

**The number and title of each element included in the document:**

**Figure S1.** Flowchart of the included patients

**Figure S2.** Heat map of cumulative incidence ratio (CIR) of different sites of second primary cancer by first primary cancer.

**Figure S3.** Heat map of standardized incidence ratio (SIR) of different sites of second primary cancer by first primary cancer.

**Figure S4.** Heat map of female cancer survivors using cumulative incidence and standardized incidence of different sites

**Figure S5.** Heat map of male cancer survivors using cumulative incidence and standardized incidence of different sites

**Figure S6.** Cumulative incidence function using the subdistribution hazards model

**Figure S7.** The common SNPs between lung cancer and other 7 cancer.

**Figure S8 - S14.** Forest plots of each included SNP in Mendelian randomization.

**Table S1.** Patient characteristics of the study population in SEER.

**Table S2.** The specific values of CIR of different sites of second primary cancer by first primary cancer.

**Table S3.** The specific values of SIR of different sites of second primary cancer by first primary cancer.

**Table S4.** Risk factors of developing SPC stratified by sites using competing risk model.  
(Breast, Lung, Kidney, Colon)

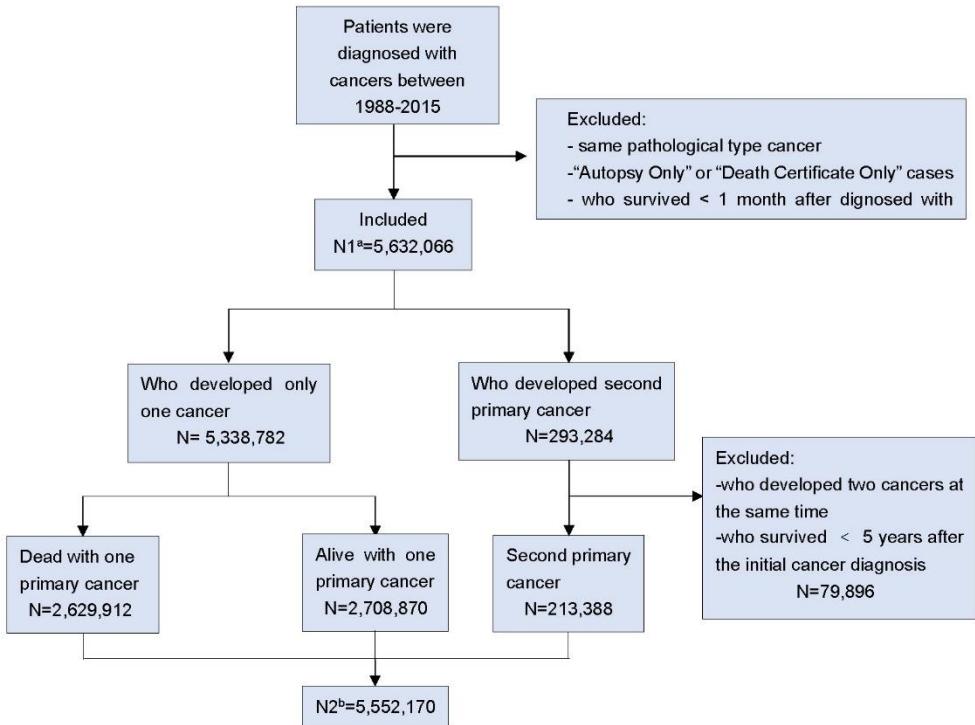
**Table S5.** Risk factors of developing SPC stratified by sites using competing risk model.

(Bladder, Endocrine, Prostate, Female Genital)

**Table S6.** Features of each included SNP in Mendelian randomization.

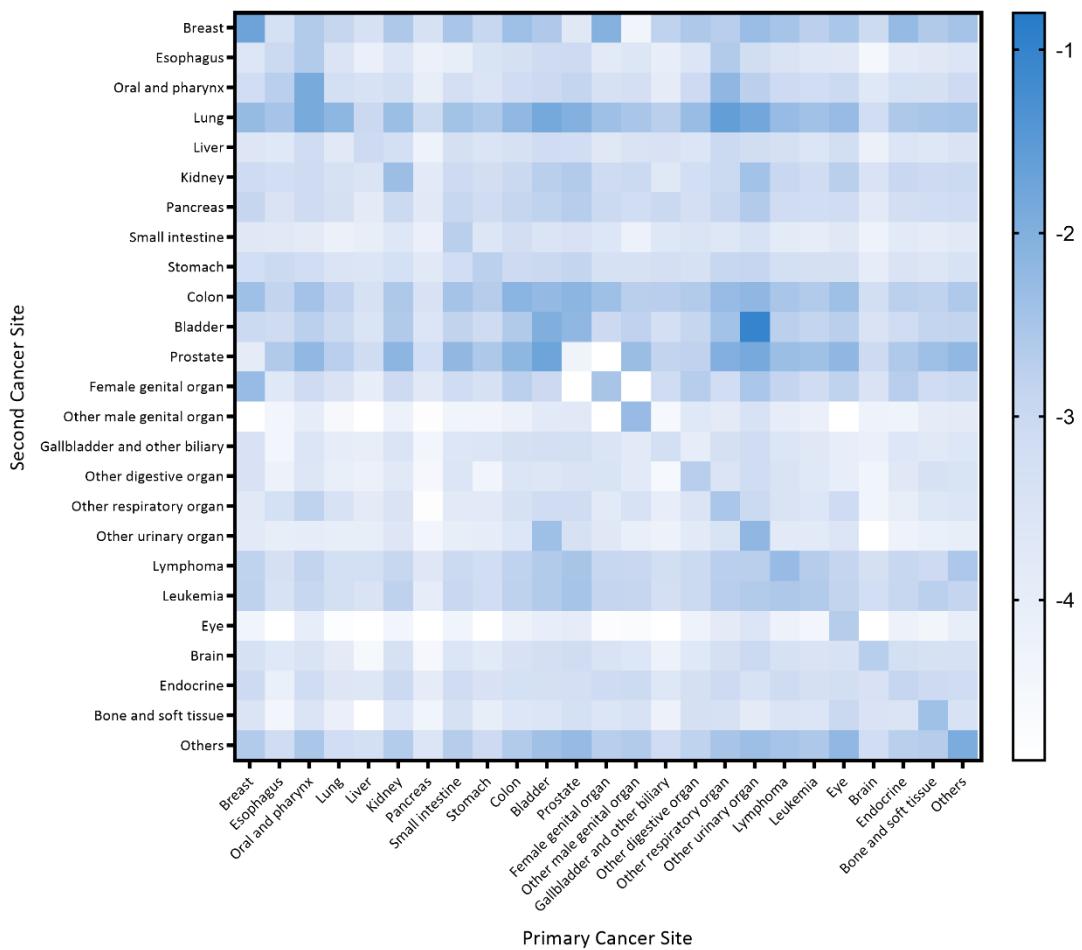
**Table S7.** Statistically significant associations of genetical predisposition to exposures

with lung cancer.

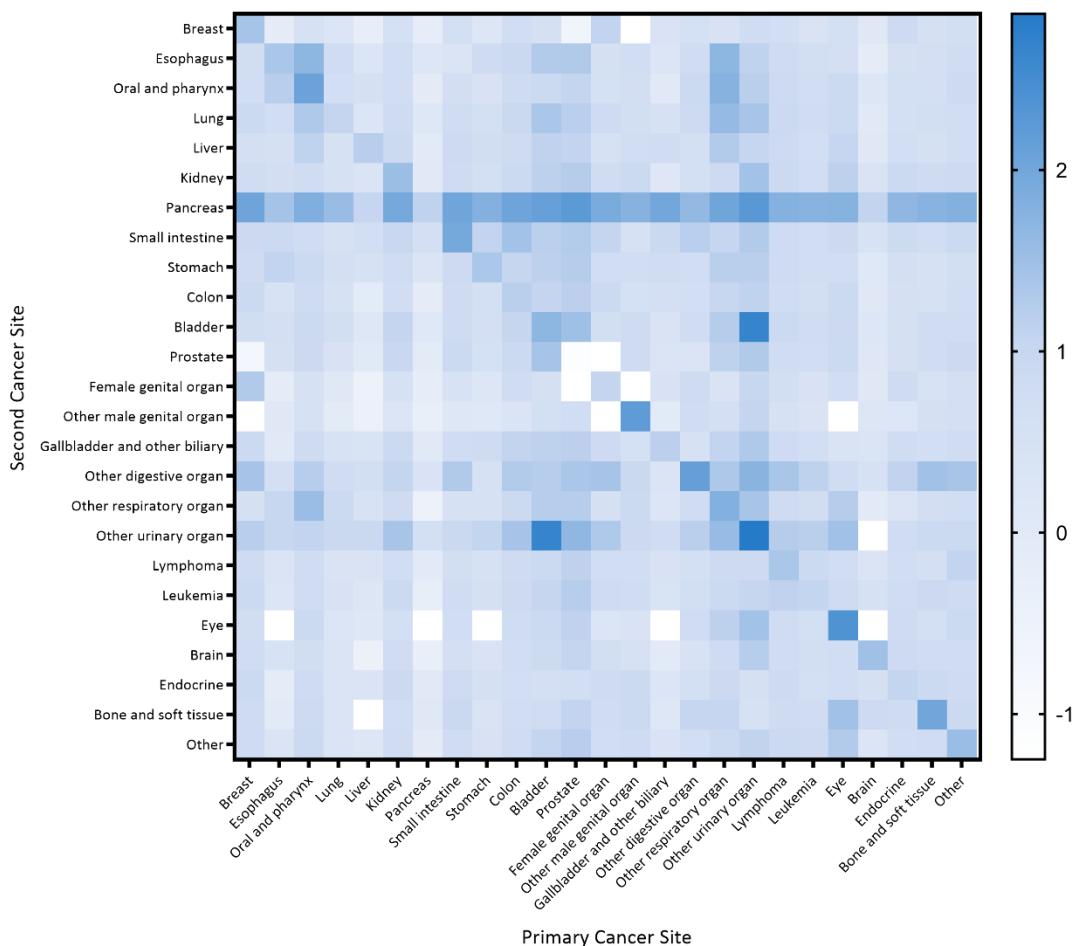


**Figure S1.** Flowchart of the included patients

<sup>a</sup>N1: This group of patients were used to estimate CIR and SIR of SPC; <sup>b</sup>N2: This group of patients were included to calculate hazard ratio using competing risk model. CIR, cumulative incidence ratio; SIR, standardized incidence ratio; SPC, second primary cancer.

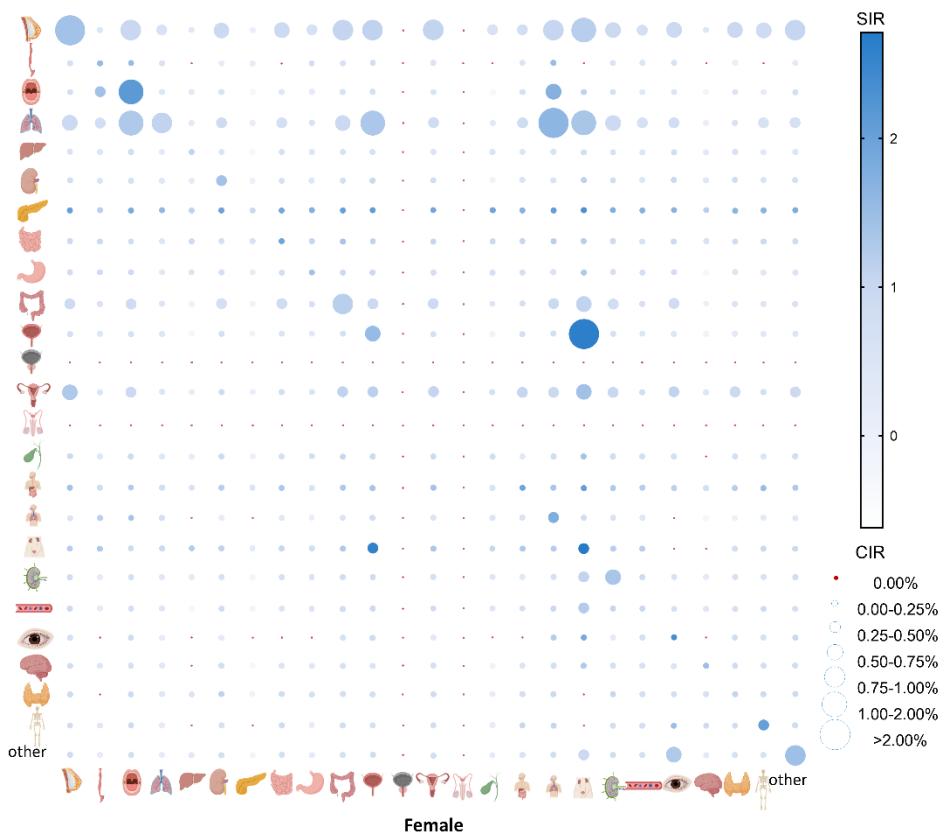


**Figure S2.** Heat map of cumulative incidence ratio of different sites of second primary cancer by first primary cancer.

