

## **Additional File 1**

### **Supplementary Information for:**

#### **Genome-wide Analysis of Sex Disparities in the Genetic Architecture of Lung and Colorectal Cancers**

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## Supporting Acknowledgment

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## Tables

**Table S1.** Demographic information about the analyzed datasets.

Cohort	Females					Males					Comparison		
	N	Case%	Smoke%	BY (SD)	BMI (SD)	N	Case%	Smoke%	BY (SD)	BMI (SD)	P <sub>Smoke</sub>	P <sub>BY</sub>	P <sub>BMI</sub>
<b>CRCa</b>													
<b>CHS</b>	1943	2.47	43.39	1915.01 (5.30)	26.42 (4.90)	1282	3.82	66.77	1913.92 (5.82)	26.44 (3.63)	< 0.05	< 0.05	> 0.05
<b>FHS</b>	2809	2.60	56.89	1930.73 (15.67)	26.29 (4.91)	2276	2.86	68.76	1931.18 (14.32)	27.64 (3.75)	< 0.05	> 0.05	< 0.05
<b>HRS</b>	3841	2.34	60.77	1933.20 (8.22)	26.74 (4.99)	2940	2.45	77.45	1933.40 (7.71)	27.52 (3.95)	< 0.05	> 0.05	< 0.05
<b>LCa</b>													
<b>CHS</b>	1943	3.24	43.39	1915.01 (5.30)	26.42 (4.90)	1282	3.59	66.77	1913.92 (5.82)	26.44 (3.63)	< 0.05	< 0.05	> 0.05
<b>FHS</b>	2809	2.63	56.89	1930.73 (15.67)	26.29 (4.91)	2276	3.95	68.76	1931.18 (14.32)	27.64 (3.75)	< 0.05	> 0.05	< 0.05
<b>HRS</b>	3839	2.60	60.64	1933.23 (8.19)	26.75 (5.00)	2940	2.86	77.38	1933.42 (7.69)	27.54 (3.95)	< 0.05	> 0.05	< 0.05

Abbreviations: CRCa = colorectal cancer; LCa = lung cancer; CHS = Cardiovascular Health Study [1]; FHS = Framingham Heart Study [2,3]; HRS = Health and Retirement Study [4]; N = numbers of subjects in analyzed datasets; Case% = percent of cases; Smoke% = percent of smokers; BY (SD) = average birth year and its standard deviation; BMI (SD) = average body mass index and its standard deviation; P<sub>Smoke</sub>, P<sub>BY</sub>, and P<sub>BMI</sub> = P-values of the differences in the distributions of covariates between the two sexes obtained by chi-square test (smoking history) or Student's t-test (birth year and BMI)

**Table S2.** Numbers (and percentages) of analyzed SNPs along with the genomic inflation factors ( $\lambda$ ) resulted from our genome-wide association analyses.

Cohort	SNPs-G	SNPs-IMP	$\lambda$ -G	$\lambda$ -IMP
<b>CRCa-F</b>				
HRS	1270859	396123	1.010	1.023
FHS	342070	1005527	1.009	1.006
CHS	315263	1176540	1.023	1.023
<b>LCa-F</b>				
HRS	1270744	396232	1.000	1.000
FHS	342119	1005542	1.036	1.025
CHS	315308	1176805	1.007	1.008
<b>CRCa-M</b>				
HRS	1271669	396746	1.025	1.027
FHS	349661	1006039	0.999	0.993
CHS	315246	1176611	1.002	0.999
<b>LCa-M</b>				
HRS	1271601	396833	1.007	1.002
FHS	349752	1006061	1.006	1.011
CHS	314979	1176675	1.019	1.018

Abbreviations: SNP = single-nucleotide polymorphism; CRCa-F = colorectal cancer in females; LCa-F = lung cancer in females; CRCa-M = colorectal cancer in males; LCa-M = lung cancer in males; CHS = Cardiovascular Health Study [1]; FHS = Framingham Heart Study [2,3]; HRS = Health and Retirement Study [4]; SNPs-G= number of genotyped SNPs; SNPs-IMP= number of imputed SNPs;  $\lambda$ -G: genomic inflation factor of genotyped SNPs;  $\lambda$ -IMP: genomic inflation factor of imputed SNPs

**Table S3.** The odds ratios of fixed-effects covariates in females and males from conducted meta-analyses.

Covariate	Females			Males			Comparison	
	OR	se	P-value	OR	se	P-value	Chi-square	P-value
<b>CRCa</b>								
<b>Smoking history</b>	1.643	0.122	4.56x10 <sup>-5</sup>	1.441	0.153	1.69x10 <sup>-2</sup>	0.451	5.02x10 <sup>-1</sup>
<b>Birth year</b>	1.276	0.058	2.73x10 <sup>-5</sup>	1.185	0.067	1.15x10 <sup>-2</sup>	0.696	4.04x10 <sup>-1</sup>
<b>BMI</b>	1.027	0.010	7.74x10 <sup>-3</sup>	1.058	0.014	8.96x10 <sup>-5</sup>	2.756	9.69x10 <sup>-2</sup>
<b>LCa</b>								
<b>Smoking history</b>	4.281	0.146	2.32x10 <sup>-23</sup>	3.464	0.206	1.74x10 <sup>-9</sup>	0.702	4.02x10 <sup>-1</sup>
<b>Birth year</b>	1.473	0.059	5.31x10 <sup>-11</sup>	1.428	0.066	6.57x10 <sup>-8</sup>	0.119	7.30x10 <sup>-1</sup>
<b>BMI</b>	0.995	0.011	6.27x10 <sup>-1</sup>	0.974	0.015	7.74x10 <sup>-2</sup>	1.364	2.43x10 <sup>-1</sup>

Abbreviations: CRCa = colorectal cancer; LCa = lung cancer; BMI = body mass index; OR and se = odds ratio and its standard error

