

Supplementary Information

Associations of mRNA expression of DNA repair genes and genetic polymorphisms with cancer risk: a bioinformatics analysis and meta-analysis

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Outline

● Supplemental data

- **Table S1.** Characteristics of studies included in the meta-analysis.
- **Table S2.** Meta-analysis of the association between genetic polymorphisms of DNA repair pathway and cancer risk by homozygous and additive models
- **Figure S1.** Flowchart presents the identification, inclusion, exclusion of the literature research.
- **Figure S2.** Funnel plots to detect publication bias with pseudo 95% CIs under the dominant model. A: *XPA* rs10817938; B: *XPA* rs2808668; C: *XPC* rs1870134; D: *XPD* rs238406; E: *XPF* rs3136038; F and G: WRN rs1801195 and rs1346044. Each point represents an independent study for the indicated association.
- **Figure S3.** Forest plots represents the correlation of cancer risk with polymorphism of *XPA* rs10817938 (A), *XPA* rs2808668 (B), *XPC* rs1870134 (C), *XPD* rs238406 (D), *XPF* rs3136038 (E), WRN rs1801195(F) and rs1346044(G) assessing by overall and subgroup analysis under the homozygous model. Estimates of OR(95% CIs) are plotted with a box and a horizontal line for each study. ◇, pooled ORs (95% CIs).
- **Figure S4.** Forest plots illustrates the association of cancer risk with polymorphism of *XPA* rs10817938 (A), *XPA* rs2808668 (B), *XPC* rs1870134 (C), *XPD* rs238406 (D), *XPF* rs3136038 (E), WRN rs1801195(F) and rs1346044(G) assessing by overall and subgroup analysis under additive model. Estimates of OR(95% CIs) are plotted with a box and a horizontal line for each study. ◇, pooled ORs (95% CIs).

Table S1. Characteristics of studies included in the meta-analysis.