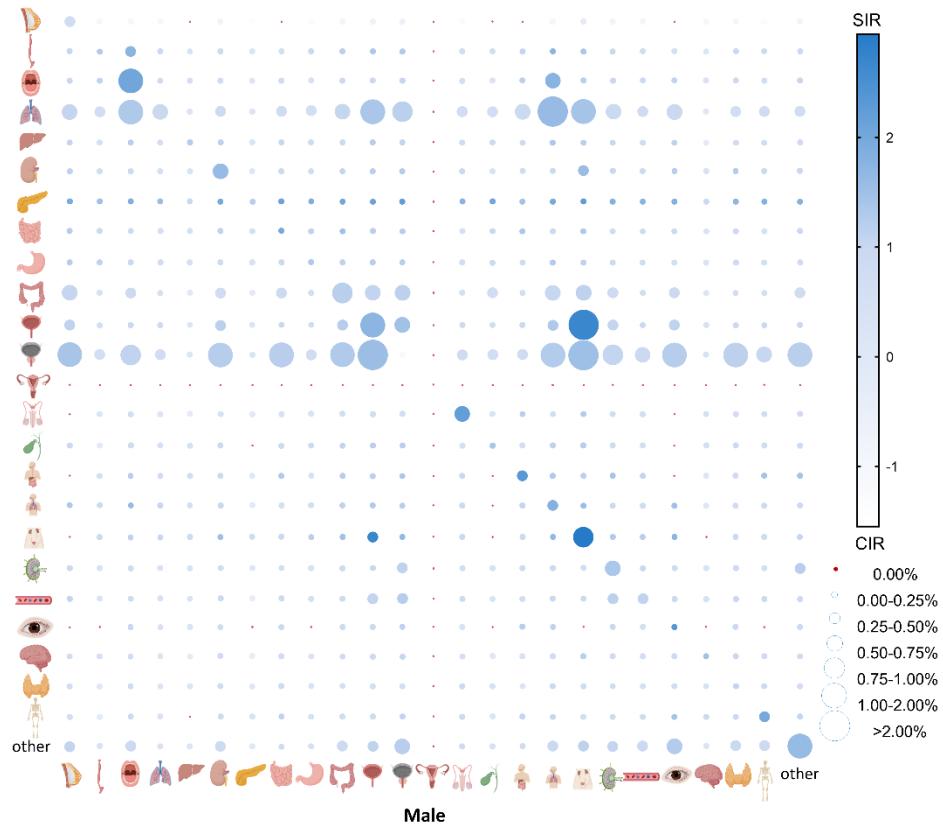


**Figure S3.** Heat map of standardized incidence ratio of different sites of second primary cancer by first primary cancer.

Figure S2&S3: X-axis represents the first primary cancer site, Y-axis represents the second primary cancer site. The color depth represents the LN-converted SIR.

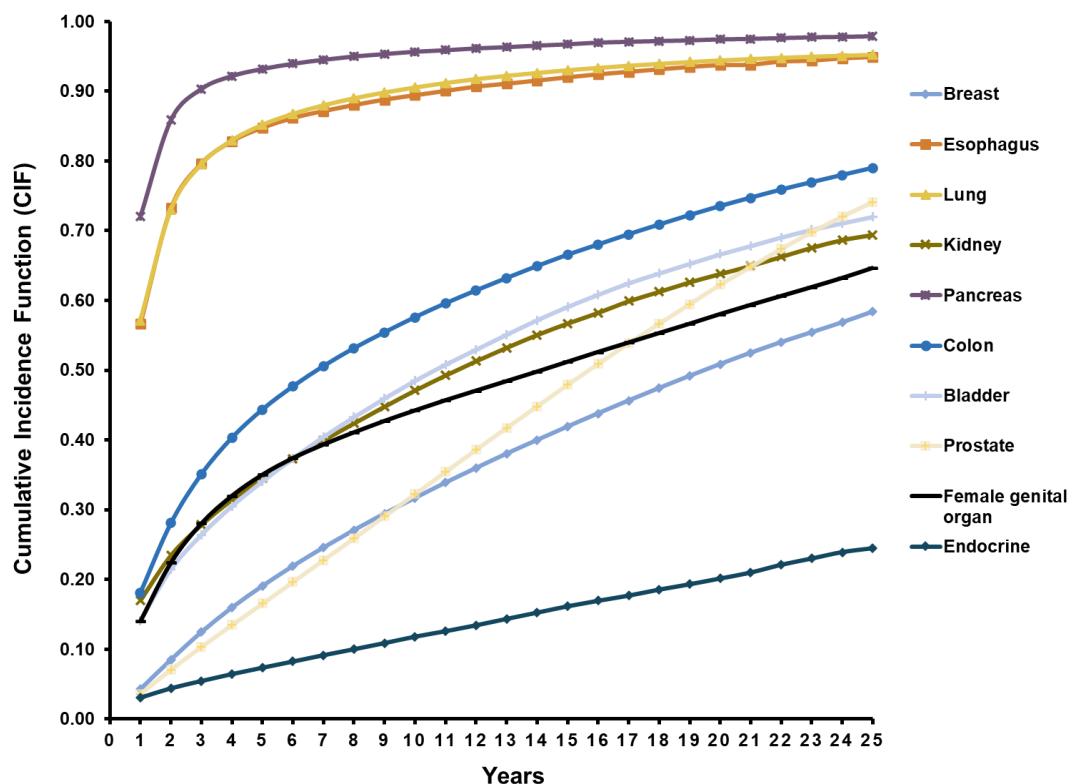


**Figure S4.** Heat map of female cancer survivors using cumulative incidence and standardized incidence of different sites

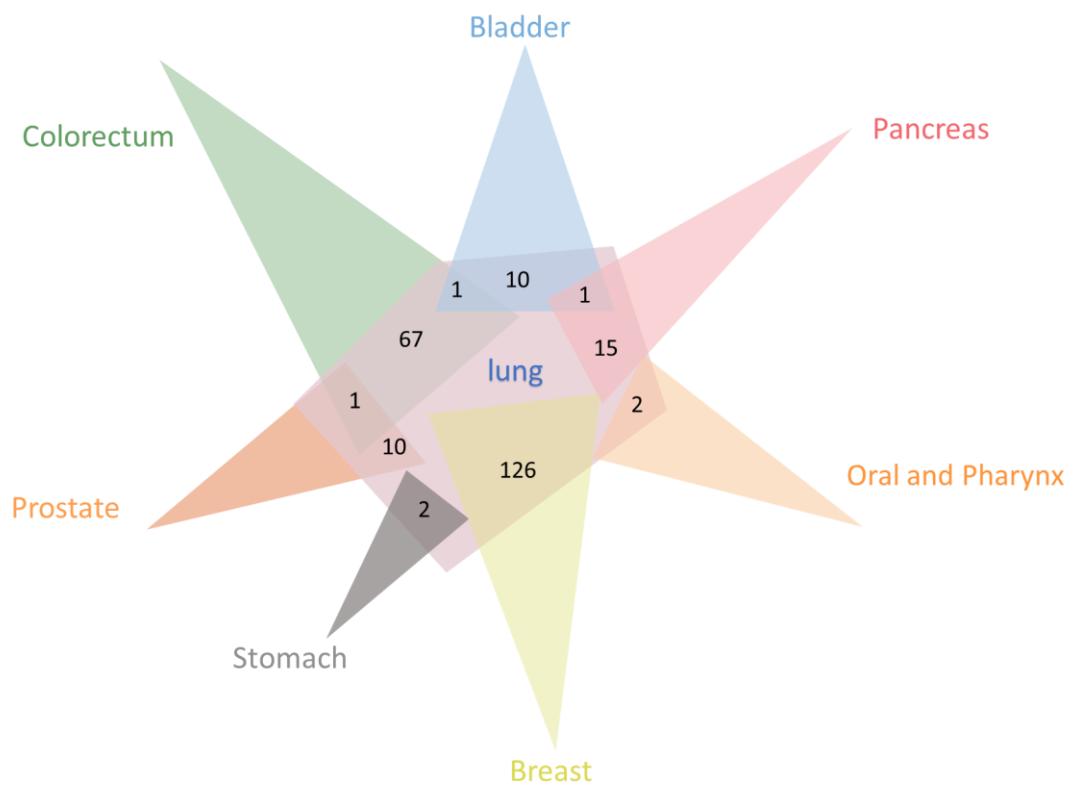


**Figure S5.** Heat map of male cancer survivors using cumulative incidence and standardized incidence of different sites

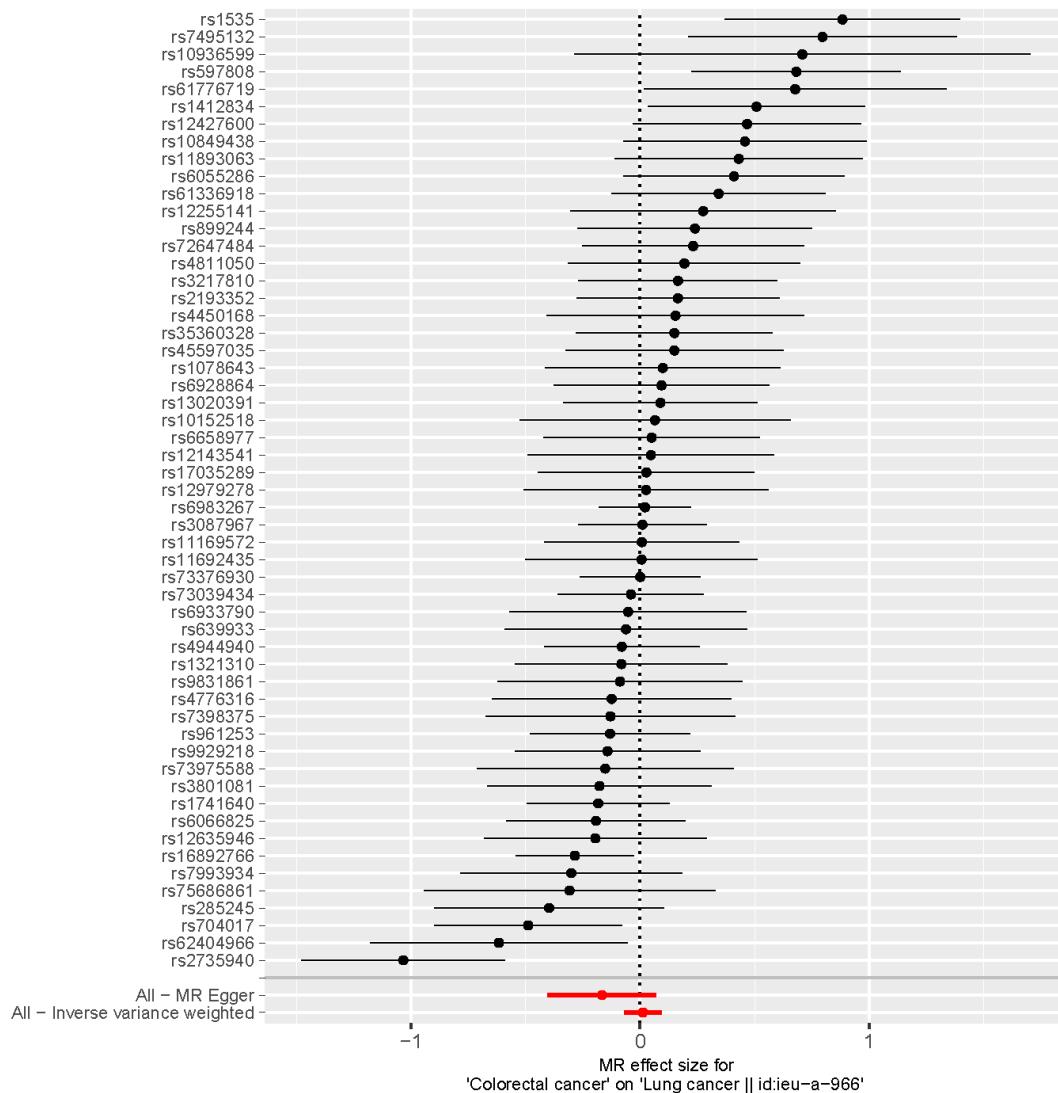
Figure S4&S5: The X-axis represent the first primary cancer site, and Y-axis represent the second primary cancer site. The size of the circle represents LN-converted CIR, and colour depth represents the LN-converted SIR. From left to right, top to bottom, the site of cancer were: Breast, Esophagus, Oral and Pharynx, Lung, Liver, Kidney, Pancreas, Small intestine, Stomach, Colon, Bladder, Prostate, Female genital organ, Other male genital organs, Gallbladder and other biliary, Other digestive organs, Other respiratory organs, Other urinary organs, Lymphoma, Leukemia, Eye, Brain, Endocrine, Bone and soft tissue, Others.