**Table S4.** Cancer-associated SNPs from genome-wide association analyses.

Detected Associations					HRS				FHS				CHS				Meta-analysis							Previous Findings					
Chr	Gene	SNP	Pos	A1	Freq	OR	se	P <sub>HRS</sub>	Freq	OR	se	P <sub>FHS</sub>	Freq	OR	se	P <sub>CHS</sub>	Freq	OR	se	P <sub>META</sub>	P <sub>Q</sub>	i <sup>2</sup>	Effects	N	1Mb?	Proxy?	Region?	Gene?	Prognostic?
CRCa-F																													
8q22.3	SNX31	rs1078186	100613251	C	0.579	0.582	0.153	4.19x10 <sup>-4</sup>	0.567	0.563	0.174	9.48x10 <sup>-4</sup>	0.572	0.775	0.208	2.21x10 <sup>-1</sup>	0.574	0.615	0.056	1.60x10 <sup>-6</sup>	4.49x10 <sup>-1</sup>	0	---	8590	N	N	S	N	O
8q24.23	KHDRBS3	rs118174020	135843271	C	NA	NA	NA	NA	0.949	0.370	0.281	3.92x10 <sup>-4</sup>	0.948	0.340	0.324	8.73x10 <sup>-4</sup>	0.949	0.357	0.062	1.41x10 <sup>-6</sup>	8.49x10 <sup>-1</sup>	0	?--	4752	N	N	N	O	O
10q26.3	GLRX3	rs3118492	130435775	A	0.227	1.624	0.162	2.74x10 <sup>-3</sup>	0.232	1.711	0.203	8.05x10 <sup>-3</sup>	0.230	1.720	0.227	1.69x10 <sup>-2</sup>	0.229	1.672	0.168	4.15x10 <sup>-6</sup>	9.71x10 <sup>-1</sup>	0	+++	8544	N	N	N	N	O
10q26.3	GLRX3	rs372813	130442933	A	0.227	1.619	0.162	2.89x10 <sup>-3</sup>	0.243	1.678	0.189	6.08x10 <sup>-3</sup>	0.230	1.721	0.227	1.68x10 <sup>-2</sup>	0.233	1.661	0.163	3.25x10 <sup>-6</sup>	9.75x10 <sup>-1</sup>	0	+++	8592	N	N	N	N	O
10q26.3	GLRX3	rs359063	130452326	T	0.225	1.585	0.163	4.64x10 <sup>-3</sup>	0.239	1.732	0.190	3.89x10 <sup>-3</sup>	0.227	1.751	0.228	1.39x10 <sup>-2</sup>	0.230	1.669	0.164	2.86x10 <sup>-6</sup>	9.14x10 <sup>-1</sup>	0	+++	8545	N	N	N	N	O
10q26.3	GLRX3	rs307385	130452402	T	0.225	1.604	0.162	3.61x10 <sup>-3</sup>	0.238	1.754	0.192	3.50x10 <sup>-3</sup>	0.227	1.751	0.228	1.39x10 <sup>-2</sup>	0.230	1.684	0.167	2.16x10 <sup>-6</sup>	9.23x10 <sup>-1</sup>	0	+++	8543	N	N	N	N	O
LCA-F																													
2p21	LOC102723824	rs7593032*	42122050	T	0.712	0.506	0.149	4.63x10 <sup>-6</sup>	0.709	0.841	0.179	3.32x10 <sup>-1</sup>	0.719	0.663	0.197	3.68x10 <sup>-2</sup>	0.713	0.631	0.057	3.66x10 <sup>-6</sup>	9.14x10 <sup>-2</sup>	0.582	---	8577	N	N	S	N	N
5q13.2	LINC02056	rs42775	72584687	T	0.329	1.701	0.145	2.43x10 <sup>-4</sup>	0.328	1.527	0.181	1.97x10 <sup>-2</sup>	0.315	1.381	0.188	8.54x10 <sup>-2</sup>	0.325	1.561	0.138	4.98x10 <sup>-6</sup>	6.74x10 <sup>-1</sup>	0	+++	8516	S	N	S	N	N
10q21.1	PRKG1	rs11000463*	52014359	T	0.897	0.427	0.186	4.60x10 <sup>-6</sup>	0.908	0.588	0.255	3.77x10 <sup>-2</sup>	0.906	1.097	0.311	7.65x10 <sup>-1</sup>	0.903	0.558	0.067	1.75x10 <sup>-5</sup>	3.31x10 <sup>-2</sup>	0.707	---	8591	N	N	N	O	N
10q21.1	PRKG1	rs11000467*	52015312	G	0.897	0.427	0.186	4.67x10 <sup>-6</sup>	0.914	0.552	0.272	2.87x10 <sup>-2</sup>	0.906	1.097	0.311	7.65x10 <sup>-1</sup>	0.905	0.548	0.066	1.37x10 <sup>-5</sup>	3.41x10 <sup>-2</sup>	0.704	---	8570	N	N	N	O	N
10q26.13	ZRANB1	rs76972397	124961380	T	0.925	0.455	0.210	1.70x10 <sup>-4</sup>	NA	NA	NA	NA	0.938	0.390	0.295	1.43x10 <sup>-3</sup>	0.930	0.432	0.063	9.62x10 <sup>-7</sup>	6.72x10 <sup>-1</sup>	0	-?	5770	N	N	G	O	N
18q11.2	HRH4	rs482962	24532843	A	0.272	1.408	0.152	2.41x10 <sup>-2</sup>	0.237	1.871	0.203	2.04x10 <sup>-3</sup>	0.277	1.747	0.196	4.52x10 <sup>-3</sup>	0.262	1.607	0.151	4.90x10 <sup>-6</sup>	4.75x10 <sup>-1</sup>	0	+++	8585	N	N	S	N	N
CRCa-M																													
3p24.2	THR8	rs57751578	24486090	T	0.902	0.459	0.224	5.16x10 <sup>-4</sup>	0.919	0.587	0.281	5.80x10 <sup>-2</sup>	0.917	0.423	0.302	4.39x10 <sup>-3</sup>	0.911	0.483	0.064	1.89x10 <sup>-6</sup>	6.98x10 <sup>-1</sup>	0	---	6491	N	N	N	O	O
5q31.1	FSTL4	rs4631227	133152748	A	0.284	1.914	0.173	1.81x10 <sup>-4</sup>	0.299	1.410	0.181	5.77x10 <sup>-2</sup>	0.303	1.702	0.218	1.49x10 <sup>-2</sup>	0.293	1.663	0.163	3.20x10 <sup>-6</sup>	4.76x10 <sup>-1</sup>	0	+++	6481	N	N	G	O	N
6q14.3	HTR1E	rs72907251	86515650	C	0.933	0.386	0.240	7.49x10 <sup>-5</sup>	0.942	0.425	0.270	1.55x10 <sup>-3</sup>	0.941	0.743	0.405	4.64x10 <sup>-1</sup>	0.937	0.446	0.063	1.06x10 <sup>-6</sup>	3.73x10 <sup>-1</sup>	0	---	6496	N	N	N	O	N
13q12.11	MPHOSPH8	rs9579517*	19603453	C	0.902	0.375	0.208	2.43x10 <sup>-6</sup>	0.895	0.961	0.292	8.91x10 <sup>-1</sup>	0.904	0.523	0.291	2.62x10 <sup>-2</sup>	0.900	0.519	0.066	8.88x10 <sup>-6</sup>	3.31x10 <sup>-2</sup>	0.707	---	6490	N	N	N	N	N
13q12.11	MPHOSPH8	rs56357430*	19632421	C	0.902	0.375	0.208	2.43x10 <sup>-6</sup>	0.897	1.031	0.301	9.20x10 <sup>-1</sup>	0.900	0.544	0.292	3.69x10 <sup>-2</sup>	0.900	0.528	0.068	1.77x10 <sup>-5</sup>	2.25x10 <sup>-2</sup>	0.736	+-	6498	N	N	N	N	N
LCA-M																													
5p15.33	LINC01377	rs12657742	3123661	A	0.869	0.577	0.200	5.98x10 <sup>-3</sup>	0.857	0.547	0.201	2.66x10 <sup>-3</sup>	0.867	0.527	0.281	2.27x10 <sup>-2</sup>	0.864	0.555	0.062	3.67x10 <sup>-6</sup>	9.63x10 <sup>-1</sup>	0	---	6490	N	N	G	O	N
5q23.2	LINC02039	rs77914729	126003571	C	0.925	0.528	0.233	6.07x10 <sup>-3</sup>	0.933	0.418	0.272	1.33x10 <sup>-3</sup>	0.931	0.464	0.346	2.67x10 <sup>-2</sup>	0.929	0.475	0.065	2.67x10 <sup>-6</sup>	8.09x10 <sup>-1</sup>	0	---	6495	N	N	S	N	N
5q23.2	LINC02039	rs75874914	126003878	C	0.925	0.529	0.233	6.25x10 <sup>-3</sup>	0.933	0.425	0.271	1.64x10 <sup>-3</sup>	0.932	0.464	0.346	2.66x10 <sup>-2</sup>	0.929	0.478	0.065	3.24x10 <sup>-6</sup>	8.29x10 <sup>-1</sup>	0	---	6496	N	N	S	N	N
5q23.2	LINC02039	rs11954381	126006435	G	0.926	0.521	0.234	5.32x10 <sup>-3</sup>	0.933	0.430	0.269	1.73x10 <sup>-3</sup>	0.932	0.464	0.346	2.66x10 <sup>-2</sup>	0.929	0.477	0.065	2.81x10 <sup>-6</sup>	8.63x10 <sup>-1</sup>	0	---	6491	N	N	S	N	N
6q23.3	MAP7	rs9399183	136496350	A	0.832	0.468	0.172	1.03x10 <sup>-5</sup>	0.839	0.711	0.192	7.56x10 <sup>-2</sup>	0.823	0.679	0.258	1.33x10 <sup>-1</sup>	0.833	0.585	0.060	3.33x10 <sup>-6</sup>	2.19x10 <sup>-1</sup>	0.341	---	6494	N	N	N	N	O
6q23.3	MAP7	rs3799451	136508794	A	0.851	0.448	0.176	4.91x10 <sup>-6</sup>	0.860	0.684	0.201	5.78x10 <sup>-2</sup>	0.842	0.691	0.263	1.61x10 <sup>-1</sup>	0.852	0.565	0.060	1.62x10 <sup>-6</sup>	2.01x10 <sup>-1</sup>	0.377	---	6495	N	N	N	N	O
6q23.3	MAP7	rs3799453	136518050	G	0.852	0.447	0.176	4.70x10 <sup>-6</sup>	0.860	0.684	0.201	5.78x10 <sup>-2</sup>	0.843	0.728	0.271	2.42x10 <sup>-1</sup>	0.853	0.570	0.061	2.46x10 <sup>-6</sup>	1.72x10 <sup>-1</sup>	0.432	---	6495	N	N	N	N	O
6q23.3	MAP7	rs3799454	136518078	T	0.835	0.462	0.172	6.90x10 <sup>-6</sup>	0.841	0.706	0.191	6.85x10 <sup>-2</sup>	0.824	0.724	0.261	2.16x10 <sup>-1</sup>	0.835	0.586	0.060	3.58x10 <sup>-6</sup>	1.76x10 <sup>-1</sup>	0.425	---	6498	N	N	N	N	O
6q23.3	MAP7	rs3799462	136524611	G	0.852	0.459	0.177	1.10x10 <sup>-5</sup>	0.860	0.684	0.201	5.78x10 <sup>-2</sup>	0.843	0.728	0.271	2.42x10 <sup>-1</sup>	0.853	0.577	0.062	4.49x10 <sup>-6</sup>	2.12x10 <sup>-1</sup>	0.356	---	6498	N	N	N	N	O
8p23.2	CSMD1	rs13261356	4605119	C	0.904	0.502	0.210	1.04x10 <sup>-3</sup>	0.895	0.458	0.233	8.05x10 <sup>-4</sup>	NA	NA	NA	NA	0.900	0.482	0.065	3.23x10 <sup>-6</sup>	7.69x10 <sup>-1</sup>	0	-?	5209	G	N	G	SO	N
10p12.31	MIR4675	rs11012129	20545511	T	0.947	0.461	0.253	2.15x10 <sup>-3</sup>	0.942	0.284	0.292	1.68x10 <sup>-5</sup>	NA	NA	NA	NA	0.945	0.375	0.060	3.21x10 <sup>-7</sup>	2.14x10 <sup>-1</sup>	0.352	---	5207	N	N	S	O	N
18q21.31	ATP8B1	rs2437037	57795758	A	0.909	0.458	0.213	2.39x10 <sup>-4</sup>	NA	NA	NA	NA	0.910	0.432	0.296	4.50x10 <sup>-3</sup>	0.909	0.449	0.066	3.95x10 <sup>-6</sup>	8.71x10 <sup>-1</sup>	0	-?	4216	N	N	N	N	O
21q21.3	GRIK1	rs363433	29588811	C	0.855	0.535	0.187	8.08x10 <sup>-4</sup>	0.865	0.571	0.219	1.03x10 <sup>-2</sup>	0.876	0.499	0.277	1.20x10 <sup>-2</sup>	0.863	0.539	0.061	1.14x10 <sup>-6</sup>	9.30x10 <sup>-1</sup>	0	---	6490	N	N	N	O	O
21q21.3	GRIK1	rs363432	29591270	G	0.857	0.570	0.191	3.23x10 <sup>-3</sup>	0.862	0.573	0.217	1.03x10 <sup>-2</sup>	0.877	0.496	0.277	1.12x10 <sup>-2</sup>	0.863	0.554	0.063	4.10x10 <sup>-6</sup>	9.03x10 <sup>-1</sup>	0	---	6495	N	N	N	O	O
21q21.3	GRIK1	rs2832405	29591425	T	0.849	0.530	0.184	5.58x10 <sup>-4</sup>	0.852	0.589	0.211	1.24x10 <sup>-2</sup>	0.871	0.523	0.278	1.98x10 <sup>-2</sup>	0.854	0.548	0.061	1.50x10 <sup>-6</sup>	9.16x10 <sup>-1</sup>	0	---	6497	N	N	N	O	O
21q21.3	GRIK1	rs363472	29595793	G	0.852	0.559	0.186	1.77x10 <sup>-3</sup>	0.852	0.594	0.210	1.29x10 <sup>-2</sup>	0.872	0.518	0.278	1.78x10 <sup>-2</sup>	0.856	0.562	0.062	4.23x10 <sup>-6</sup>	9.26x10 <sup>-1</sup>	0	---	6490	N	N	N	O	O