Variant	Author[ref]	Year	Country	Ethnicity	Tumor type	Control source	Genotyping method	Case				Controls			HWE (cases)	HWE (controls)	
								CC	CT	TT	Total	CC	CT	TT			Total
XPA rs10817938								CC	CT	TT	Total	CC	CT	TT	Total		
	Liu, J.	2015	China	Asian	Gastric cancer	HB	Sequencing	13	51	105	169	15	172	311	169	0.064	0.129
	Gao, C.	2016	China	Asian	OSCC	PB	Sequencing	37	307	307	932	38	299	595	891	0.000	0.955
	Wang, B.	2016	China	Asian	HCC	PB	Taqman assay	26	150	150	350	11	123	216	362	0.171	0.191
	Wang, B.	2016	China	Asian	HCC	PB	Sequencing	16	129	129	379	14	124	241	353	0.026	0.691
XPA rs2808668								CC	CT	TT	Total	CC	CT	TT	Total		
	Han, W.	2011	Korea	Asian	Breast cancer	PB	Sequencing	76	190	80	346	103	171	87	361	0.067	0.335
	Mei, C.	2013	China	Asian	Lung cancer	HB	Taqman assay	49	142	60	251	93	139	69	301	0.034	0.221
	Liu, J.	2015	China	Asian	Gastric cancer	HB	Sequencing	239	435	216	890	223	482	224	929	0.515	0.251
	Sun, Y.	2015	China	Asian	Laryngeal cancer	HB	PCR-RFLP	44	118	109	271	39	111	121	271	0.211	0.106
	Zhao, F.	2015	China	Asian	Pancreatic cancer	HB	PCR-RFLP	29	132	85	246	25	126	95	246	0.039	0.072
	Ravegnini, G.	2016	Italy	Caucasian	Gastric cancer	HB	Taqman assay	38	32	11	81	51	81	14	146	0.317	0.025
	Gao, C.	2016	China	Asian	OSCC	PB	Taqman assay	79	161	122	362	70	160	120	350	0.063	0.212
	Wang, B.	2016	China	Asian	HCC	PB	Sequencing	43	84	42	169	114	265	116	495	0.939	0.116
XPC rs1870134								GG	GC	CC	Total	GG	GC	CC	Total		
	He, J.	2013	China	Asian	Gastric cancer	HB	Taqman assay	439	417	69	925	606	496	94	1196	0.026	0.591
	Liu, J.	2015	China	Asian	Gastric cancer	HB	Sequencing	473	356	65	891	481	390	63	932	0.859	0.176
	Hua, R.X.	2016	China	Asian	Gastric cancer	PB	Sequence	711	378	53	1142	742	374	57	1173	0.761	0.268
	Wang, B.	2016	China	Asian	HCC	PB	Sequencing	230	114	15	359	197	160	24	381	0.854	0.257
	Wang, M.	2016	China	Asian	Prostate cancer	HB	Taqman assay	588	356	60	1004	551	430	74	1055	0.532	0.424
	Zhu, J.	2018	China	Asian	Wilms Tumor	HB	Taqman assay	92	51	2	145	339	166	26	521	0.082	0.335
	Sun, Y.	2015	China	Asian	laryngeal cancer	HB	PCR-RFLP	111	123	37	271	125	117	29	271	0.753	0.835
	McWilliams, R.R.	2009	USA	Mix	pancreatic	HB	PCR-RFLP	418	22	0	440	520	30	0	550	0.590	0.511
XPD rs238406								CC	CA	AA	Total	CC	CA	AA	Total		
	Sturgis, M.E.	2000	USA	Mix	HNC	PB	PCR-RFLP	62	97	30	189	154	241	101	496	0.435	0.705
	Caggana, M.	2001	USA	Mix	Glioma	PB	Taqman assay	38	49	39	126	55	60	24	139	0.013	0.281
	Vogel, U.	2001	Demmark	Caucasian	Basal cell cancer	PB	PCR-RFLP	16	36	14	66	42	47	22	111	0.455	0.189
	Lovatt, T.	2005	UK	Mix	Basal cell cancer	HB	PCR-RFLP	123	179	77	379	183	238	88	509	0.421	0.483
	Vogel U.	2005	Demmark	Caucasian	Basal cell cancer	PB	Real-time PCR	84	145	90	319	90	164	68	322	0.106	0.674
	Wrensch, M.	2005	USA	Mix	Glioma	PB	PCR-RFLP	40	67	31	138	51	72	22	145	0.770	0.678
	Wrensch, M.	2005	USA	Mix	Glioma	PB	PCR-RFLP	97	133	51	281	104	189	81	374	0.647	0.779
	Casson, A.G.	2005	Canada	NC	ESCC	HB	Taqman assay	35	43	17	95	14	30	12	56	0.552	0.586
	Garcia-C.,M.	2006	Spanish	Caucasian	Bladder cancer	HB	PCR-RFLP	287	578	268	1133	270	528	327	1125	0.488	0.048
	Shao, J.	2007	China	Asian	Bladder cancer	HB	PCR-RFLP	61	103	51	215	92	122	31	245	0.560	0.334
	Kipikasova, L.	2008	Slovak	Caucasian	Breast cancer	HB	PCR-RFLP	27	55	32	114	46	55	12	113	0.722	0.455
	Chang, J.S.	2008	USA	Caucasian	Lung cancer	PB	Sequencing	43	37	34	114	113	123	61	297	0.000	0.012
	Chang, J.S.	2008	USA	African	Lung cancer	PB	Sequencing	190	58	6	254	207	68	4	279	0.534	0.550
	Harth, V.	2008	German	Caucasian	NSCC	HB	PCR-RFLP	114	144	54	312	98	146	56	300	0.464	0.901
	Worrillow, L.	2009	UK	Caucasian	NHL	PB	Taqman assay	199	300	153	652	232	377	152	761	0.055	0.959
	Yin, J.	2009	China	Asian	breast cancer	HB	PCR-RFLP	41	56	32	129	55	102	48	205	0.147	0.958
	Yin, J.	2012	China	Asian	breast cancer	HB	PCR-RFLP	15	14	11	40	11	23	8	42	0.064	0.513
	Yin, J.	2012	China	Asian	breast cancer	HB	PCR-RFLP	37	79	51	167	33	81	46	160	0.542	0.808
	El-Din, M.A.K.	2013	Egyptian	Mix	LBCL	HB	PCR-RFLP	20	36	25	81	34	48	18	100	0.332	0.883
	Zhou, C.	2013	China	Asian	Prostate cancer	HB	PCR-RFLP	26	53	21	100	38	49	13	100	0.531	0.650
	Szczur, K.P.	2014	Polish	Caucasian	CRC	PB	Taqman assay	231	363	160	754	356	672	211	1239	0.434	0.000
	Mirecka, A.	2014	Poland	Caucasian	Prostate cancer	PB	Taqman assay	113	300	99	512	141	411	126	678	0.000	0.000
	Michalska, M.M.	2015	Polish	Caucasian	Endometrial cancer	HB	PCR-RFLP	136	144	1080	1360	264	840	216	1320	0.000	0.000
	Romanowicz, H.	2016	Poland	Caucasian	ovarian	HB	PCR-RFLP	76	135	189	400	122	186	92	400	0.000	0.195
	Carrera-L., P.	2017	Spain	Caucasian	Gastric cancer	PB	Sequencing	169	268	166	603	162	282	159	603	0.006	0.112
	Yan, D.	2018	China	Asian	pancreatic	PB	PCR-RFLP	226	253	113	81	32	128	97	38	0.007	0.008
XPF rs3136038								CC	CT	TT	Total	CC	CT	TT	Total		
	Shao, M.	2007	China	Asian	Lung cancer	HB	Taqman assay	601	297	73	971	558	364	51	973	0.000	0.399
	Han, J.	2008	USA	Mixed	Breast cancer	PB	Sequencing	119	94	23	236	193	221	52	466	0.485	0.341