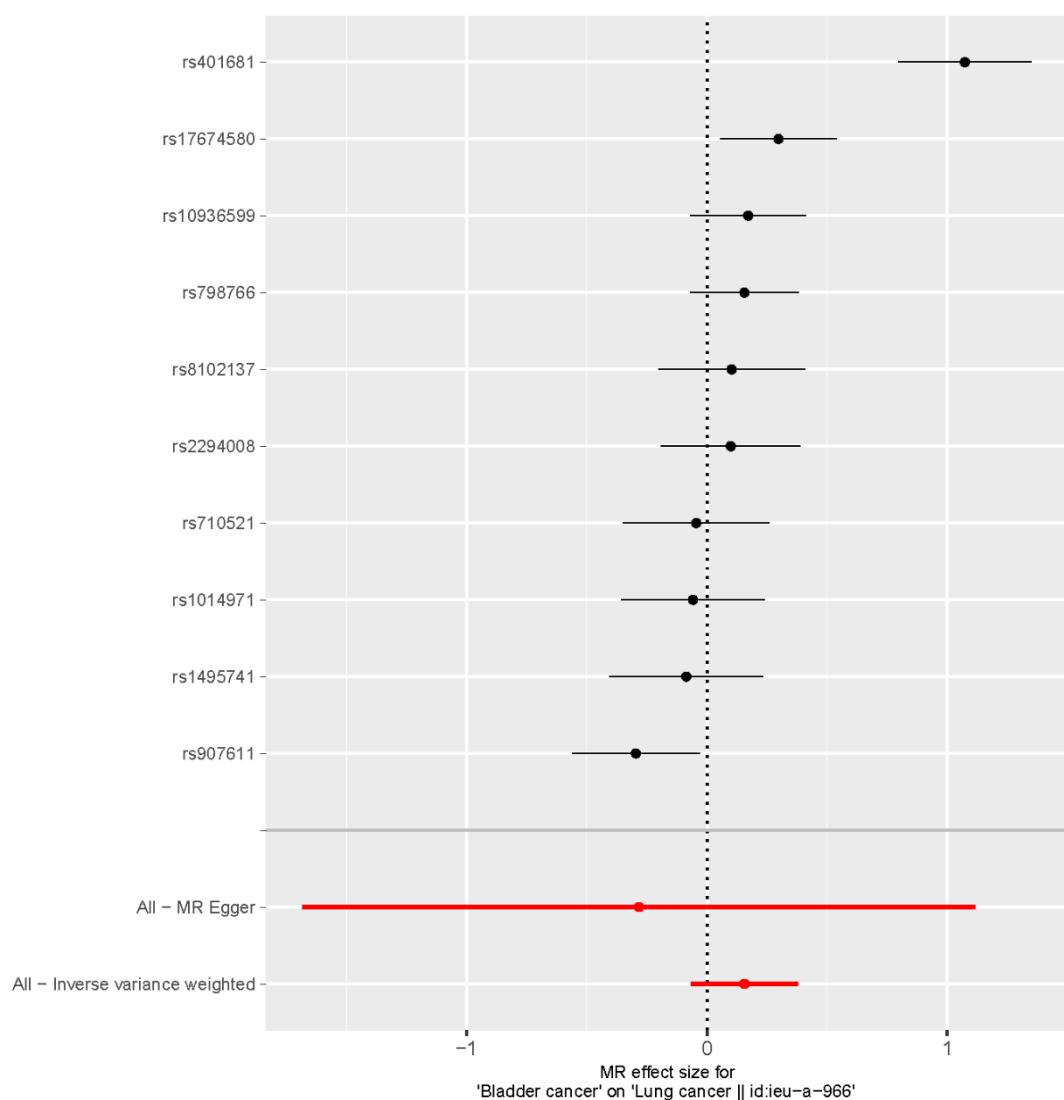
**Figure S6.** Cumulative incidence function using the subdistribution hazards mode



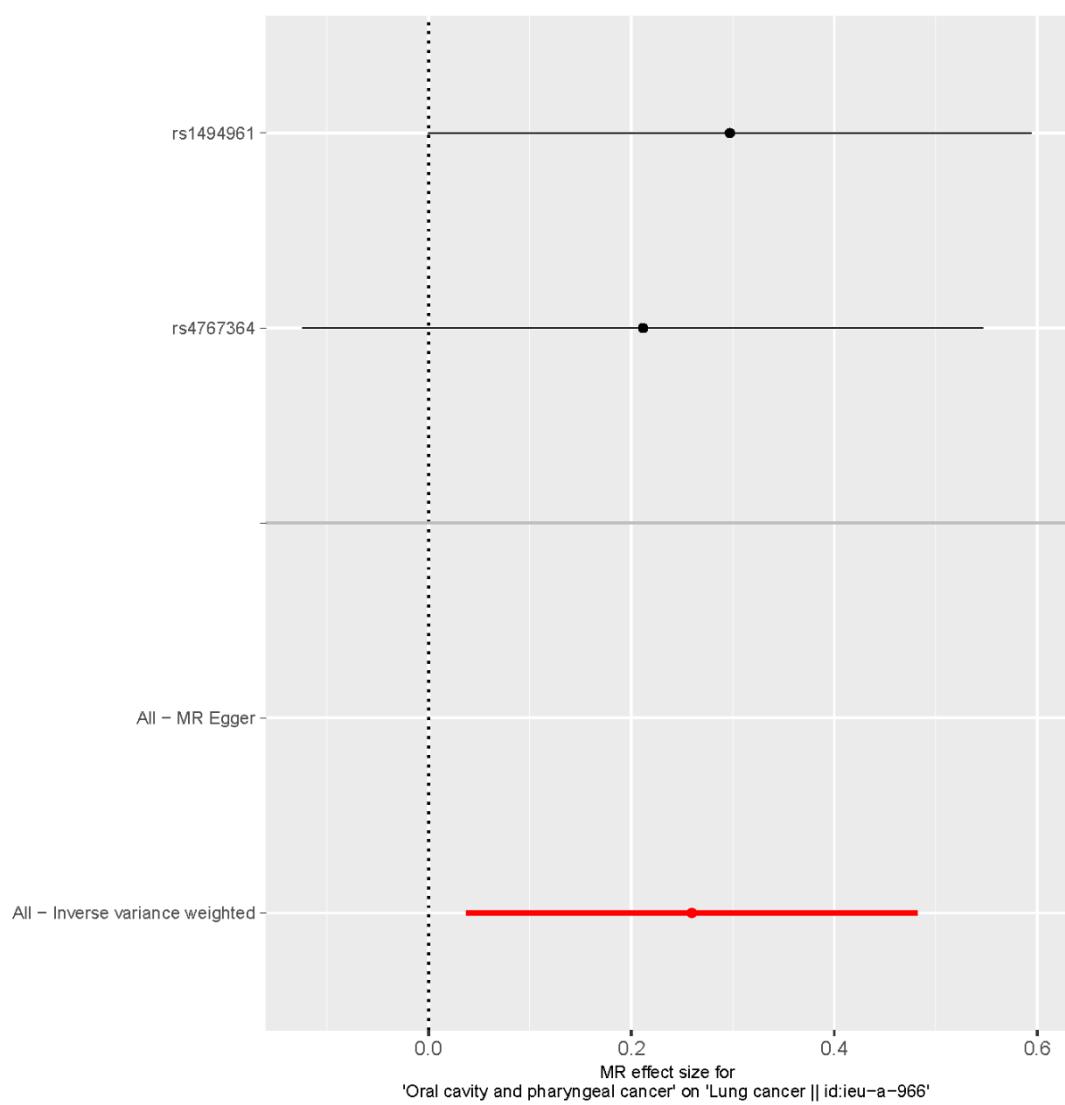
**Figure S7.** The common SNPs between lung cancer and other 7 cancer.



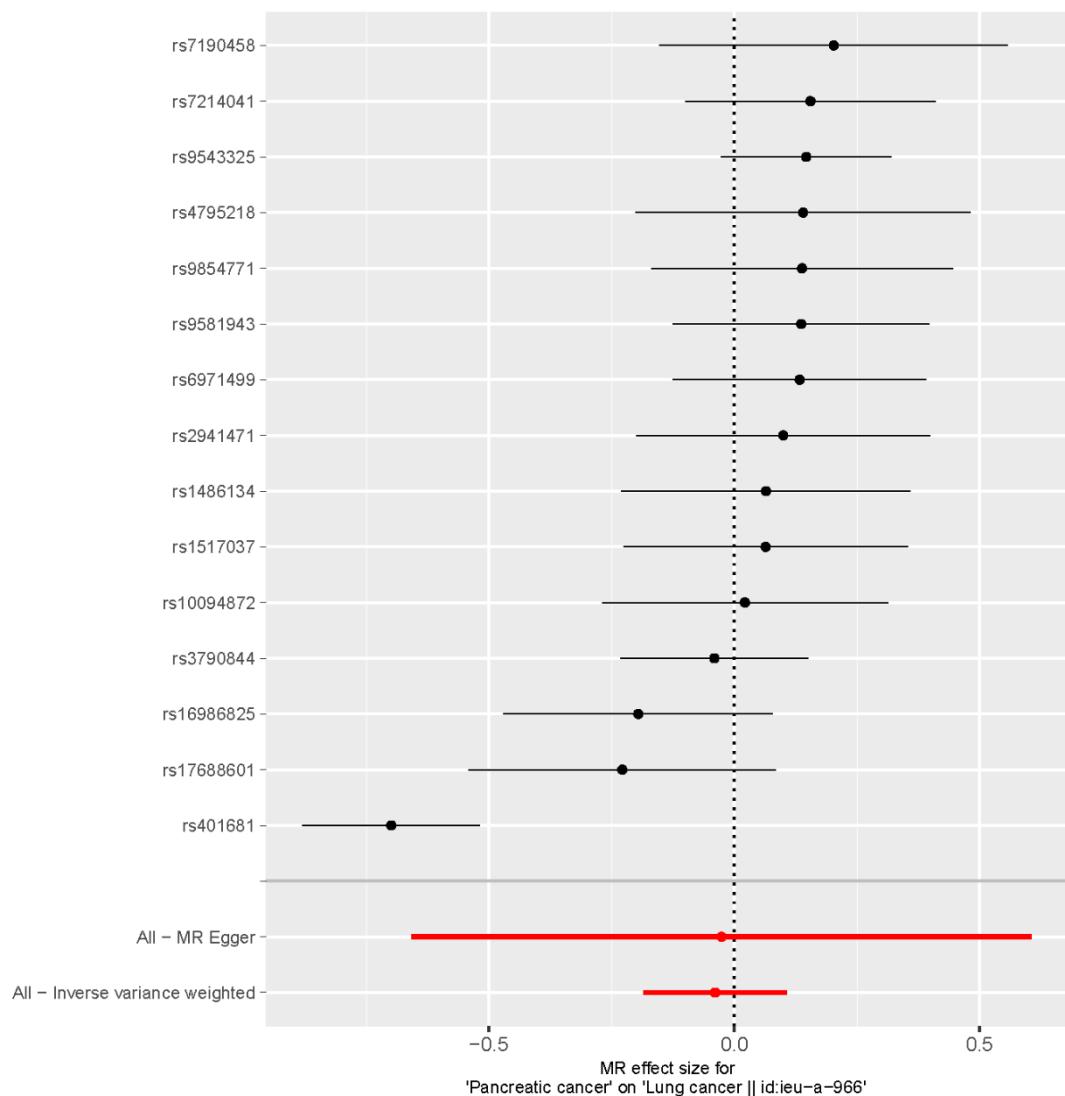
**Figure S8.** Forest plots of included SNP between colorectal cancer and lung cancer in Mendelian randomization.