Abbreviations: SNP = single-nucleotide polymorphism; CRCA-F = colorectal cancer in females; LCA-F = lung cancer in females; CRCA-M = colorectal cancer in males; LCA-M = lung cancer in males; CHS = Cardiovascular Health Study [1]; FHS = Framingham Heart Study [2,3]; HRS = Health and Retirement Study [4]; Chr = chromosomal region (i.e., cytogenetic band); Gene = the gene within which the SNP is located or else the closest gene to the SNP; Pos = SNP position based on Human Genome version 38 (hg38); A1 = effect allele; Freq = frequency of effect allele; OR (se) = odds ratio and its standard error; P<sub>HRS</sub>, P<sub>FHS</sub>, and P<sub>CHS</sub> = P-values of the SNP in HRS, FHS, and CHS datasets, respectively; P<sub>META</sub> = P-value in conducted meta-analysis; P<sub>Q</sub> = P-value of Q-statistics (Cochran's heterogeneity test); i<sup>2</sup> = i-squared inconsistency metric; Effects = directions of SNP's effects in HRS, FHS, and CHS datasets, respectively (Positive, Negative, Missing); N = Number of subjects with non-missing genotype data in conducted meta-analysis; 1Mb? = whether any polymorphism associated with the same cancer was previously discovered within the ±1 Mb of the SNP detected here (G: polymorphism with P <

**Table S5.** Linkage disequilibrium measures among SNPs with significant association signals that were mapped to the same gene.