YU, D.K.	2010	China	Asian	Lung cancer	HB	PCR-RFLP	577	355	56	988	547	362	77	986	0.886	0.118
Yu, H.	2012	USA	Caucasian	Glioma	HB	Sequencing	452	483	105	1040	458	452	136	1046	0.145	0.143
Cheng, H.	2013	China	Asian	Glioma	HB	Sequencing	90	89	29	208	105	100	31	236	0.358	0.356
Zhou, W.	2014	China	Asian	Glioma	HB	Sequencing	94	100	31	225	111	114	34	259	0.594	0.580
Liu, Y.	2014	China	Asian	ESCC	HB	PCR-RFLP	297	175	28	500	277	176	47	500	0.740	0.017
Banescu, C.	2016	Romania	Caucasian	AML	HB	PCR-RFLP	57	35	16	108	71	76	16	163	0.012	0.504
Carrera-L., P.	2017	Spanish	Caucasian	Gastric cancer	HB	Sequencing	258	277	66	601	222	298	81	601	0.515	0.225
Lawania, S.	2017	India	Asian	Lung cancer	HB	PCR-RFLP	181	141	48	370	199	118	60	377	0.016	0.000
WRN rs1801195							GG	GT	TT	Total	GG	GT	TT	Total		
Wang, Z.	2009	China	Asian	Breast cancer	HB	PCR-RFLP	394	382	228	1004	392	451	165	1008	0.000	0.069
Frank, B.	2009	German	Caucasian	CRC	HB	Sequencing	17	61	69	147	12	61	38	111	0.533	0.086
Wang, L.	2011	China	Asian	Prostate cancer	PB	Sequencing	609	828	323	1795	623	829	328	1805	0.159	0.075
Huang, G.	2018	China	Asian	Meningiomas	HB	PCR-RFLP	37	92	86	215	36	90	92	218	0.154	0.087
WRN rs1346044							TT	TC	CC	Total	TT	TC	CC	Total		
Shen, M.	2006	USA	Mixed	Lymphoma	PB	PCR-RFLP	305	161	29	495	313	238	39	590	0.213	0.487
Wirtenberger, M.	2006	German	European	Breast cancer	PB	Taqman assay	407	339	65	811	565	375	65	1005	0.632	0.794
Ding, S.L.	2007	China	Asian	Breast cancer	HB	Taqman assay	738	181	13	932	1225	300	19	1544	0.617	0.896
Pinto, G. R.	2008	Brazil	Mixed	Glioma	PB	PCR-RFLP	48	43	3	94	59	38	3	100	0.070	0.284
Frank, B.	2009	German	Caucasian	CRC	PB	Sequencing	926	708	137	1795	963	686	140	1805	0.918	0.250
Wang, Z.	2009	China	Asian	Breast cancer	PB	PCR-RFLP	826	168	10	1004	847	158	3	1008	0.656	0.122
LI, T.	2012	China	Asian	ESCC	HB	PCR-RFLP	80	36	1	117	114	17	1	132	0.156	0.680
Sun, K.	2014	China	Asian	CRC	PB	PCR-RFLP	675	202	13	890	680	189	41	910	0.631	0.000
Wang, K.	2014	China	Asian	Skull cancer	PB	PCR-RFLP	45	19	0	64	41	24	0	65	0.163	0.068
Wang, K.	2014	China	Asian	Skull cancer	PB	PCR-RFLP	45	19	0	64	185	54	5	244	0.163	0.652
Zins, K.	2015	European	Caucasian	Breast cancer	HB	Taqman assay	140	111	21	272	140	103	11	254	0.877	0.139

