19E-12	5.43E-12	6.26E-12	intergenic	*PITX2; C4orf32*
		rs6847935	chr4:111696651_A/T	0.99	0.1930	1.81E-76	8.87E-12	5.92E-12	6.83E-12	intergenic	*PITX2; C4orf32*
		rs2634074	chr4:111677041_T/A	0.99	0.1930	2.50E-76	1.10E-11	7.41E-12	8.52E-12	intergenic	*PITX2; C4orf32*
		rs2466455	chr4:111685615_C/T	0.99	0.1930	1.51E-76	1.16E-11	7.81E-12	8.98E-12	intergenic	*PITX2; C4orf32*
		rs2723334	chr4:111688752_T/C	0.99	0.1932	2.97E-76	1.49E-11	1.01E-11	1.15E-11	intergenic	*PITX2; C4orf32*
Vigorous Physical Activity	Hyperlipidemia	rs10950866	chr7:21691020_A/G	0.99	0.4230	0.257	3.64E-09	3.82E-09	3.75E-09	intronic	*DNAH11*
		rs2030672	chr7:21687925_G/C	0.99	0.4403	0.142	4.99E-09	5.19E-09	5.14E-09	intronic	*DNAH11*
		rs72766601	chr16:4487228_T/C	0.94	0.0262	0.238	6.76E-09	1.47E-09	4.01E-09	intronic	*DNAJA3*
		rs10260140	chr7:21690063_A/T	0.99	0.4200	0.221	7.08E-09	7.45E-09	7.31E-09	intronic	*DNAH11*
		rs11762779	chr7:21713592_C/T	0.98	0.4499	0.344	1.23E-08	1.27E-08	1.26E-08	intronic	*DNAH11*
		rs6975512	chr7:21706255_G/A	1.00	0.4337	0.392	1.56E-08	1.61E-08	1.59E-08	intronic	*DNAH11*
		rs7793951	chr7:21700039_C/G	1.00	0.4279	0.542	2.74E-08	2.83E-08	2.79E-08	intronic	*DNAH11*
		rs2390549	chr7:21697779_A/T	0.99	0.4312	0.560	3.01E-08	3.11E-08	3.06E-08	intronic	*DNAH11*
		rs148392361	chr5:134774969_G/C	0.77	0.0014	0.696	3.58E-08	5.83E-08	4.04E-08	intergenic	*H2AFY; DCANP1*
		rs751416555	chr12:5324708_A/T	0.68	0.0002	0.156	3.89E-08	1.90E-07	1.93E-06	intergenic	*KCNA5; LINC02443*
		rs714423	chr7:21712615_C/A	0.99	0.3945	0.835	4.13E-08	4.29E-08	4.17E-08	intronic	*DNAH11*
		rs970020	chr7:21711019_G/A	1.00	0.4352	0.340	4.92E-08	5.07E-08	5.01E-08	intronic	*DNAH11*
		rs10950869	chr7:21711860_C/T	0.99	0.3915	0.811	4.92E-08	5.12E-08	4.97E-08	intronic	*DNAH11*