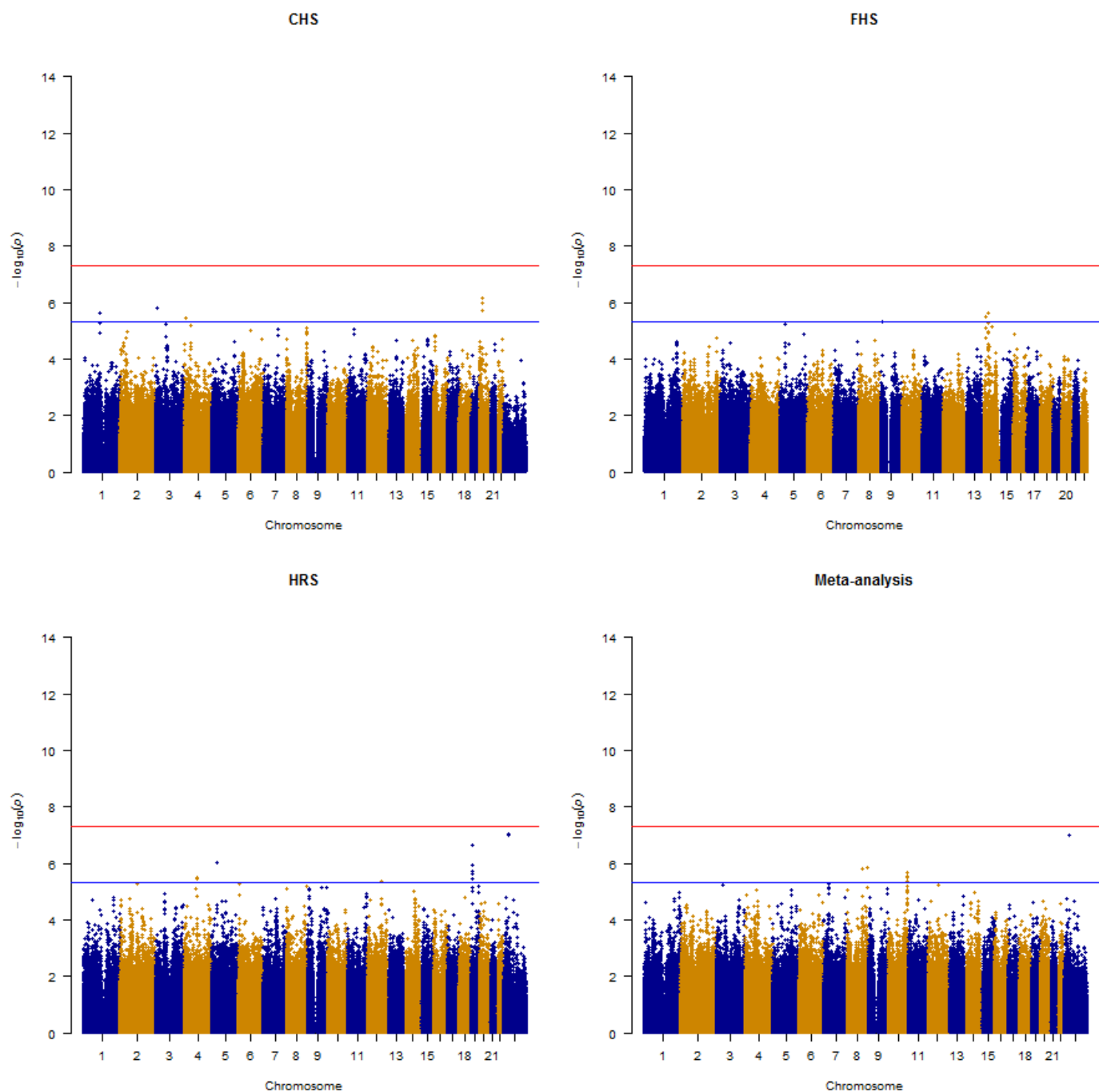
SNP1	SNP2	D'	r <sup>2</sup>
<b>GLRX3</b>			
rs3118492	rs372813	1	1
rs3118492	rs359063	1	0.971
rs3118492	rs307385	1	0.971
rs372813	rs359063	1	0.971
rs372813	rs307385	1	0.971
rs359063	rs307385	1	1
<b>PRKG1</b>			
rs11000463	rs11000467	1	1
<b>MPHOSPH8</b>			
rs9579517	rs56357430	1	1
<b>LINC02039</b>			
rs77914729	rs75874914	1	1
rs77914729	rs11954381	1	1
rs75874914	rs11954381	1	1
<b>MAP7</b>			
rs9399183	rs3799451	1	0.855
rs9399183	rs3799453	1	0.855
rs9399183	rs3799454	1	1
rs9399183	rs3799462	1	0.855
rs3799451	rs3799453	1	1
rs3799451	rs3799454	1	0.855
rs3799451	rs3799462	1	1
rs3799453	rs3799454	1	0.855
rs3799453	rs3799462	1	1
rs3799454	rs3799462	1	0.855
<b>GRIK1</b>			
rs363433	rs363432	1	1
rs363433	rs2832405	1	0.957
rs363433	rs363472	1	0.957
rs363432	rs2832405	1	0.957
rs363432	rs363472	1	0.957
rs2832405	rs363472	1	1

The LD measures were obtained for the CEU population (i.e., Utah Residents with Northern and Western European Ancestry) using *LDlink* web-tool [6].