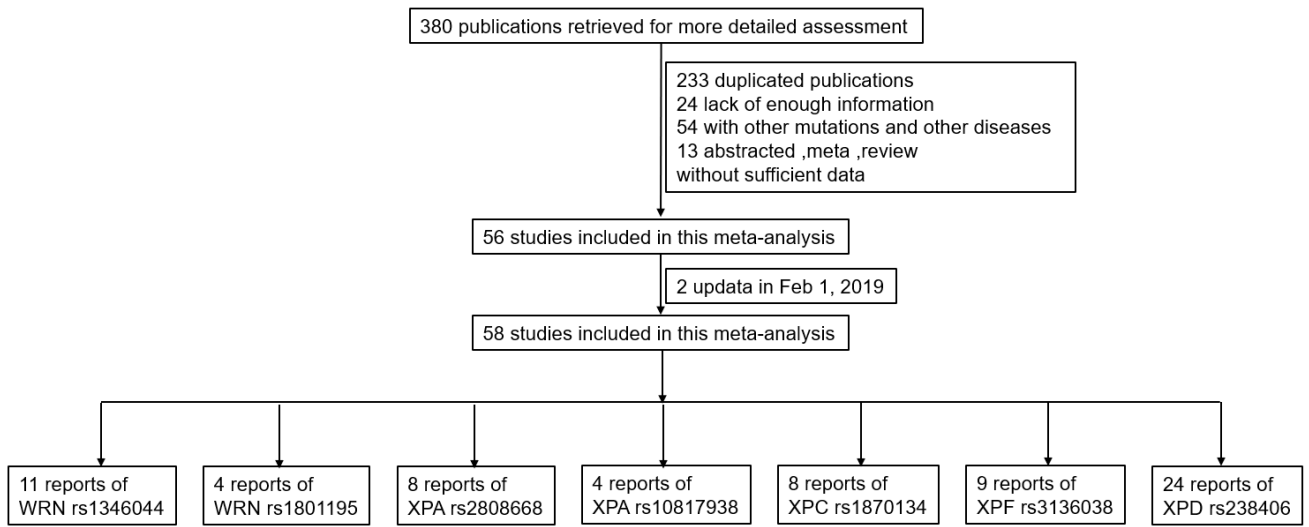
HB, Hospital based; PB, Population based; PCR-RFLP, polymorphism chain reaction- restriction fragment length polymorphism; OSCC, oral squamous cell cancer; HCC, hepatocellular cancer; CRC, colorectal cancer; ESCC, Esophageal squamous cell carcinoma; AML, Acute myeloid leukemia; HNC, Head and neck cancer; NHL, Non-Hodgkinlymphoma; NSCC, Neck squamous cell cancer; LBCL, Large B cell lymphoma.

Table S2. Meta-analysis of the association between genetic polymorphisms of DNA repair pathway and cancer risk by homozygous and additive models