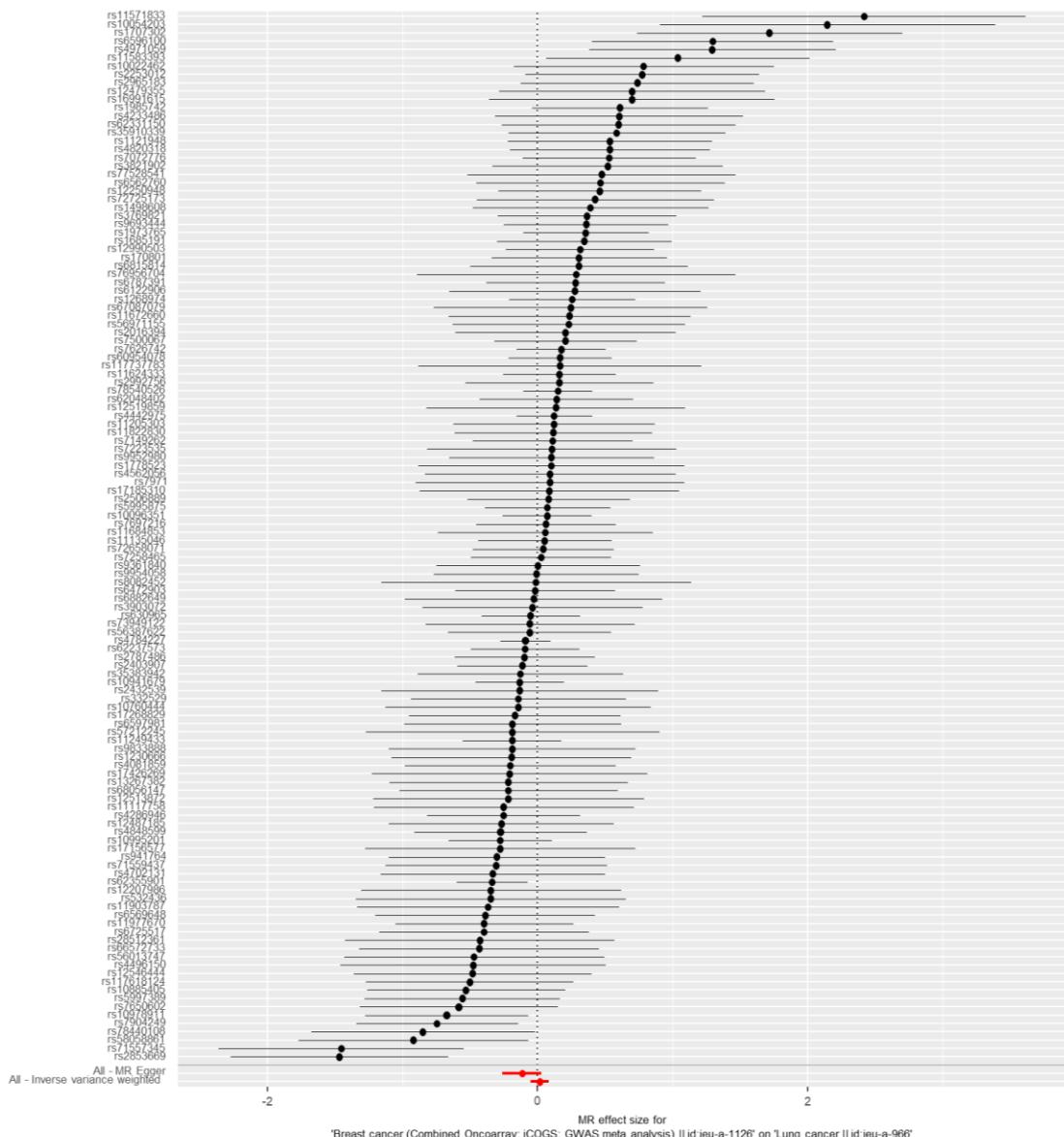
**Figure S9.** Forest plots of included SNP between bladder cancer and lung cancer in Mendelian randomization.



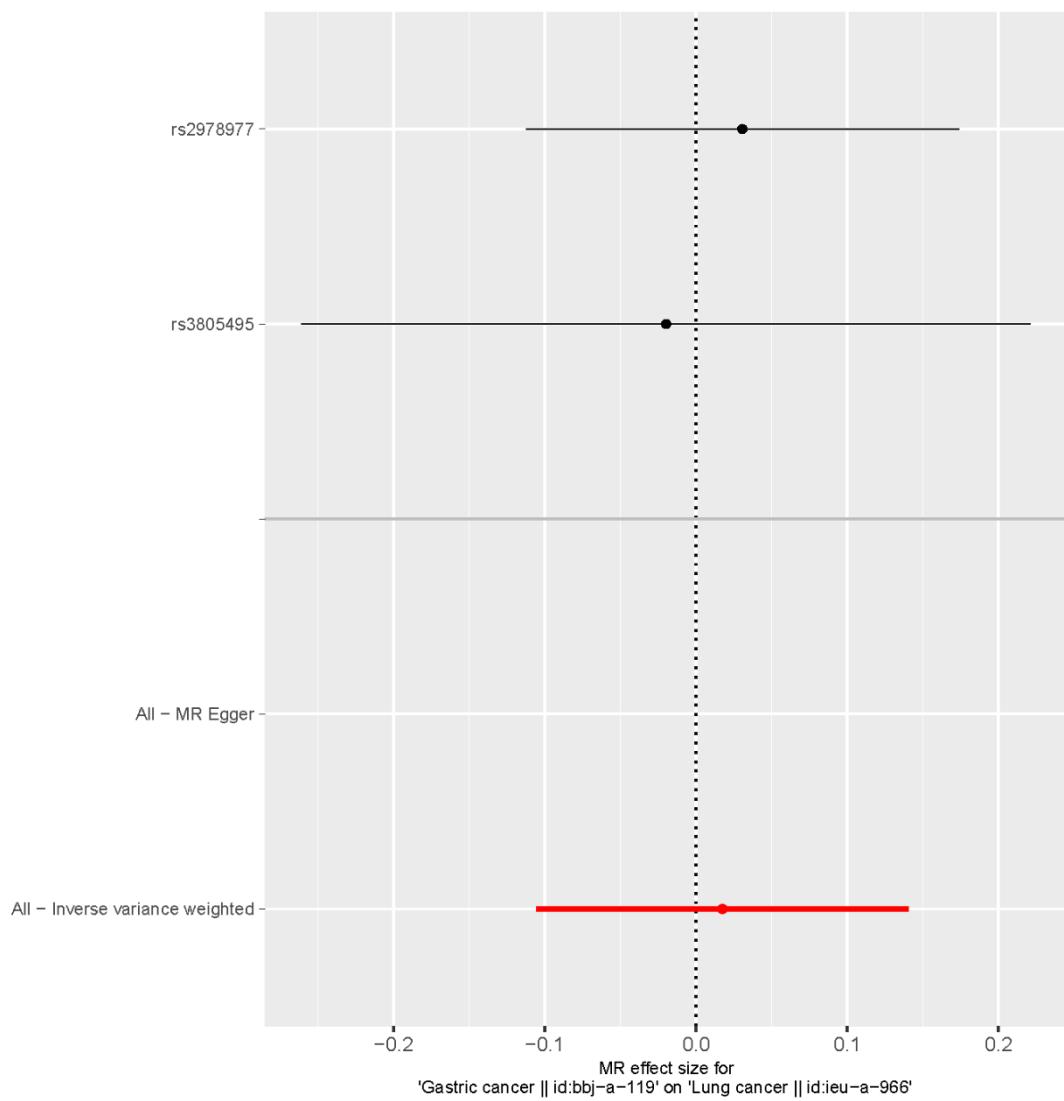
**Figure S10.** Forest plots of included SNP between oral and pharynx cancer and lung cancer in Mendelian randomization.



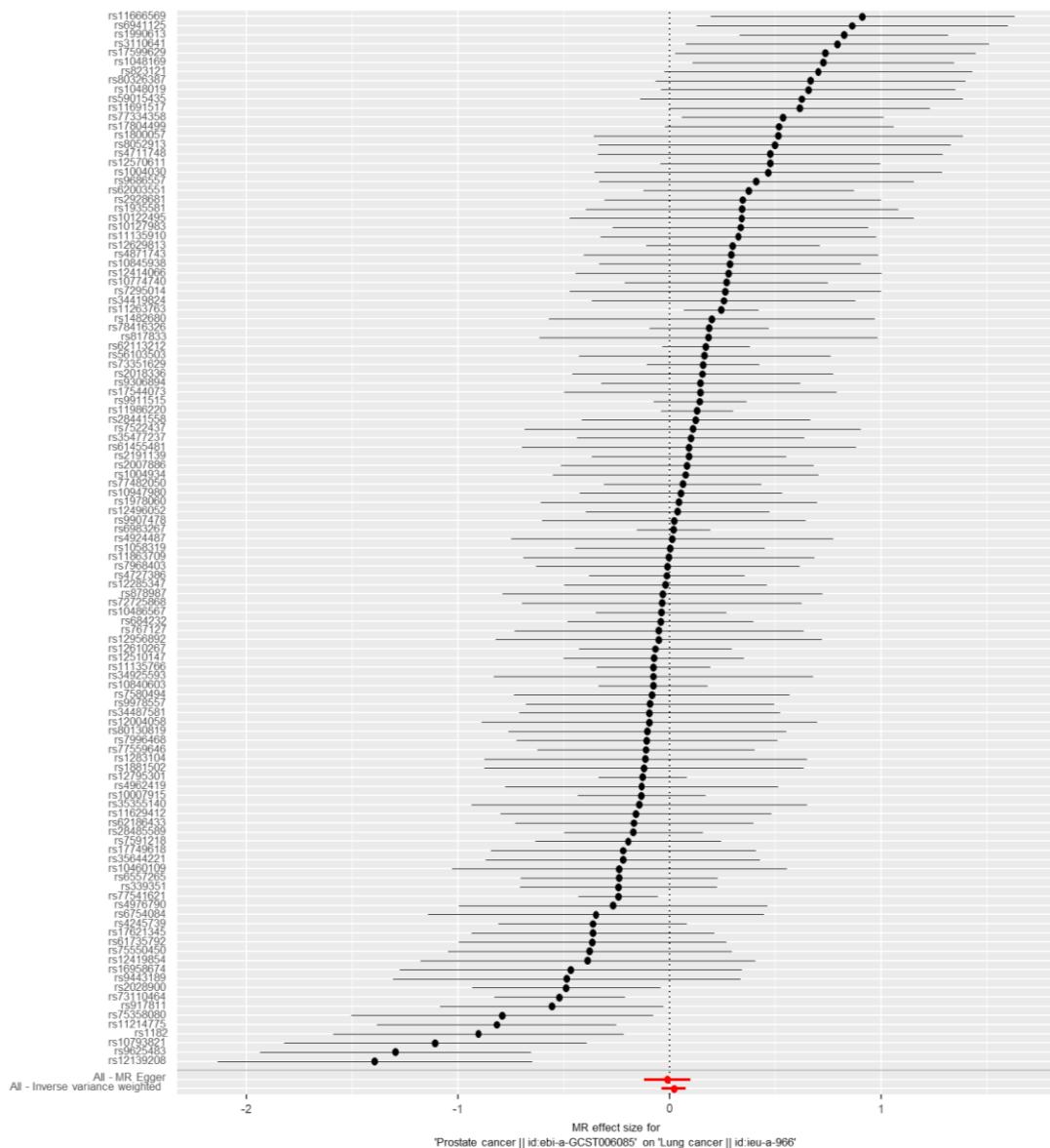
**Figure S11.** Forest plots of included SNP between pancreas cancer and lung cancer in Mendelian randomization.