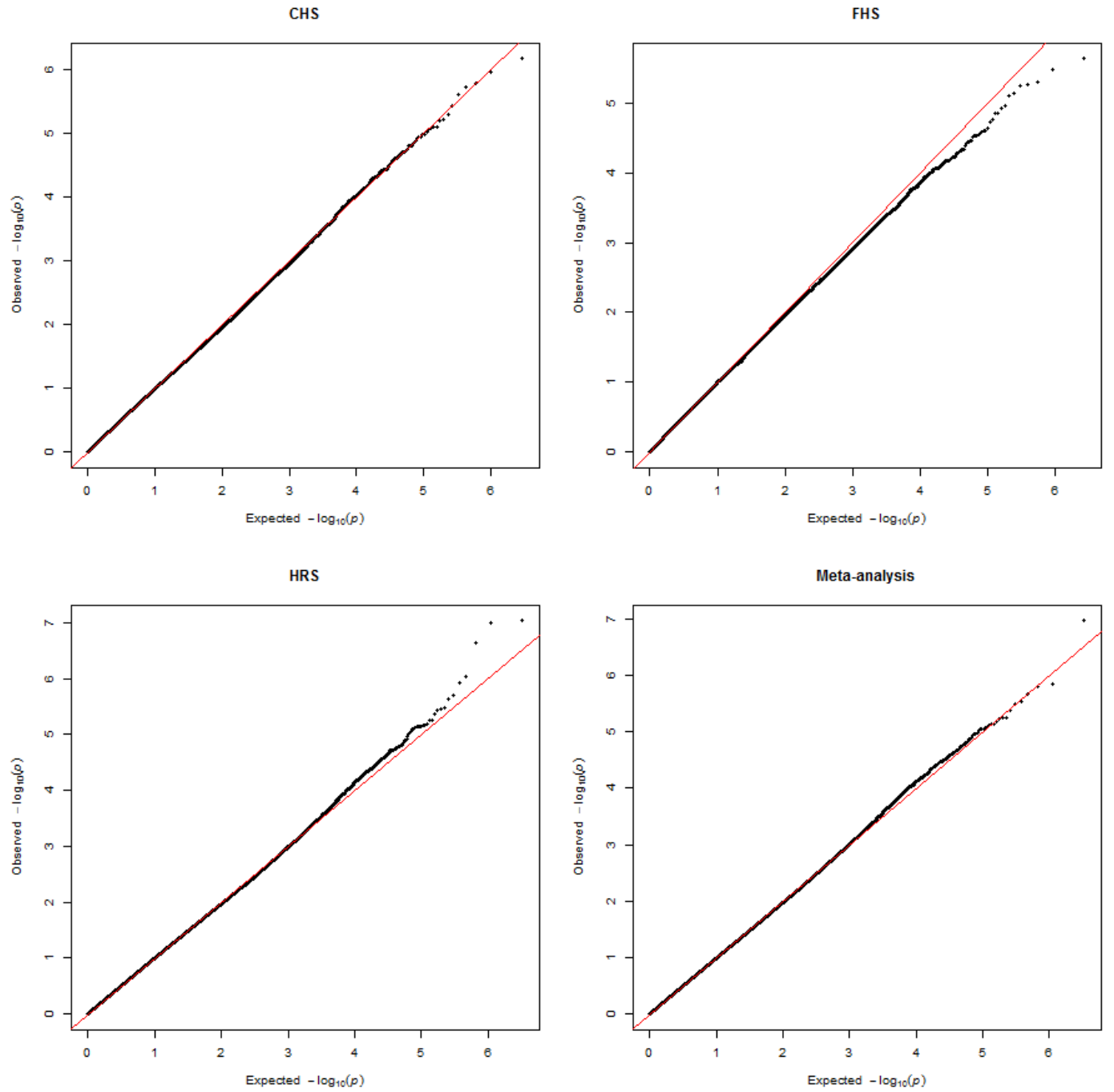
## Figures

**Figure S1.** Manhattan plot of the genome-wide association analyses of colorectal cancer in females (CRCa-F).



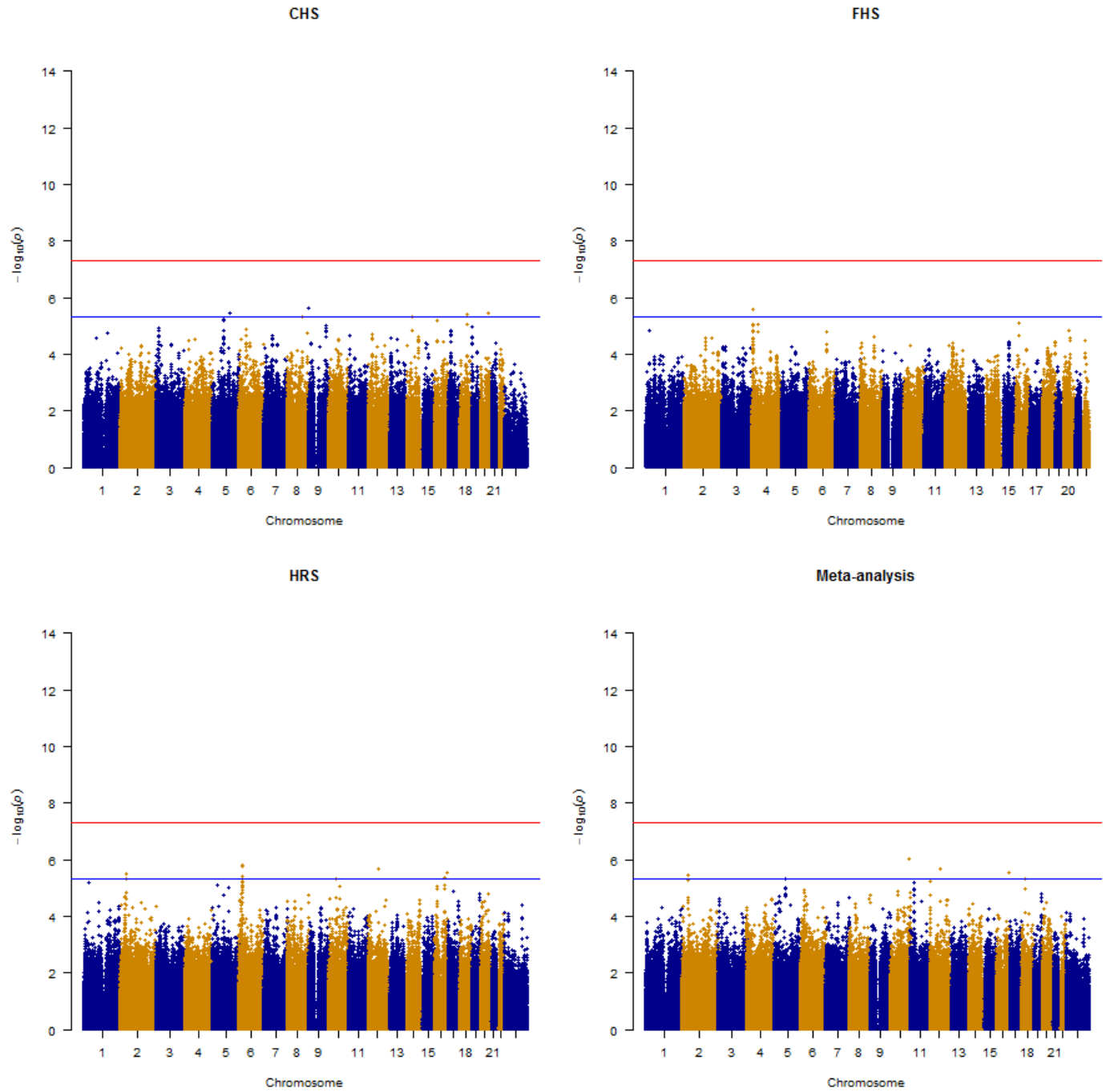
Abbreviations: CHS = Cardiovascular Health Study [1]; FHS = Framingham Heart Study [2,3]; HRS = Health and Retirement Study [4]; Red and blue lines display the genome-wide (i.e.,  $P < 5.0 \times 10^{-8}$ ) and suggestive (i.e.,  $5.0 \times 10^{-8} \leq P < 5.0 \times 10^{-6}$ ) significance levels, respectively.