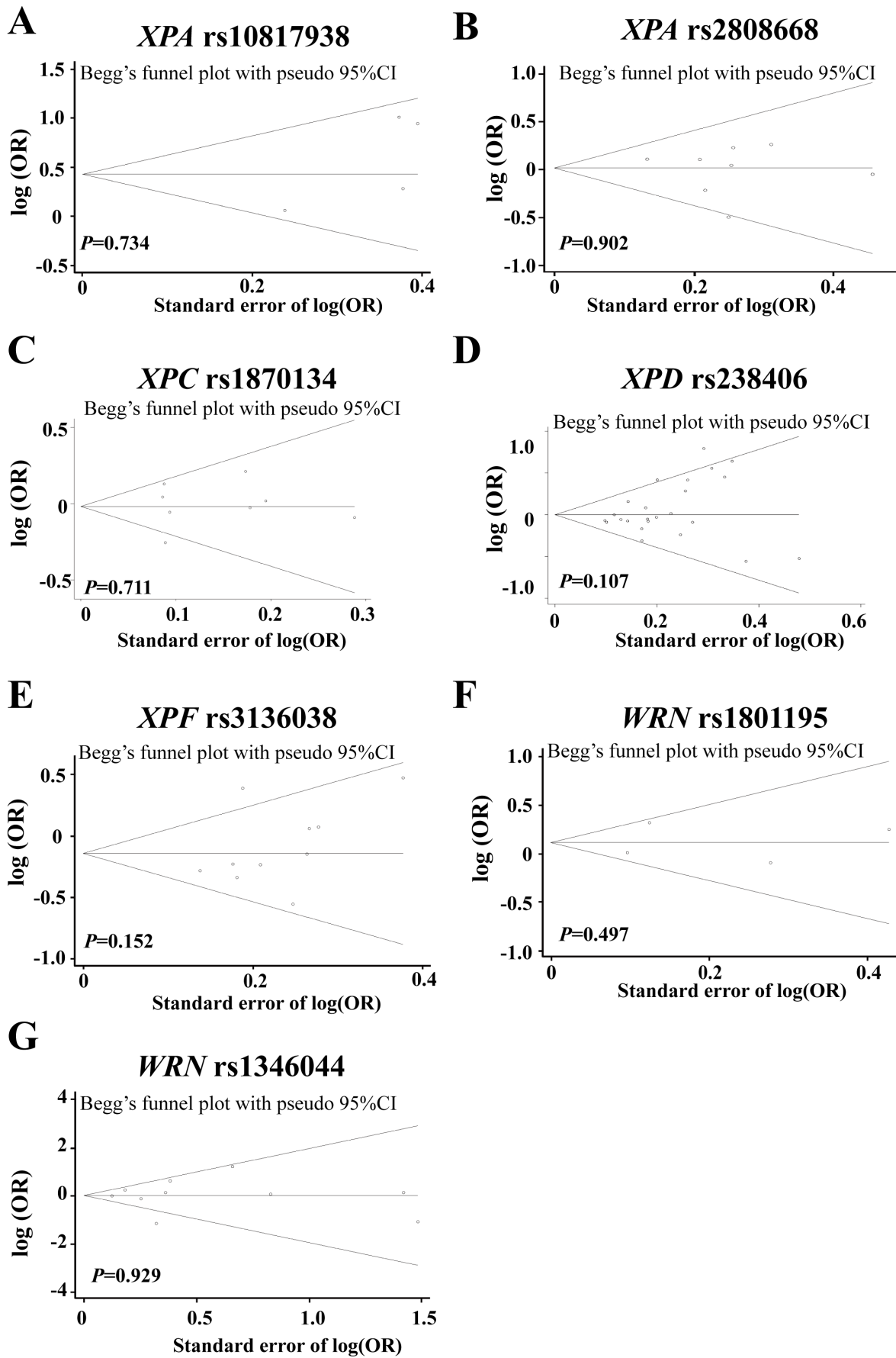
Variables	No. of cases/ controls	p^{z*}	Homozygous OR(95%CI)	$p^{het\#}$	$I^2\#$ (%)	p^{z*}	Additive OR(95%CI)	$p^{het\#}$	$I^2\#$ (%)
XPA rs10817938			CC VS. TT				C VS. T		
Digestive system [†]	1775/2156	0.04	1.68 (1.02,2.76)	0.08	55.2	0.01	1.20 (1.04,1.38)	0.21	33.5
Overall	1775/2156	0.04	1.68 (1.02,2.76)	0.08	55.2	0.01	1.20 (1.04,1.38)	0.21	33.5
XPA rs2808668			CC VS. TT				C VS. T		
Digestive system [†]	2019/2437	0.19	1.13 (0.94,1.34)	0.99	0.0	0.10	1.07 (0.99,1.17)	0.97	0.0
Others	597/662	0.04	0.71 (0.52,0.98)	0.40	0.0	0.03	0.84 (0.72,0.99)	0.40	0.0
Overall	2616/3099	0.91	1.01 (0.86,1.19)	0.39	5.7	0.76	1.01 (0.93,1.11)	0.27	19.8
XPC rs1870134			CC VS. GG				C VS. G		
Digestive system [†]	3567/4346	0.69	0.95 (0.74,1.22)	0.26	25.4	0.78	1.01 (0.94,1.09)	0.66	0.0
Others	1420/1847	0.61	0.85 (0.45,1.61)	0.05	67.0	0.70	0.95 (0.75,1.21)	0.04	69.3
Overall	4987/6193	0.48	0.92 (0.72,1.16)	0.11	42.1	0.57	0.98 (0.89,1.07)	0.12	39.5
XPD rs238406			AA VS. CC				A VS. C		
Nervous system [§]	545/658	0.45	1.38 (0.60,3.13)	0.003	82.9	0.46	1.18 (0.76,1.81)	0.002	84.2
Basal cell cancer	764/942	0.02	1.38 (1.05,1.81)	0.88	0.0	0.02	1.18 (1.03,1.35)	0.78	0.0
Digestive system [†]	1678/2151	0.60	1.05 (0.87,1.26)	0.49	0.0	0.88	1.01 (0.92,1.10)	0.53	0.0
Urinary system [‡]	1348/1370	0.61	1.35 (0.43,4.22)	0.000	93.2	0.64	1.14 (0.66,1.95)	0.000	92.9
Genital system [¶]	1062/1298	0.18	1.38 (0.86,2.23)	0.009	67.2	0.20	1.17 (0.92,1.48)	0.007	68.4