**Figure S12.** Forest plots of included SNP between breast cancer and lung cancer in Mendelian randomization



**Figure S13.** Forest plots of included SNP between stomach cancer and lung cancer in Mendelian randomization



**Figure S14.** Forest plots of included SNP between prostate cancer and lung cancer in Mendelian randomization

**Table S1** Patient characteristics of the study population in SEER

VARIABLE	ALIVE WITH OPC <sup>1</sup> (%)	DEAD WITH OPC <sup>1</sup> (%)	SPC <sup>2</sup> (%)
TOTAL	2,708,870	2,629,912	213388
Age at diagnosis			
0-39	328,271(12.1)	91,555(3.5)	8,120(3.8)
40-49	389,833(14.4)	169,842(6.5)	17,991(8.4)
50-59	685,171(25.3)	390,168(14.8)	39,574(18.5)
60-69	749,592(27.7)	636,365(24.2)	68,206(32.0)
70-79	423,728(15.6)	770,994(29.3)	60,382(28.3)
80+	132,275(4.9)	570,988(21.7)	19,115(9.0)
Race			
White	2,183,913(80.6)	2,148,537(81.7)	182,556(85.6)
Black	263,979(9.7)	301,280(11.5)	18,006(8.4)
Asian Pacific	191,851(7.1)	159,898(6.1)	11,771(5.5)
Other	69,127(2.6)	20,197(0.8)	1,055(0.5)
Sex			
Male	1,321,864(48.8)	1,416,339(53.9)	120,296(56.4)
Female	1,387,006(51.2)	1,213,573(46.1)	93,092(43.6)
Tumor size			
micro	952,371(35.2)	1,183,467(45.0)	91,301(42.8)
<1cm	255,885(9.4)	67,037(2.5)	17,938(8.4)
1-2cm	398,164(14.7)	154,437(5.9)	27,312(12.8)
2-3cm	286,381(10.6)	206,279(7.8)	21,576(10.1)
3-4cm	190,930(7.0)	209,870(8.0)	15,144(7.1)
4-5cm	132,260(4.9)	183,063(7.0)	10,566(5.0)
>5cm	492,879(18.2)	625,759(23.8)	29,551(13.8)
Grade			
unknown	720,581(26.6)	1,017,585(38.7)	56,895(26.7)
well differentiated	334,567(12.4)	151,060(5.7)	25,777(12.1)
moderate differentiated	875,468(32.3)	611,822(23.3)	76,932(36.1)
poorly differentiated	553,620(20.4)	608,030(23.1)	40,298(18.9)
undifferentiated	64,176(2.4)	137,308(5.2)	6,022(2.8)
other	160,458(5.9)	104,107(4.0)	7,464(3.5)
Positive Nodes			
0	1,891,281(69.8)	1,019,001(38.7)	135,697(63.6)
≥1	619,574(22.9)	906,092(34.5)	34,133(16.0)
unknown	198,015(7.3)	704,819(26.8)	43,558(20.4)
Radiation			
Yes	833,861(30.8)	788,181(30.0)	66,487(31.2)
No	1,875,009(69.2)	1,841,731(70.0)	146,901(68.8)
Chemotherapy			
Yes	696,346(25.7)	938,235(35.7)	172,835(81.0)
No	2,012,524(74.3)	1,691,677(64.3)	40,553(19.0)
Surgery			
Yes	1,990,410(73.5)	1,160,833(44.1)	159,417(74.7)
No	698,174(25.8)	1,440,739(54.8)	53,255(25.0)
unknown	20,286(0.7)	28,340(1.1)	716(0.3)

NOTE. Characteristics are overall and according to subdistribution hazards regression model; ALIVE WITH OPC: patients who only developed one cancer and still alive up to the last follow-up time, DEAD WITH OPC: patients who only developed one cancer and died up to the last follow-up time due to various causes, SPC: patients who developed second primary cancer. Abbreviations: <sup>1</sup>OPC: one primary cancer, <sup>2</sup>SPC: second primary cancer

**Table S2.**

Site CIR \ Site	Breast	Esophagus	Oral and pharynx	Lung	Liver	Kidney	Pancreas	Small intestine	Stomach	Colon	Bladder	Prostate	Female genital organ	Other male genital organ	Gallbladder	Other digestive organ	Other respiratory organ	Other urinary organ	Lymphoma	Leukemia	Eye	Brain	Endocrine	Bone and soft tissue	Others	
Breast	1.85%	0.05%	0.23%	0.13%	0.04%	0.27%	0.04%	0.30%	0.12%	0.41%	0.25%	0.02%	0.88%	0.00%	0.16%	0.27%	0.19%	0.48%	0.34%	0.18%	0.30%	0.09%	0.55%	0.24%	0.35%	
Esophagus	0.02%	0.11%	0.23%	0.03%	0.01%	0.02%	0.01%	0.01%	0.03%	0.05%	0.08%	0.09%	0.02%	0.02%	0.01%	0.03%	0.22%	0.06%	0.03%	0.02%	0.02%	0.00%	0.02%	0.02%	0.03%	
Oral and pharynx	0.07%	0.18%	1.33%	0.05%	0.04%	0.06%	0.01%	0.05%	0.03%	0.08%	0.10%	0.14%	0.04%	0.05%	0.01%	0.09%	0.66%	0.18%	0.09%	0.06%	0.10%	0.02%	0.05%	0.05%	0.09%	
Lung	0.55%	0.33%	1.28%	0.71%	0.11%	0.46%	0.09%	0.38%	0.26%	0.63%	1.43%	0.94%	0.42%	0.30%	0.19%	0.50%	2.48%	1.54%	0.52%	0.38%	0.52%	0.07%	0.27%	0.31%	0.33%	
Liver	0.02%	0.02%	0.08%	0.02%	0.09%	0.05%	0.01%	0.05%	0.03%	0.04%	0.08%	0.07%	0.02%	0.03%	0.04%	0.02%	0.10%	0.06%	0.04%	0.03%	0.06%	0.01%	0.03%	0.02%	0.03%	
Kidney	0.08%	0.06%	0.09%	0.04%	0.03%	0.46%	0.01%	0.09%	0.06%	0.12%	0.19%	0.23%	0.08%	0.11%	0.02%	0.06%	0.10%	0.36%	0.12%	0.08%	0.19%	0.03%	0.12%	0.09%	0.11%	
Pancreas	0.13%	0.03%	0.08%	0.04%	0.01%	0.11%	0.02%	0.12%	0.08%	0.13%	0.16%	0.21%	0.10%	0.07%	0.11%	0.05%	0.12%	0.23%	0.07%	0.07%	0.01%	0.06%	0.07%	0.08%		
Small intestine	0.02%	0.02%	0.01%	0.01%	0.01%	0.02%	0.01%	0.18%	0.02%	0.06%	0.03%	0.04%	0.02%	0.01%	0.02%	0.03%	0.02%	0.04%	0.01%	0.01%	0.02%	0.01%	0.02%	0.01%	0.02%	
Stomach	0.06%	0.10%	0.07%	0.03%	0.03%	0.05%	0.02%	0.06%	0.18%	0.09%	0.11%	0.14%	0.04%	0.04%	0.05%	0.04%	0.12%	0.13%	0.05%	0.04%	0.01%	0.03%	0.02%	0.04%		
Colon	0.42%	0.14%	0.36%	0.15%	0.04%	0.27%	0.04%	0.36%	0.21%	0.77%	0.57%	0.72%	0.41%	0.19%	0.19%	0.22%	0.53%	0.66%	0.31%	0.23%	0.41%	0.06%	0.18%	0.15%	0.25%	
Bladder	0.11%	0.08%	0.18%	0.10%	0.03%	0.24%	0.03%	0.15%	0.09%	0.24%	1.03%	0.65%	0.10%	0.16%	0.05%	0.13%	0.36%	9.56%	0.18%	0.14%	0.19%	0.03%	0.08%	0.14%	0.14%	
Prostate	0.01%	0.24%	0.63%	0.18%	0.07%	0.74%	0.06%	0.61%	0.27%	0.70%	1.81%	0.00%	0.00%	0.48%	0.14%	0.16%	0.98%	1.37%	0.46%	0.40%	0.66%	0.09%	0.26%	0.41%	0.62%	
Female genital organ	0.53%	0.02%	0.08%	0.03%	0.01%	0.09%	0.02%	0.08%	0.04%	0.18%	0.10%	0.00%	0.32%	0.00%	0.07%	0.20%	0.06%	0.30%	0.13%	0.07%	0.16%	0.03%	0.20%	0.08%	0.11%	
Other male genital organ	0.00%	0.00%	0.01%	0.00%	0.00%	0.01%	0.00%	0.00%	0.00%	0.01%	0.01%	0.02%	0.00%	0.53%	0.00%	0.02%	0.01%	0.04%	0.01%	0.01%	0.00%	0.01%	0.01%	0.01%	0.01%	
Gallbladder and other biliary	0.04%	0.00%	0.03%	0.01%	0.01%	0.03%	0.00%	0.02%	0.03%	0.04%	0.05%	0.05%	0.03%	0.01%	0.05%	0.01%	0.05%	0.08%	0.02%	0.02%	0.01%	0.02%	0.02%	0.02%		
Other digestive organ	0.04%	0.01%	0.02%	0.01%	0.01%	0.02%	0.00%	0.03%	0.00%	0.03%	0.02%	0.03%	0.04%	0.01%	0.01%	0.00%	0.19%	0.03%	0.08%	0.03%	0.02%	0.01%	0.00%	0.02%	0.03%	
Other respiratory organ	0.02%	0.05%	0.16%	0.04%	0.01%	0.03%	0.00%	0.01%	0.01%	0.04%	0.08%	0.08%	0.02%	0.02%	0.04%	0.01%	0.03%	0.30%	0.11%	0.03%	0.02%	0.08%	0.00%	0.01%	0.02%	
Other urinary organ	0.01%	0.01%	0.01%	0.01%	0.01%	0.02%	0.00%	0.01%	0.01%	0.02%	0.42%	0.04%	0.02%	0.01%	0.01%	0.01%	0.03%	0.65%	0.02%	0.01%	0.03%	0.00%	0.01%	0.01%	0.01%	
Lymphoma	0.16%	0.05%	0.15%	0.05%	0.05%	0.12%	0.02%	0.11%	0.07%	0.16%	0.22%	0.32%	0.12%	0.12%	0.06%	0.10%	0.18%	0.19%	0.52%	0.22%	0.13%	0.05%	0.12%	0.09%	0.28%	
Leukemia	0.17%	0.04%	0.12%	0.05%	0.03%	0.17%	0.01%	0.12%	0.07%	0.16%	0.23%	0.34%	0.13%	0.13%	0.05%	0.10%	0.19%	0.23%	0.26%	0.23%	0.14%	0.06%	0.12%	0.18%	0.13%	
Eye	0.00%	0.00%	0.01%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.01%	0.01%	0.01%	0.00%	0.00%	0.00%	0.01%	0.01%	0.03%	0.01%	0.01%	0.00%	0.01%	0.00%	0.01%		
Brain	0.04%	0.02%	0.03%	0.01%	0.00%	0.04%	0.00%	0.03%	0.01%	0.04%	0.05%	0.08%	0.03%	0.02%	0.01%	0.02%	0.05%	0.11%	0.04%	0.03%	0.04%	0.20%	0.05%	0.04%	0.04%	
Endocrine	0.09%	0.01%	0.07%	0.02%	0.02%	0.10%	0.01%	0.08%	0.04%	0.05%	0.04%	0.05%	0.08%	0.09%	0.02%	0.04%	0.09%	0.04%	0.09%	0.05%	0.06%	0.04%	0.13%	0.09%	0.07%	
Bone and soft tissue	0.03%	0.00%	0.03%	0.01%	0.00%	0.02%	0.00%	0.04%	0.01%	0.02%	0.02%	0.05%	0.03%	0.04%	0.01%	0.04%	0.04%	0.01%	0.03%	0.03%	0.12%	0.03%	0.39%	0.04%		
Others	0.23%	0.07%	0.30%	0.07%	0.05%	0.22%	0.03%	0.21%	0.09%	0.23%	0.40%	0.55%	0.20%	0.23%	0.08%	0.16%	0.31%	0.43%	0.33%	0.26%	0.62%	0.06%	0.19%	0.22%	1.20%	

NOTE: The first row of site represents the primary cancer site and the first column represents the second primary site.