**Figure S2.** QQ plot of the genome-wide association analyses of colorectal cancer in females (CRCa-F).



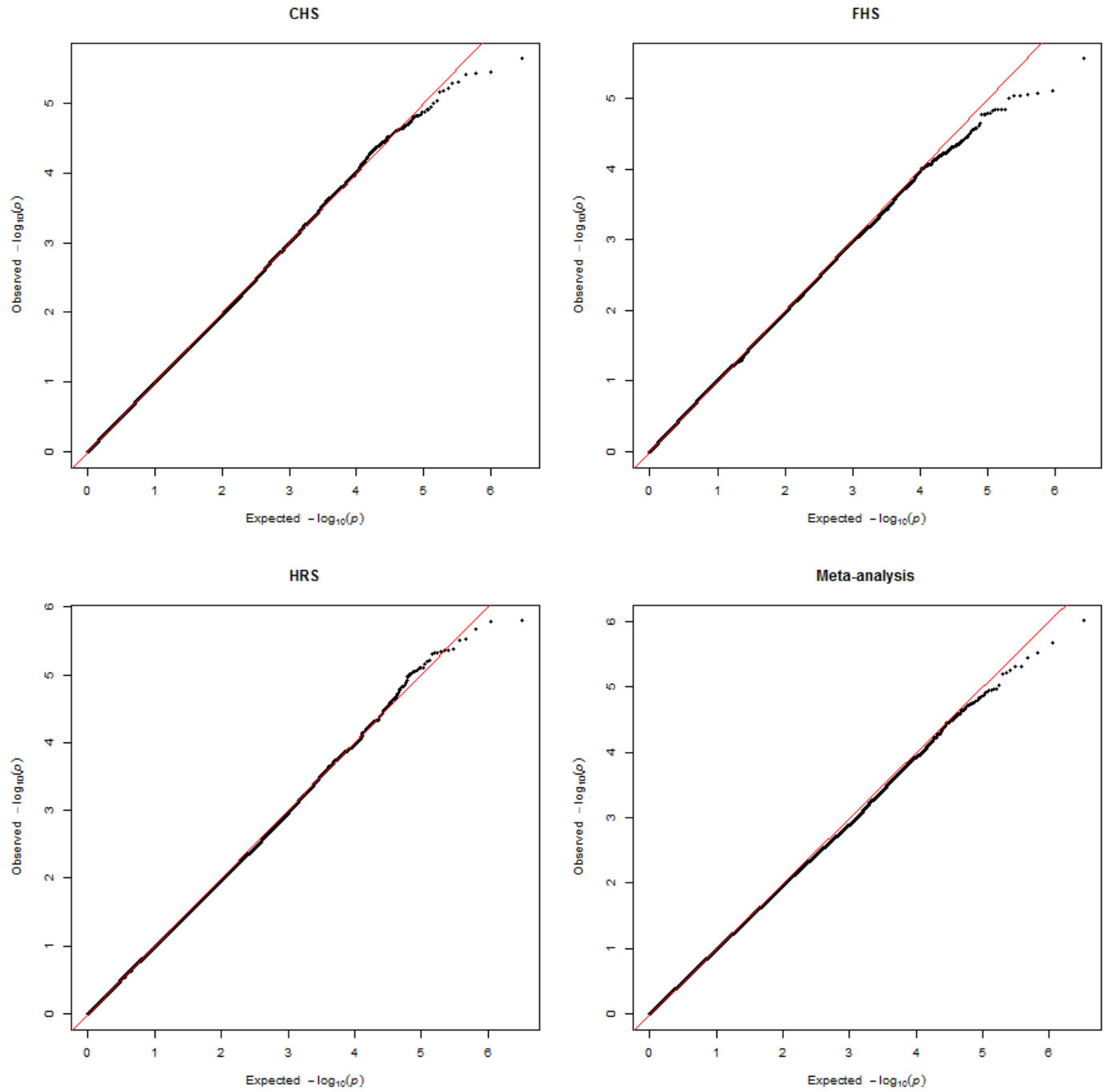
Abbreviations: CHS = Cardiovascular Health Study [1]; FHS = Framingham Heart Study [2,3]; HRS = Health and Retirement Study [4]

**Figure S3.** Manhattan plot of the genome-wide association analyses of lung cancer in females (LCa-F).



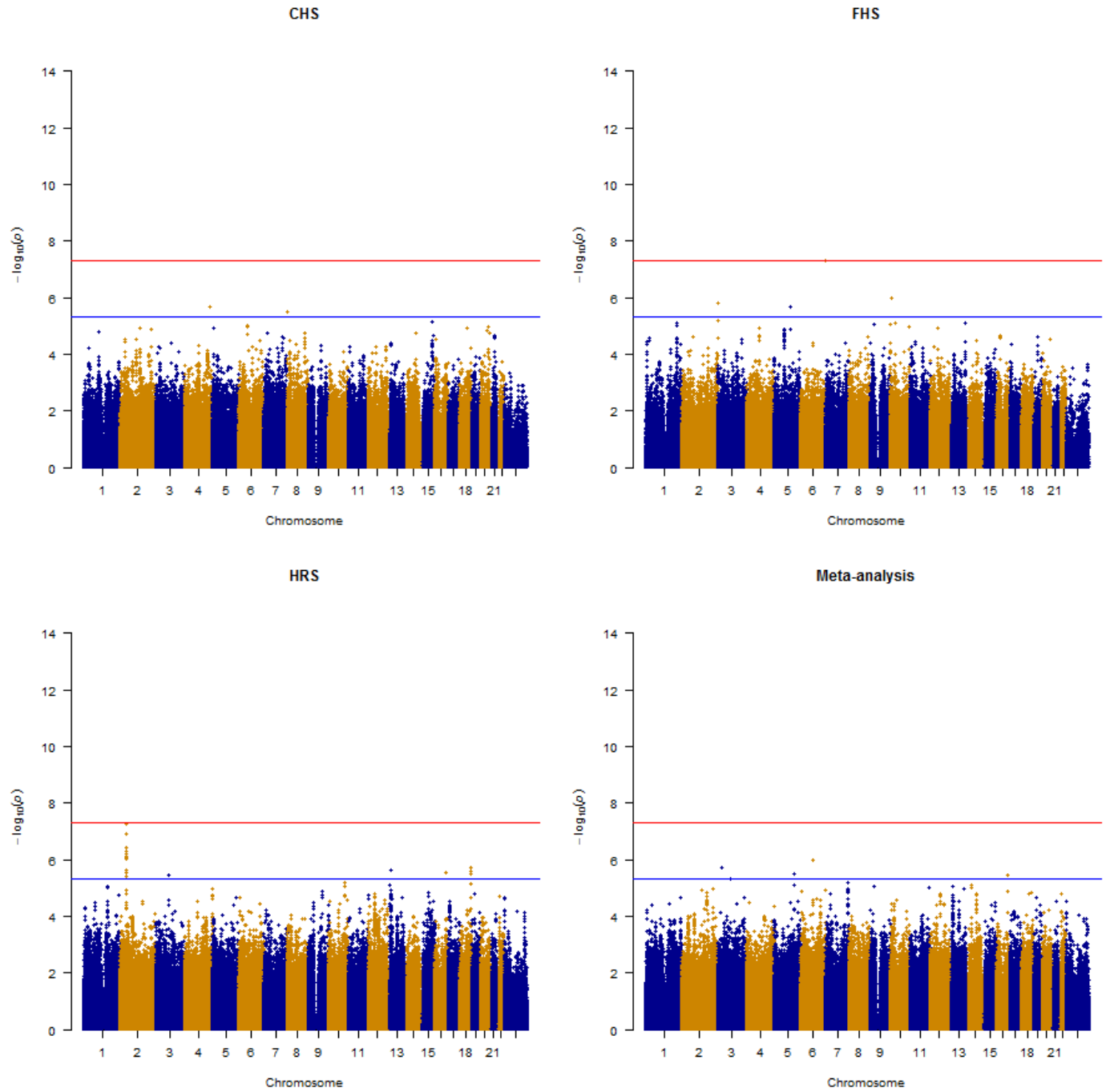
Abbreviations: CHS = Cardiovascular Health Study [1]; FHS = Framingham Heart Study [2,3]; HRS = Health and Retirement Study [4]; Red and blue lines display the genome-wide (i.e.,  $P < 5.0 \times 10^{-8}$ ) and suggestive (i.e.,  $5.0 \times 10^{-8} \leq P < 5.0 \times 10^{-6}$ ) significance levels, respectively.