Respiratory system [¶]	368/576	0.12	1.49 (0.90,2.46)	0.88	0.0	0.32	1.12 (0.89,1.41)	0.44	0.0
Others	1234/1657	0.78	1.05 (0.73,1.53)	0.07	58.4	0.80	1.02 (0.85,1.23)	0.07	57.7
Overall	6999/8652	0.03	1.20 (1.02,1.41)	0.000	61.1	0.05	1.08 (1.00,1.18)	0.00	61.9
XPF rs3136038			TT VS. CC				T VS. C		
Respiratory system [¶]	2329/2336	0.72	0.93 (0.63,1.38)	0.05	67.4	0.10	0.92 (0.84,1.02)	0.49	0.0
Nervous system [§]	1473/1541	0.252	0.87 (0.69,1.10)	0.32	0.0	0.62	0.97 (0.88,1.08)	0.70	0.0
Digestive system [†]	1101/1101	0.004	0.64 (0.48,0.87)	0.46	0.0	0.003	0.82 (0.72,0.94)	0.86	0.0
others	344/629	0.628	0.88 (0.52,1.48)	0.42	0.0	0.06	0.82 (0.67,1.00)	0.53	0.0
Overall	5247/5607	0.06	0.85 (0.71,1.00)	0.14	33.7	0.001	0.91 (0.86,0.96)	0.58	0.0
WRN rs1801195			TT VS. GG				T VS. G		
Genital system [¶]	1151/1119	0.009	1.37 (1.08,1.73)	0.88	0.0	0.02	1.15 (1.02,1.29)	0.49	0.0
Others	2010/2023	0.97	1.00 (0.83,1.19)	0.73	0.0	0.99	1.00 (0.91,1.09)	0.80	0.0
Overall	3161/3142	0.25	1.13 (0.92,1.39)	0.21	34.2	0.24	1.06 (0.96,1.16)	0.25	26.6
WRN rs1346044			CC VS. TT				C VS. T		
Breast cancer	3019/3811	0.01	1.47 (1.10,1.97)	0.44	0.0	0.005	1.15 (1.04,1.26)	0.51	0.0
Digestive system [†]	2802/2847	0.41	0.65 (0.24,1.79)	0.004	82.3	0.48	1.22 (0.81,1.56)	0.001	84.9
Others	717/999	0.31	0.78 (0.48,1.26)	0.76	0.0	0.53	0.92 (0.71,1.19)	0.20	35.9
Overall	6538/7657	0.88	1.03 (0.72,1.47)	0.005	61.7	0.36	1.06 (0.94,1.20)	0.001	66.5