**Table S3.**

SIR \ Site	Breast	Esophagus	Oral and pharynx	Lung	Liver	Kidney	Pancreas	Small intestine	Stomach	Colon	Bladder	Prostate	Female genital organ	Other male genital organ	Gallbladder and other biliary	Other digestive organ	Other respiratory organ	Other urinary organ	Lymphoma	Leukemia	Eye	Brain	Endocrine	Bone and soft tissue	Others
Breast	25.82	0.70	3.25	1.78	0.56	3.82	0.60	4.24	1.67	5.70	3.51	0.24	12.37	0.06	2.22	3.72	2.67	6.66	4.71	2.46	4.21	1.24	7.75	3.41	4.93
Esophagus	4.99	22.87	49.30	6.33	1.73	5.38	1.52	2.00	7.44	10.22	18.06	19.59	3.41	5.29	1.92	6.02	48.68	13.62	7.12	4.73	3.85	0.73	3.42	4.08	5.93
Oral and pharynx	5.78	15.94	116.89	4.61	3.38	5.43	0.82	4.43	2.63	6.89	9.06	11.88	3.71	4.45	1.03	8.26	57.65	15.38	8.14	5.62	8.55	1.67	4.36	3.95	8.09
Lung	8.79	5.24	20.54	11.36	1.82	7.48	1.41	6.07	4.18	10.16	22.99	15.11	6.71	4.90	2.98	8.07	39.98	24.81	8.42	6.12	8.42	1.10	4.29	4.93	5.37
Liver	3.88	3.36	13.48	2.96	16.33	9.37	0.95	8.06	5.07	6.97	13.29	12.22	3.19	5.69	6.19	4.37	18.20	10.99	7.86	4.66	10.88	1.18	4.52	3.62	5.75
Kidney	6.09	4.46	6.55	3.12	2.20	34.27	1.05	6.91	4.26	8.66	14.01	17.44	6.34	8.23	1.33	4.37	7.80	27.31	8.73	5.73	13.99	2.36	8.79	6.91	8.16
Pancreas	106.70	27.10	69.56	37.18	11.08	90.61	13.56	103.36	63.27	108.74	132.38	171.99	81.94	57.46	95.57	41.53	101.64	187.90	62.21	55.54	59.05	12.16	46.61	54.73	62.66
Small intestine	9.01	8.61	6.28	3.34	4.65	10.42	3.88	91.88	12.30	28.04	14.69	17.87	11.49	3.04	10.29	15.23	10.92	18.79	6.74	5.45	8.86	2.81	7.54	5.63	8.54
Stomach	7.21	12.43	8.49	3.89	3.16	6.19	2.03	8.04	22.19	11.30	14.23	17.35	5.18	5.32	6.25	5.19	15.47	15.66	6.78	5.77	5.54	1.26	4.01	3.05	4.85
Colon	8.45	2.87	7.27	3.01	0.83	5.40	0.74	7.25	4.31	15.59	11.60	14.59	8.32	3.82	3.93	4.54	10.65	13.44	6.23	4.74	8.25	1.23	3.59	3.11	5.14
Bladder	5.00	3.99	8.37	4.92	1.32	11.45	1.29	6.97	4.05	11.17	48.63	30.58	4.78	7.40	2.37	6.04	17.25	452.98	8.44	6.42	8.82	1.54	3.60	6.49	6.63
Prostate	0.17	3.39	8.92	2.57	1.02	10.42	0.83	8.65	3.76	9.89	25.69	0.07	0.00	6.81	2.04	2.20	13.95	19.34	6.52	5.63	9.28	1.30	3.62	5.85	8.82
Female genital organ	19.00	0.69	3.06	1.16	0.33	3.26	0.59	2.81	1.58	6.39	3.63	0.00	11.49	0.00	2.64	7.27	2.29	10.81	4.75	2.65	5.74	1.21	7.05	2.77	4.00
Other male genital organ	0.00	1.16	3.13	0.83	0.40	1.78	0.47	1.39	1.30	2.20	4.31	5.08	0.00	160.39	0.89	5.87	3.86	11.39	3.09	2.38	0.00	1.70	1.52	3.41	4.01
Gallbladder and other biliary	9.74	1.03	7.19	2.91	2.52	8.27	1.05	6.21	7.23	12.07	13.90	14.61	8.18	3.84	14.31	2.99	12.30	20.31	6.69	4.71	2.39	2.12	6.11	4.56	6.10
Other digestive organ	25.08	4.10	16.88	5.96	4.75	11.63	2.21	19.69	3.06	18.41	17.05	23.11	25.01	10.14	2.10	136.45	20.80	53.69	23.67	13.69	6.33	3.21	13.02	29.49	24.59
Other respiratory organ	3.44	10.81	34.52	8.38	2.89	6.94	0.34	3.00	3.02	8.80	16.47	16.75	3.41	8.38	1.92	6.62	64.90	24.51	7.05	5.02	17.33	0.98	2.05	4.49	5.39
Other urinary organ	16.06	10.63	12.31	10.12	10.34	24.60	4.31	10.21	11.88	25.41	468.29	45.21	20.23	9.01	6.53	15.38	38.43	723.76	17.40	15.49	29.53	0.00	6.28	8.34	10.10
Lymphoma	6.90	2.00	6.35	2.34	2.32	5.29	0.88	4.81	2.94	7.01	9.82	13.88	5.43	5.22	2.70	4.23	7.95	8.21	22.69	9.42	5.80	2.06	5.38	4.10	12.18
Leukemia	8.27	1.91	6.06	2.67	1.66	8.27	0.54	5.97	3.53	8.20	11.32	16.94	6.74	6.39	2.50	4.85	9.65	11.27	13.11	11.63	7.09	2.97	6.19	8.91	6.69
Eye	4.97	0.00	9.85	1.85	1.48	4.34	0.00	5.10	0.00	6.45	9.69	13.23	1.87	2.25	0.00	6.15	14.16	27.84	6.47	4.36	236.22	0.00	6.98	4.17	10.10
Brain	6.56	2.86	4.96	1.95	0.40	6.22	0.46	4.11	2.23	5.53	7.54	11.44	4.85	3.33	0.88	2.89	6.79	16.83	6.14	4.94	5.29	29.98	7.88	6.44	6.58
Endocrine	8.58	0.72	6.83	2.07	1.99	8.88	1.09	7.30	3.40	4.65	4.12	4.70	7.44	8.34	1.92	4.14	8.85	3.51	8.13	4.40	5.80	3.46	11.81	8.77	6.87
Bone and soft tissue	7.40	0.96	7.76	1.93	0.00	5.70	1.16	10.34	2.41	5.76	6.20	12.23	6.58	9.63	1.47	11.07	10.92	3.13	7.01	6.43	28.79	7.85	7.07	98.52	9.71
Others	6.76	2.19	8.69	1.96	1.60	6.47	0.75	6.20	2.63	6.63	11.79	16.22	5.79	6.72	2.24	4.71	9.18	12.49	9.66	7.72	18.18	1.88	5.57	6.33	35.21

NOTE: The first row of site represents the primary cancer site and the first column represents the second primary site.

**Table S4.** Risk factors of developing SPC stratified by sites using competing risk model.

Site	Breast	Lung	Kidney	Colon				
Variable	HR (95% CL)	P Value						
40-49y	1.03(0.99-1.08)	0.17	1.87(1.53-2.29)	<0.01	2.37(1.96-2.86)	<0.01	1.37(1.22-1.54)	<0.01
50-59y	1.23(1.18-1.29)	<0.01	2.78(2.31-3.36)	<0.01	3.74(3.14-4.46)	<0.01	1.99(1.79-2.21)	<0.01
60-69y	1.68(1.60-1.75)	<0.01	3.90(3.24-4.69)	<0.01	5.48(4.60-6.52)	<0.01	3.28(2.95-3.63)	<0.01
70-79y	1.95(1.86-2.04)	<0.01	3.96(3.28-4.77)	<0.01	6.68(5.60-7.97)	<0.01	4.03(3.63-4.47)	<0.01
≥ 80y	1.77(1.67-1.87)	<0.01	3.39(2.78-4.12)	<0.01	6.05(4.95-7.40)	<0.01	3.64(3.26-4.05)	<0.01
Black	1.04(1.00-1.08)	<0.05	1.12(1.05-1.19)	<0.01	1.32(1.22-1.44)	<0.01	0.98(0.93-1.02)	0.30
Asian	0.93(0.89-0.96)	<0.01	0.85(0.79-0.92)	<0.01	1.10(0.98-1.24)	0.12	0.87(0.82-0.91)	<0.01
Unmarried	1.06(1.04-1.09)	<0.01	0.95(0.91-0.99)	<0.01	0.93(0.87-0.99)	<0.05	1.01(0.98-1.04)	0.49
Node	1.00(0.98-1.03)	0.70	0.89(0.85-0.93)	<0.01	0.94(0.76-1.17)	0.58	0.97(0.94-1.00)	0.08
Surgery	1.50(1.39-1.62)	<0.01	1.72(1.62-1.82)	<0.01	1.61(1.41-1.85)	<0.01	1.87(1.72-2.03)	<0.01
Size<1cm	1.01(0.96-1.05)	0.82	0.99(0.86-1.13)	0.83	1.12(0.83-1.52)	0.46	0.93(0.87-1.00)	0.04
Size:1-2cm	1.02(0.97-1.06)	0.48	0.99(0.92-1.06)	0.73	0.86(0.73-1.02)	0.08	0.89(0.84-0.95)	<0.01
Size:2-3cm	1.04(0.99-1.09)	0.09	0.95(0.89-1.02)	0.19	0.92(0.80-1.06)	0.23	0.96(0.91-1.01)	0.11
Size:3-4cm	1.06(1.00-1.12)	0.04	0.98(0.91-1.06)	0.62	0.90(0.78-1.03)	0.13	0.98(0.94-1.03)	0.43
Size:4-5cm	0.97(0.91-1.04)	0.43	0.93(0.86-1.01)	0.09	0.96(0.83-1.11)	0.58	0.99(0.95-1.04)	0.77
Size:>5cm	1.03(0.97-1.09)	0.29	0.92(0.86-0.99)	<0.05	0.94(0.83-1.07)	0.35	1.04(1.00-1.08)	0.06
Grade1	0.75(0.72-0.77)	<0.01	1.00(0.93-1.07)	0.90	0.80(0.73-0.87)	<0.01	0.97(0.92-1.02)	0.22
Grade2	0.78(0.76-0.81)	<0.01	1.15(1.09-1.21)	<0.01	0.76(0.72-0.82)	<0.01	0.93(0.89-0.97)	<0.01
Grade3	0.83(0.80-0.85)	<0.01	1.09(1.03-1.15)	<0.01	0.75(0.69-0.82)	<0.01	0.95(0.90-1.01)	0.09
Grade4	0.98(0.91-1.05)	0.54	1.29(1.19-1.39)	<0.01	0.65(0.54-0.78)	<0.01	0.90(0.77-1.05)	0.18
Chemotherapy	0.87(0.85-0.90)	<0.01	0.80(0.76-0.84)	<0.01	0.51(0.40-0.64)	<0.01	0.86(0.83-0.90)	<0.01
Radiation	1.19(1.16-1.21)	<0.01	1.41(1.35-1.48)	<0.01	0.76(0.60-0.96)	<0.05	1.03(0.98-1.08)	0.21
Sex	0.62(0.56-0.69)	<0.01	0.72(0.70-0.75)	<0.01	0.69(0.65-0.73)	<0.01	0.68(0.66-0.70)	<0.01

**Table S5.** Risk factors of developing SPC stratified by sites using competing risk model.

Site	Bladder		Endocrine		Prostate		Female Genital	
Variable	HR (95% CL)	P Value	HR (95% CL)	P Value	HR (95% CL)	P Value	HR (95% CL)	P Value
40-49y	2.10(1.74-2.53)	<0.01	2.17(1.96-2.41)	<0.01	2.23(1.11-4.5)	<0.05	1.82(1.66-1.99)	<0.01
50-59y	3.39(2.85-4.03)	<0.01	3.46(3.13-3.82)	<0.01	4.00(2.00-8.00)	<0.01	2.60(2.40-2.83)	<0.01
60-69y	5.05(4.25-5.99)	<0.01	6.03(5.45-6.67)	<0.01	6.79(3.39-13.58)	<0.01	3.58(3.30-3.89)	<0.01
70-79y	5.94(5.00-7.05)	<0.01	6.95(6.18-7.83)	<0.01	9.60(4.80-19.20)	<0.01	4.51(4.14-4.90)	<0.01
≥ 80y	4.97(4.17-5.92)	<0.01	8.10(6.66-9.85)	<0.01	11.06(5.53-22.14)	<0.01	4.59(4.13-5.10)	<0.01
Black	0.98(0.91-1.07)	0.71	1.04(0.92-1.19)	0.51	0.95(0.93-0.98)	<0.01	1.03(0.96-1.11)	0.42
Asian	0.85(0.78-0.92)	<0.01	0.96(0.86-1.06)	0.41	0.87(0.83-0.90)	<0.01	0.92(0.86-0.99)	<0.05
Unmarried	0.96(0.93-1.00)	<0.05	0.97(0.91-1.04)	0.46	1.00(0.98-1.03)	0.83	1.01(0.97-1.05)	0.64
Node	1.21(1.08-1.37)	<0.01	1.15(1.06-1.25)	<0.01	1.39(1.3-1.49)	<0.01	1.03(0.96-1.12)	0.42
Surgery	1.16(1.07-1.26)	<0.01	1.28(1.06-1.55)	<0.01	1.08(1.06-1.11)	<0.01	1.09(1.02-1.17)	<0.05
Size<1cm	0.91(0.83-1.00)	0.05	0.94(0.84-1.06)	0.32	1.14(1.11-1.19)	<0.01	0.98(0.90-1.06)	0.62
Size:1-2cm	0.97(0.91-1.03)	0.29	0.86(0.77-0.96)	<0.05	0.97(0.92-1.01)	0.13	0.94(0.87-1.02)	0.13
Size:2-3cm	0.88(0.83-0.93)	<0.01	0.88(0.78-0.99)	<0.05	1.04(0.98-1.11)	0.18	0.98(0.91-1.05)	0.51
Size:3-4cm	0.91(0.86-0.96)	<0.01	0.83(0.72-0.95)	<0.01	1.05(0.95-1.17)	0.34	0.90(0.84-0.98)	<0.05
Size:4-5cm	0.92(0.85-0.99)	<0.05	0.78(0.66-0.92)	<0.01	0.88(0.74-1.04)	0.12	0.94(0.87-1.03)	0.17
Size:>5cm	0.90(0.85-0.96)	<0.01	0.99(0.86-1.13)	0.85	0.76(0.62-0.93)	<0.01	0.88(0.83-0.93)	<0.01
Grade1	0.98(0.92-1.04)	0.48	0.91(0.83-1.01)	0.07	1.22(1.16-1.28)	<0.01	0.83(0.79-0.88)	<0.01
Grade2	1.11(1.05-1.17)	<0.01	0.95(0.81-1.12)	0.56	0.97(0.93-1.02)	0.23	0.88(0.83-0.93)	<0.01
Grade3	1.20(1.13-1.28)	<0.01	0.99(0.77-1.27)	0.93	0.88(0.84-0.92)	<0.01	0.87(0.82-0.93)	<0.01
Grade4	1.18(1.10-1.25)	<0.01	0.89(0.59-1.33)	0.56	1.12(0.95-1.31)	0.18	0.89(0.80-0.99)	<0.05
Chemotherapy	1.18(1.12-1.24)	<0.01	1.03(0.81-1.30)	0.81	1.40(1.25-1.58)	<0.01	0.88(0.83-0.92)	<0.01
Radiation	0.74(0.66-0.83)	<0.01	1.01(0.95-1.08)	0.68	1.27(1.24-1.30)	<0.01	1.39(1.33-1.45)	<0.01
Sex	0.66(0.64-0.69)	<0.01	0.69(0.65-0.74)	<0.01	-	-	-	-

**NOTE of Table S4-S5 :**

Grade, Reference: unknown; Grade1: well differentiated, Grade2: moderate differentiated,

Grade3: poorly differentiated, Grade4: undifferentiated,

Age, Reference: 0-39;

Race, Reference: White;

Marital, Reference: Married;

Node, Reference: positive node=0;

Size, Reference: micro;

Chemotherapy, Reference: no;

Radiation, Reference: no;

Sex, Reference: Male.