**Figure S4.** QQ plot of the genome-wide association analyses of lung cancer in females (LCa-F).



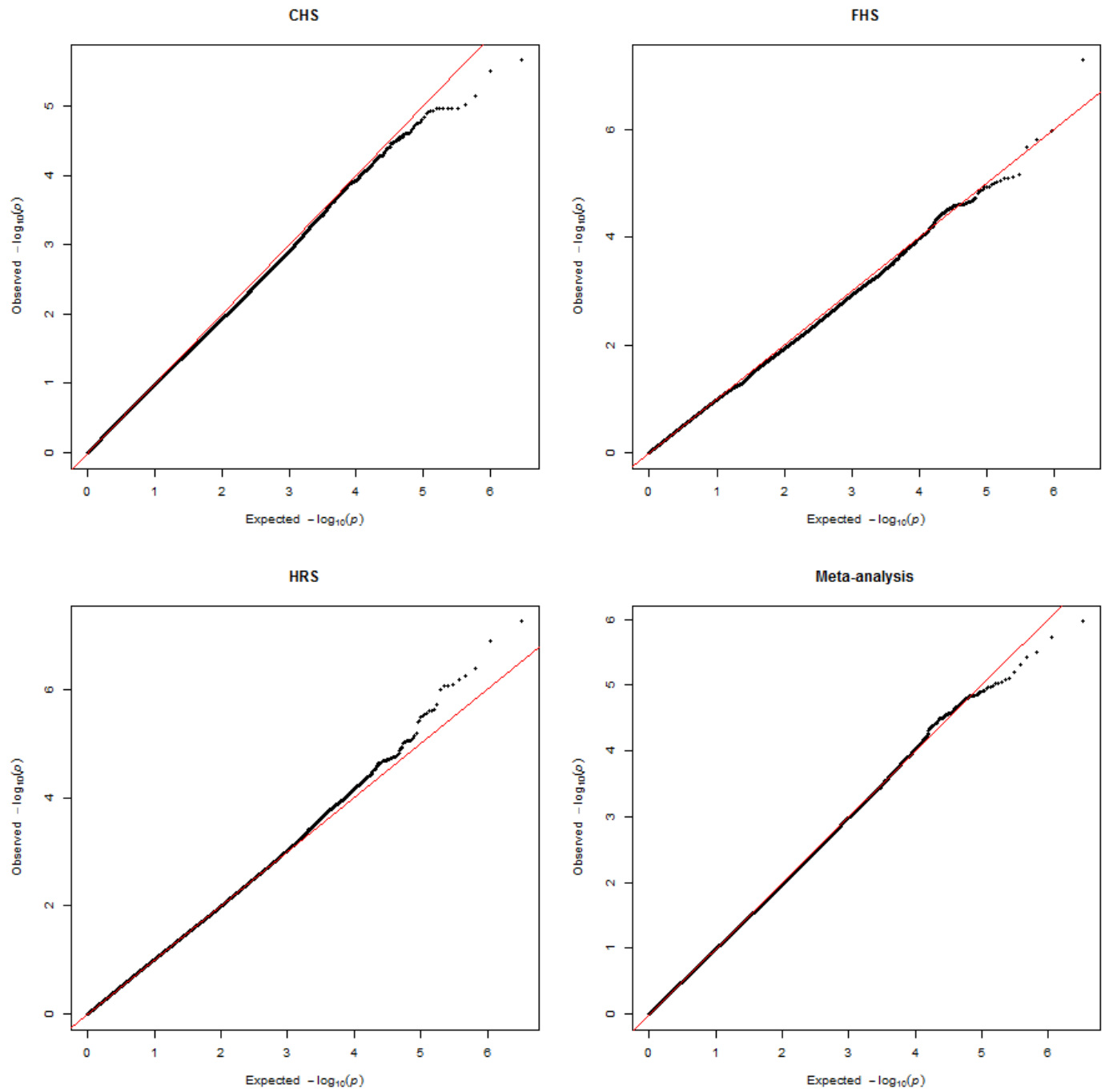
Abbreviations: CHS = Cardiovascular Health Study [1]; FHS = Framingham Heart Study [2,3]; HRS = Health and Retirement Study [4]