* P_z : the significance of the pooled OR was determined by Z-test, and $P < 0.05$ was considered statistically significant. # P_{het} and I^2 were calculated by Chi square-based Q-test. [¶]Respiratory system cancer: lung cancer; [‡]Urinary system cancer: bladder cancer; [†]Digestive system cancer: gastric cancer, ESCC, hepatocellular cancer, colorectal cancer, laryngeal cancer, OSCC, pancreatic cancer; [§]Nervous system cancer: glioma; [¶]Genital system cancer: breast cancer, prostate cancer.

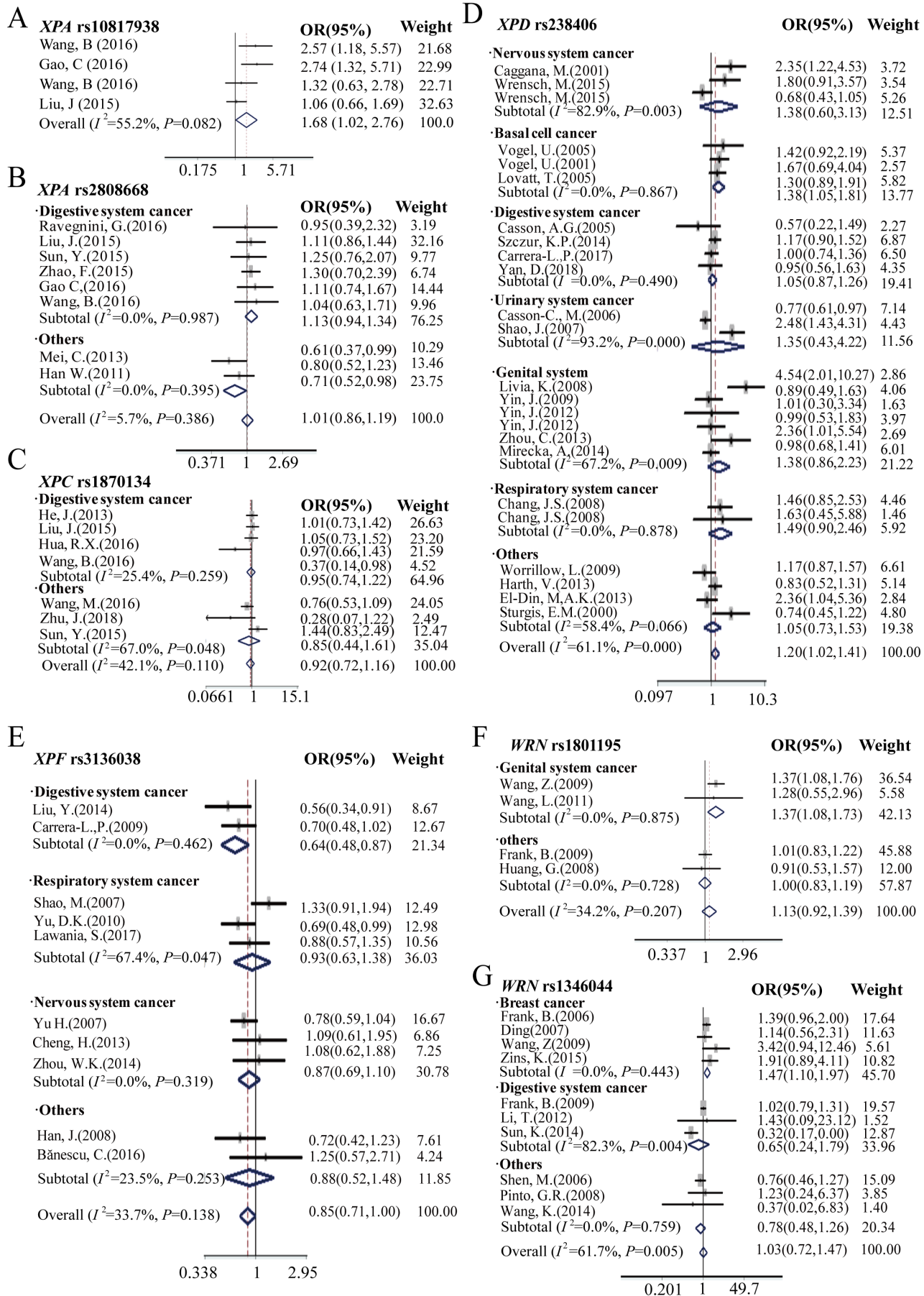
FigureS1



FigureS2



FigureS3



FigureS4