Table S6. Features of each included SNP in Mendelian randomization.

Number	exposure	outcome	Colorectal Cancer					<b>b</b>	<b>se</b>	<b>p</b>
			<b>id.exposure</b>	<b>id.outcome</b>	<b>samplesize</b>	<b>SNP</b>				
1	Colorectal cancer	Lung cancer    idieu-a-966	9xChou	ieu-a-966	27209	rs10512518	0.064870744	0.302100903	0.829976239	
2	Colorectal cancer	Lung cancer    idieu-a-966	9xChou	ieu-a-966	27209	rs1078643	0.099335911	0.262399681	0.705009286	
3	Colorectal cancer	Lung cancer    idieu-a-966	9xChou	ieu-a-966	27209	rs10849438	0.458299678	0.270752281	0.090514489	
4	Colorectal cancer	Lung cancer    idieu-a-966	9xChou	ieu-a-966	27209	rs10936599	0.708911128	0.508965758	0.163666241	
5	Colorectal cancer	Lung cancer    idieu-a-966	9xChou	ieu-a-966	27209	rs11169572	0.007424137	0.217724548	0.972798399	
6	Colorectal cancer	Lung cancer    idieu-a-966	9xChou	ieu-a-966	27209	rs11692435	0.006055263	0.258363537	0.981301701	
7	Colorectal cancer	Lung cancer    idieu-a-966	9xChou	ieu-a-966	27209	rs11893063	0.431455559	0.276550011	0.118727805	
8	Colorectal cancer	Lung cancer    idieu-a-966	9xChou	ieu-a-966	27209	rs12143541	0.047191916	0.273821748	0.863166002	
9	Colorectal cancer	Lung cancer    idieu-a-966	9xChou	ieu-a-966	27209	rs12255141	0.275663049	0.295151356	0.350318429	
10	Colorectal cancer	Lung cancer    idieu-a-966	9xChou	ieu-a-966	27209	rs12427600	0.467738194	0.254497404	0.066078639	
11	Colorectal cancer	Lung cancer    idieu-a-966	9xChou	ieu-a-966	27209	rs12635946	-0.195820504	0.248034586	0.429815713	
12	Colorectal cancer	Lung cancer    idieu-a-966	9xChou	ieu-a-966	27209	rs12979278	0.025961796	0.272204669	0.924016169	
13	Colorectal cancer	Lung cancer    idieu-a-966	9xChou	ieu-a-966	27209	rs13020391	0.08869035	0.21586792	0.68117908	
14	Colorectal cancer	Lung cancer    idieu-a-966	9xChou	ieu-a-966	27209	rs1321310	-0.081828713	0.236557728	0.729407082	
15	Colorectal cancer	Lung cancer    idieu-a-966	9xChou	ieu-a-966	27209	rs1412834	0.50855601	0.240979068	0.034826137	
16	Colorectal cancer	Lung cancer    idieu-a-966	9xChou	ieu-a-966	27209	rs1535	0.88449003	0.261829055	0.000729832	
17	Colorectal cancer	Lung cancer    idieu-a-966	9xChou	ieu-a-966	27209	rs16892766	-0.285298382	0.130711674	0.029061287	
18	Colorectal cancer	Lung cancer    idieu-a-966	9xChou	ieu-a-966	27209	rs17035289	0.027304324	0.241023572	0.909804713	
19	Colorectal cancer	Lung cancer    idieu-a-966	9xChou	ieu-a-966	27209	rs1741640	-0.183373528	0.158900412	0.248493841	
20	Colorectal cancer	Lung cancer    idieu-a-966	9xChou	ieu-a-966	27209	rs2193352	0.165258696	0.22566114	0.463966434	
21	Colorectal cancer	Lung cancer    idieu-a-966	9xChou	ieu-a-966	27209	rs2735940	-1.035301691	0.226416889	4.82E-06	
22	Colorectal cancer	Lung cancer    idieu-a-966	9xChou	ieu-a-966	27209	rs285245	-0.397944556	0.256688349	0.121068958	
23	Colorectal cancer	Lung cancer    idieu-a-966	9xChou	ieu-a-966	27209	rs3087967	0.010281554	0.142513761	0.942487078	
24	Colorectal cancer	Lung cancer    idieu-a-966	9xChou	ieu-a-966	27209	rs3127810	0.165708201	0.221698407	0.454792718	
25	Colorectal cancer	Lung cancer    idieu-a-966	9xChou	ieu-a-966	27209	rs35360328	0.149713258	0.219092772	0.94936629	
26	Colorectal cancer	Lung cancer    idieu-a-966	9xChou	ieu-a-966	27209	rs3801081	-0.17788091	0.250282477	0.477257398	
27	Colorectal cancer	Lung cancer    idieu-a-966	9xChou	ieu-a-966	27209	rs450168	0.154650847	0.286747964	0.589661416	
28	Colorectal cancer	Lung cancer    idieu-a-966	9xChou	ieu-a-966	27209	rs45597035	0.149463934	0.242928107	0.538383063	
29	Colorectal cancer	Lung cancer    idieu-a-966	9xChou	ieu-a-966	27209	rs4776316	-0.124388	0.266563442	0.640760589	
30	Colorectal cancer	Lung cancer    idieu-a-966	9xChou	ieu-a-966	27209	rs4811050	0.193369691	0.258776135	0.454914478	
31	Colorectal cancer	Lung cancer    idieu-a-966	9xChou	ieu-a-966	27209	rs4944940	-0.080115281	0.1730789	0.643448232	
32	Colorectal cancer	Lung cancer    idieu-a-966	9xChou	ieu-a-966	27209	rs597808	0.682670837	0.233076549	0.003401031	
33	Colorectal cancer	Lung cancer    idieu-a-966	9xChou	ieu-a-966	27209	rs605286	0.41020979	0.24682825	0.096528016	
34	Colorectal cancer	Lung cancer    idieu-a-966	9xChou	ieu-a-966	27209	rs6066825	-0.193081159	0.199590432	0.333350683	
35	Colorectal cancer	Lung cancer    idieu-a-966	9xChou	ieu-a-966	27209	rs61336918	0.34320133	0.238391149	0.149964649	
36	Colorectal cancer	Lung cancer    idieu-a-966	9xChou	ieu-a-966	27209	rs61776719	0.677675375	0.337399586	0.044575753	
37	Colorectal cancer	Lung cancer    idieu-a-966	9xChou	ieu-a-966	27209	rs62404966	-0.617329227	0.286131784	0.030966754	
38	Colorectal cancer	Lung cancer    idieu-a-966	9xChou	ieu-a-966	27209	rs639933	-0.061850777	0.270401499	0.81907348	
39	Colorectal cancer	Lung cancer    idieu-a-966	9xChou	ieu-a-966	27209	rs658977	0.050628213	0.240381363	0.833186757	
40	Colorectal cancer	Lung cancer    idieu-a-966	9xChou	ieu-a-966	27209	rs6928864	0.093571605	0.240464484	0.697181028	
41	Colorectal cancer	Lung cancer    idieu-a-966	9xChou	ieu-a-966	27209	rs6933790	-0.052684509	0.264085117	0.841873042	
42	Colorectal cancer	Lung cancer    idieu-a-966	9xChou	ieu-a-966	27209	rs6983267	0.021234491	0.101923903	0.834966064	
43	Colorectal cancer	Lung cancer    idieu-a-966	9xChou	ieu-a-966	27209	rs704017	-0.489632903	0.209956586	0.019697148	
44	Colorectal cancer	Lung cancer    idieu-a-966	9xChou	ieu-a-966	27209	rs72647484	0.232056532	0.247713847	0.348865184	
45	Colorectal cancer	Lung cancer    idieu-a-966	9xChou	ieu-a-966	27209	rs7303944	-0.040147617	0.162571683	0.80494435	
46	Colorectal cancer	Lung cancer    idieu-a-966	9xChou	ieu-a-966	27209	rs73376930	0.000447075	0.133994352	0.997337849	
47	Colorectal cancer	Lung cancer    idieu-a-966	9xChou	ieu-a-966	27209	rs73975588	-0.152665749	0.285562361	0.592916527	
48	Colorectal cancer	Lung cancer    idieu-a-966	9xChou	ieu-a-966	27209	rs7398375	-0.129792284	0.278738015	0.641471372	
49	Colorectal cancer	Lung cancer    idieu-a-966	9xChou	ieu-a-966	27209	rs7495132	0.797168338	0.299118392	0.007697468	
50	Colorectal cancer	Lung cancer    idieu-a-966	9xChou	ieu-a-966	27209	rs75688661	-0.308684424	0.325063331	0.342308838	
51	Colorectal cancer	Lung cancer    idieu-a-966	9xChou	ieu-a-966	27209	rs7993934	-0.300801544	0.247774715	0.224743038	
52	Colorectal cancer	Lung cancer    idieu-a-966	9xChou	ieu-a-966	27209	rs899244	0.239465673	0.260833135	0.358577037	
53	Colorectal cancer	Lung cancer    idieu-a-966	9xChou	ieu-a-966	27209	rs961253	-0.131533135	0.178679544	0.461645586	
54	Colorectal cancer	Lung cancer    idieu-a-966	9xChou	ieu-a-966	27209	rs9831861	-0.08765147	0.272145549	0.747395341	
55	Colorectal cancer	Lung cancer    idieu-a-966	9xChou	ieu-a-966	27209	rs9929218	-0.14275495	0.206882413	0.49017569	
56	Colorectal cancer	Lung cancer    idieu-a-966	9xChou	ieu-a-966	27209	All - Inverse variance weighted	0.011724872	0.041018757	0.774999358	
57	Colorectal cancer	Lung cancer    idieu-a-966	9xChou	ieu-a-966	27209	All - MR Egger	-0.166792227	0.121347978	0.175072108	
58	Bladder cancer	Lung cancer    idieu-a-966	0IE7f	ieu-a-966	27209	rs1014971	-0.058529607	0.151884794	0.699974213	
59	Bladder cancer	Lung cancer    idieu-a-966	0IE7f	ieu-a-966	27209	rs10936599	0.171055296	0.122809877	0.163666241	
60	Bladder cancer	Lung cancer    idieu-a-966	0IE7f	ieu-a-966	27209	rs1495741	-0.086488974	0.162438237	0.594419757	
61	Bladder cancer	Lung cancer    idieu-a-966	0IE7f	ieu-a-966	27209	rs17674580	0.297173796	0.123665837	0.016259465	
62	Bladder cancer	Lung cancer    idieu-a-966	0IE7f	ieu-a-966	27209	rs2294008	0.098741071	0.147785549	0.50404581	
63	Bladder cancer	Lung cancer    idieu-a-966	0IE7f	ieu-a-966	27209	rs401681	1.072808704	0.141358739	3.22F-14	
64	Bladder cancer	Lung cancer    idieu-a-966	0IE7f	ieu-a-966	27209	rs710521	-0.044789955	0.155653442	0.773534782	
65	Bladder cancer	Lung cancer    idieu-a-966	0IE7f	ieu-a-966	27209	rs798766	0.155283715	0.115493592	0.178779538	
66	Bladder cancer	Lung cancer    idieu-a-966	0IE7f	ieu-a-966	27209	rs8102137	0.102474575	0.155943128	0.511098702	
67	Bladder cancer	Lung cancer    idieu-a-966	0IE7f	ieu-a-966	27209	rs907611	-0.296429051	0.134936591	0.028034548	