**Figure S5.** Manhattan plot of the genome-wide association analyses of colorectal cancer in males (CRCa-M).



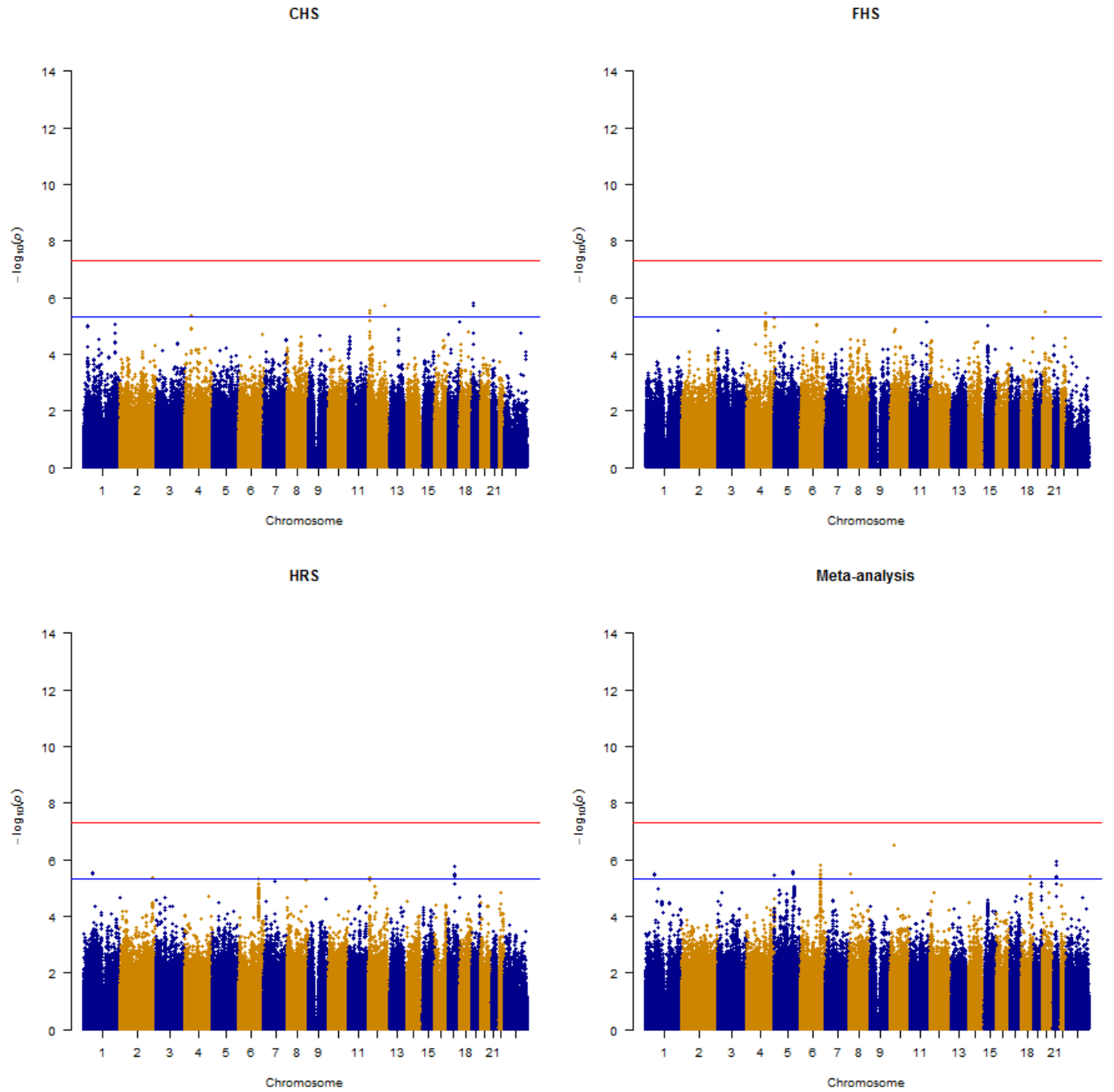
Abbreviations: CHS = Cardiovascular Health Study [1]; FHS = Framingham Heart Study [2,3]; HRS = Health and Retirement Study [4]; Red and blue lines display the genome-wide (i.e.,  $P < 5.0 \times 10^{-8}$ ) and suggestive (i.e.,  $5.0 \times 10^{-8} \leq P < 5.0 \times 10^{-6}$ ) significance levels, respectively.

**Figure S6.** QQ plot of the genome-wide association analyses of colorectal cancer in males (CRCa-M).



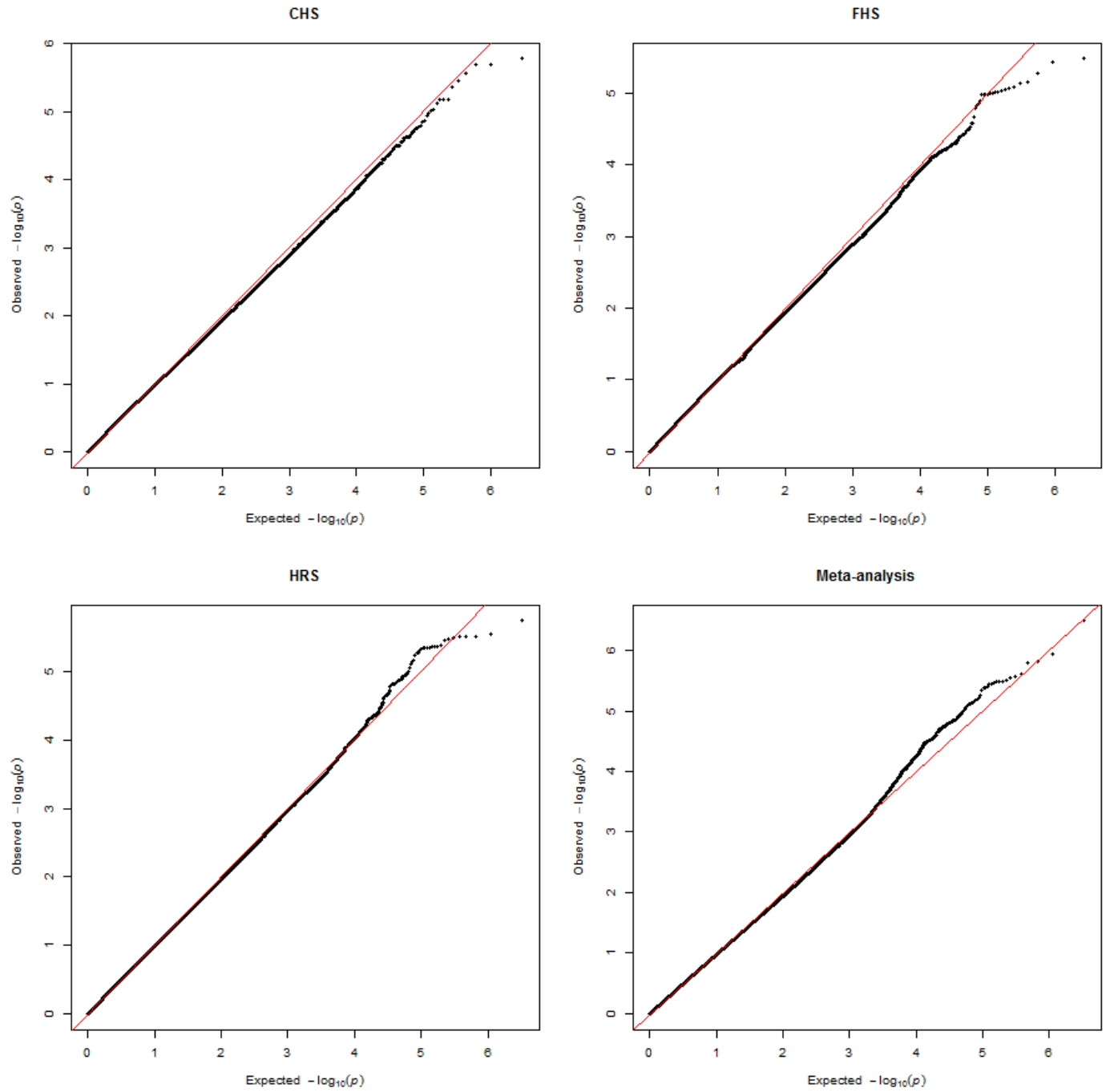
Abbreviations: CHS = Cardiovascular Health Study [1]; FHS = Framingham Heart Study [2,3]; HRS = Health and Retirement Study [4]

**Figure S7.** Manhattan plot of the genome-wide association analyses of lung cancer in males (LCa-M).



Abbreviations: CHS = Cardiovascular Health Study [1]; FHS = Framingham Heart Study [2,3]; HRS = Health and Retirement Study [4]; Red and blue lines display the genome-wide (i.e.,  $P < 5.0 \times 10^{-8}$ ) and suggestive (i.e.,  $5.0 \times 10^{-8} \leq P < 5.0 \times 10^{-6}$ ) significance levels, respectively.

**Figure S8.** QQ plot of the genome-wide association analyses of lung cancer in males (LCa-M).



Abbreviations: CHS = Cardiovascular Health Study [1]; FHS = Framingham Heart Study [2,3]; HRS = Health and Retirement Study [4]



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