Bladder Cancer						
Number	exposure	outcome	id.exposure	id.outcome	samplesize	SNP
1	Bladder cancer	Lung cancer    idieu-a-966	OlEx7f	ieu-a-966	27209	rs1014971
2	Bladder cancer	Lung cancer    idieu-a-966	OlEx7f	ieu-a-966	27209	rs10936599
3	Bladder cancer	Lung cancer    idieu-a-966	OlEx7f	ieu-a-966	27209	rs1495741
4	Bladder cancer	Lung cancer    idieu-a-966	OlEx7f	ieu-a-966	27209	rs17674580
5	Bladder cancer	Lung cancer    idieu-a-966	OlEx7f	ieu-a-966	27209	rs2294008
6	Bladder cancer	Lung cancer    idieu-a-966	OlEx7f	ieu-a-966	27209	rs401681
7	Bladder cancer	Lung cancer    idieu-a-966	OlEx7f	ieu-a-966	27209	rs710521
8	Bladder cancer	Lung cancer    idieu-a-966	OlEx7f	ieu-a-966	27209	rs798766
9	Bladder cancer	Lung cancer    idieu-a-966	OlEx7f	ieu-a-966	27209	rs8102137
10	Bladder cancer	Lung cancer    idieu-a-966	OlEx7f	ieu-a-966	27209	rs907611

Number	exposure	outcome	id.exposure	id.outcome	samplesize	SNP	b	se	p
1	Oral cavity and pharyngeal cancer	Lung cancer    idieu-a-966	0oh4Qs	ieu-a-966	27209	rs1494961	0.297096008	0.151682691	0.0501517
2	Oral cavity and pharyngeal cancer	Lung cancer    idieu-a-966	0oh4Qs	ieu-a-966	27209	rs4767364	0.211516124	0.171088243	0.216347658

Pancreas Cancer								
Number	exposure	outcome	id.exposure	id.outcome	samplesize	SNP	b	se
1	Pancreatic cancer	Lung cancer    idieu-a-966	zCRK8e	ieu-a-966	27209	rs10094872	0.021811401	0.148571
2	Pancreatic cancer	Lung cancer    idieu-a-966	zCRK8e	ieu-a-966	27209	rs1486134	0.064748703	0.150043965
3	Pancreatic cancer	Lung cancer    idieu-a-966	zCRK8e	ieu-a-966	27209	rs1517037	0.064116222	0.147992179
4	Pancreatic cancer	Lung cancer    idieu-a-966	zCRK8e	ieu-a-966	27209	rs16986825	-0.19566148	0.140005913
5	Pancreatic cancer	Lung cancer    idieu-a-966	zCRK8e	ieu-a-966	27209	rs17688601	-0.228129846	0.159770527
6	Pancreatic cancer	Lung cancer    idieu-a-966	zCRK8e	ieu-a-966	27209	rs2941471	0.100079967	0.15239354
7	Pancreatic cancer	Lung cancer    idieu-a-966	zCRK8e	ieu-a-966	27209	rs3790844	-0.040529557	0.097707381
8	Pancreatic cancer	Lung cancer    idieu-a-966	zCRK8e	ieu-a-966	27209	rs401681	-0.698923188	0.092093679
9	Pancreatic cancer	Lung cancer    idieu-a-966	zCRK8e	ieu-a-966	27209	rs4795218	0.140338976	0.174328544
10	Pancreatic cancer	Lung cancer    idieu-a-966	zCRK8e	ieu-a-966	27209	rs6971498	0.133454644	0.131709683
11	Pancreatic cancer	Lung cancer    idieu-a-966	zCRK8e	ieu-a-966	27209	rs7190458	0.202982783	0.181026894
12	Pancreatic cancer	Lung cancer    idieu-a-966	zCRK8e	ieu-a-966	27209	rs7214041	0.155457327	0.130288327
13	Pancreatic cancer	Lung cancer    idieu-a-966	zCRK8e	ieu-a-966	27209	rs9543235	0.146821614	0.08875867
14	Pancreatic cancer	Lung cancer    idieu-a-966	zCRK8e	ieu-a-966	27209	rs9581943	0.136643064	0.13319792
15	Pancreatic cancer	Lung cancer    idieu-a-966	zCRK8e	ieu-a-966	27209	rs9854771	0.138104125	0.156821439

Number	exposure	Breast Cancer									
		outcome	id.exposure	id.outcome	samplesize	SNP	b	se	p		
1	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r10022462	0.78378133	0.49117333	0.110548492		
2	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r10054203	2.145229765	0.633759791	0.000711975		
3	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r10096531	0.067796398	0.168606635	0.687611873		
4	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r10760444	-0.146107821	0.501452514	0.770768963		
5	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r1085405	-0.523593785	0.373655914	0.154095238		
6	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r10941679	-0.135007825	0.167480438	0.420178845		
7	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r10978911	-0.675584025	0.308855781	0.028715014		
8	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r1095201	-0.277413819	0.194563402	0.153918184		
9	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r1117758	-0.252966592	0.490712695	0.606197693		
10	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r1135046	0.050327476	0.251785216	0.841572424		
11	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r11205303	0.11766338	0.380523139	0.757158148		
12	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r1121948	0.533641739	0.385339313	0.166009449		
13	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r11249433	-0.191187247	0.184939274	0.310237212		
14	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r11571833	2.416912358	0.610913091	7.61E-05		
15	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r11583933	1.037434343	0.497222222	0.036936963		
16	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r11624333	0.160338843	0.212985537	0.451560709		
17	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r11672660	0.233601693	0.456610169	0.608910380		
18	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r11684853	0.053827376	0.405045249	0.894278594		
19	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r117618124	-0.505081007	0.392150338	0.197751495		
20	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r117737783	0.163574297	0.534082999	0.759298085		
21	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r11822830	0.114227523	0.372756323	0.759267786		
22	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r11903787	-0.368736142	0.493813747	0.452328047		
23	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r11977670	-0.397720307	0.335498084	0.23583474		
24	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r12027986	-0.347592	0.49048	0.478524808		
25	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r12205049	0.45734375	0.382899306	0.232312531		
26	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r1230666	-0.19464695	0.45292297	0.667371722		
27	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r12479355	0.699788732	0.502816901	0.164021446		
28	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r12487185	0.271284444	0.424177778	0.523205057		
29	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r12513872	-0.217926633	0.511210654	0.669892774		
30	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r12519859	0.133755068	0.498273973	0.784134987		
31	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r12546444	-0.48204742	0.448114505	0.28202069		
32	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r1268974	0.253760404	0.237616646	0.28554742		
33	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r1290503	0.313253425	0.280013699	0.262569445		
34	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r13267382	-0.217344622	0.45068499	0.629626694		
35	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r1498606	0.390098631	0.44494739	0.380543423		
36	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r1685191	0.343515388	0.328737201	0.296044083		
37	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r16991615	0.6698923219	0.538693931	0.195826372		
38	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r1703702	1.716771978	0.501236264	0.000614629		
39	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r170801	0.305292724	0.330930626	0.356253302		
40	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r17156577	-0.279529412	0.510103806	0.583701964		
41	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r1785310	0.085223544	0.488810127	0.861591212		
42	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r1786829	-0.196939596	0.399333333	0.670977373		
43	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r17872669	-0.207823409	0.519753593	0.689267094		
44	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r1787852	0.099721878	0.503645833	0.843045064		
45	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r1793765	0.3564744908	0.235777234	0.130557534		
46	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r1805742	0.609590136	0.319104762	0.066262803		
47	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r1806194	0.205126824	0.415529412	0.621552143		
48	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r18253012	0.772946882	0.440415704	0.079252581		
49	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r18403907	-0.11531093	0.244949749	0.637816838		
50	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r18425359	-0.135909169	0.523008596	0.794971538		
51	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r18506889	0.079069919	0.506097561	0.796162996		
52	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r18524068	0.099746834	0.263050241	0.737823939		
53	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r185261361	-0.42989527	0.508330602	0.397623052		
54	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r1853669	-1.470955453	0.410030722	0.000333976		
55	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r1865183	0.7373221348	0.440269663	0.099932333		
56	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r1899756	0.158728458	0.354071146	0.653940036		
57	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r1923290	-0.143336139	0.451495815	0.724349774		
58	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r19358942	0.128633663	0.38827093	0.740435675		
59	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r19510339	0.584465368	0.409588745	0.153592401		
60	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r1960821	0.091455658	0.242423074	0.846816183		
61	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r19621902	0.516598587	0.43578491	0.235671335		
62	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r1993072	-0.039367281	0.415207373	0.924223078		
63	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r198081859	0.20485207	0.39860142	0.606815357		
64	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r1993886	0.601988384	0.468181881	0.199184611		
65	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r19946946	-0.254196496	0.289712404	0.380366561		
66	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r1994975	0.121565149	0.143147505	0.39557552		
67	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r199491650	-0.490149038	0.501930239	0.337805909		
68	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r199562056	0.091455658	0.242400591	0.474930966		
69	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r199840480	0.137382051	0.28926221	0.634830806		
70	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r199821120	-0.188621166	0.554401284	0.733687365		
71	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r199840681	0.083310127	0.433164557	0.033044193		
72	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r199859875	0.0701824	0.236575458	0.762423885		
73	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r199870599	-0.053670728	0.186280242	0.773517079		
74	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r199872436	0.019219388	0.301992888	0.949604563		
75	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r199872670	0.465119639	0.469933288	0.322219196		
76	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r199869468	-0.390427734	0.414179688	0.345858409		
77	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r199869103	1.294790433	0.455466937	0.044722533		
78	Breast cancer (Combined Oncoarray; iCOGS; GWAS meta analysis)	idieu-a-1126	Lung cancer	idieu-a-966	27209	r199869781</					

Prostate Cancer						
Number	exposure	outcome	id.exposure	id.outcome	samplesize	SNP
1	Bladder cancer	Lung cancer    idieu-a-966	OlEx7f	ieu-a-966	27209	rs1014971
2	Bladder cancer	Lung cancer    idieu-a-966	OlEx7f	ieu-a-966	27209	rs10936599
3	Bladder cancer	Lung cancer    idieu-a-966	OlEx7f	ieu-a-966	27209	rs1495741
4	Bladder cancer	Lung cancer    idieu-a-966	OlEx7f	ieu-a-966	27209	rs17674580
5	Bladder cancer	Lung cancer    idieu-a-966	OlEx7f	ieu-a-966	27209	rs2294008
6	Bladder cancer	Lung cancer    idieu-a-966	OlEx7f	ieu-a-966	27209	rs401681
7	Bladder cancer	Lung cancer    idieu-a-966	OlEx7f	ieu-a-966	27209	rs710521
8	Bladder cancer	Lung cancer    idieu-a-966	OlEx7f	ieu-a-966	27209	rs798766
9	Bladder cancer	Lung cancer    idieu-a-966	OlEx7f	ieu-a-966	27209	rs8102137
10	Bladder cancer	Lung cancer    idieu-a-966	OlEx7f	ieu-a-966	27209	rs907611

Number	exposure	outcome	id.exposure	id.outcome	samplesize	SNP	b	se	p
1	Gastric cancer    idbbj-a-119	Lung cancer    idieu-a-966	bbj-a-119	ieu-a-966	27209	rs2978977	0.030628005	0.073030949	0.674935578
2	Gastric cancer    idbbj-a-119	Lung cancer    idieu-a-966	bbj-a-119	ieu-a-966	27209	rs3805495	-0.019754793	0.122942247	0.872342672

**Table S7.** Statistically significant associations of genetical predisposition to different cancer with lung cancer.

	Inverse variance weighted				Weighted median				MR Egger			
	OR	95% LCI	95% UCI	P-value	OR	95% LCI	95% UCI	P-value	OR	95% LCI	95% UCI	P-value
colorectum	1.042	0.928	1.132	0.334	1.010	0.920	1.110	0.829	1.042	0.928	1.132	0.07
bladder	1.157	0.930	1.441	0.191	1.099	0.972	1.242	0.132	0.539	0.121	2.406	0.442
oral and pharynx	1.296	1.038	1.619	<b>0.022</b>	NA	NA	NA	NA	NA	NA	NA	NA
pancreas	0.990	0.894	1.097	0.848	1.086	0.976	1.209	0.128	0.902	0.622	1.309	0.597
breast	1.013	0.949	1.083	0.698	1.026	0.938	1.123	0.576	0.890	0.771	1.028	0.115
stomach	1.017	0.899	1.151	0.781	NA	NA	NA	NA	NA	NA	NA	NA
prostate	1.021	0.965	1.080	0.473	1.019	0.948	1.094	0.613	0.989	0.886	1.103	0.841

NOTE: Inverse variance weighted method was carried out to assess the effect of genetically determined each cancer on lung cancer risk. MR-Egger and Weighted median estimator were used for sensitivity analysis.