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Association between the polymorphisms in *XPG* gene and gastric cancer susceptibility in Chinese populations

A PRISMA-compliant meta-analysis

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Abstract

Background: Several previous studies were carried out on the association between xeroderma pigmentosum group G (XPG) gene polymorphisms (including rs873601 G>A, rs2094258 C>T, rs2296147 T>C, and rs751402 C>T) and the risk of gastric cancer in Chinese populations. However, their conclusions were not consistent. Therefore, this meta-analysis was performed by us to investigate the association between the 4 potentially functional single nucleotide polymorphisms (SNPs) of *XPG* gene and gastric cancer risk.

Methods: The eligible literatures were identified through PubMed, Embase, Ovid MEDLINE, Web of Science, CNKI, and Wan fang databases up to July 2017. Finally, 5 studies for rs873601, 7 studies for rs2094258, 4 studies for rs2296147, and 8 studies for rs751402 were used for the current meta-analysis.

Results: Of the 4 included SNPs, only rs751402 was showed to be associated with the risk of gastric cancer [C vs T, odds ratio (OR) = 1.16, 95% confidence interval (CI) = 1.04–1.29; CC + CT vs TT, OR = 1.23, 95% CI = 1.00–1.52; CC vs CT + TT, OR = 1.15, 95% CI = 1.05–1.27; CC vs TT, OR = 1.35, 95% CI = 1.06–1.72; CC vs CT, OR = 1.13, 95% CI = 1.02–1.25].

Conclusion: The current meta-analysis demonstrated that the *XPG* gene polymorphism rs751402 was associated with increased susceptibility to gastric cancer in Chinese populations. However, studies with a larger number of subjects among different ethnic groups are needed to further validate the results.

Abbreviations: CI = confidence interval, ERCC5 = excision repair cross complementing group 5, HWE = Hardy–Weinberg equilibrium, MAF = minor allele frequency, NER = nucleotide excision repair, OR = odds ratio, SNP = single nucleotide polymorphism, XPG = xeroderma pigmentosum group G.

Keywords: Chinese, gastric cancer, polymorphism, susceptibility, *XPG*

1. Introduction

Gastric cancer is always companied with high mortality. According to the statistics, the incidence rate of gastric cancer is the highest in Eastern Asia including China.[1,2] Gastric carcinogenesis is a multifactor process involved in lifestyle, environmental factor, and host genetics.[3] The relationship between the former 2 factors and gastric cancer risk has been already well known.[4,5] Genetic susceptibility attracts increasing attention in recent years.[6–11]

In humans, DNA repair system plays a critical role in maintaining genome stability, which prevents carcinogenesis.[12] Nucleotide excision repair (NER) has been identified as a major DNA repair pathway.[13] One of the rate-limiting proteins in the NER mechanism is xeroderma pigmentosum group G (XPG).[14] The protein, also named the excision repair cross complementing group 5 (ERCC5), is an endonuclease. The endonuclease could cut the damaged DNA at the lesion during DNA repair process.[15] Therefore, genetic variations of *XPG* may affect DNA repair capacity. And it could partly explain why certain individuals have increased susceptibility to malignancies compared with others.[16]

Recently, several studies have explored the association between the polymorphisms in *XPG* gene (including rs873601 G>A, rs2094258 C>T, rs2296147 T>C, and rs751402 C>T) and gastric cancer risk in Chinese populations. However, the conclusions in these studies were controversial.[16–26]

To clarify the association between these single nucleotide polymorphisms (SNPs) and gastric cancer risk in Chinese populations, we performed this meta-analysis of eleven published studies. Meanwhile, we will learn the roles of these SNPs in gastric carcinogenesis and illustrate the possible reasons for these

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conflicting results. All of the original regions in these studies were from China and no other ethnicities or regions existed.

2. Methods

2.1. Search strategy

The potentially relevant literatures were searched in PubMed, Embase, Ovid MEDLINE, Web of Science, CNKI, and Wan fang databases up to July 2017. The search terms were "gastric cancer," "stomach cancer," "xeroderma pigmentosum group G," "*XPG*," "excision repair cross complementing group 5," "ERCC5," "polymorphism," "SNP," "rs873601," "rs2094258," "rs2296147," and "rs751402." Furthermore, all references of the retrieved eligible studies were examined for additionally relevant publications.

2.2. Inclusion criteria

The inclusion criteria for studies were as follows: evaluating the association between the SNPs of *XPG* gene and gastric cancer risk in Chinese populations; case–control study; and available data including the phenotype or allele frequencies of the SNPs of *XPG* gene in both cases and controls. More than that, unpublished articles, abstracts from conferences, case reports, and reviews were excluded.

2.3. Data extraction

Data including the following information were collected from each eligible study: the first author's name, year of publication, region and ethnicity of the sample population, the sample sizes in case and control groups, the distribution of phenotype, and minor allele frequency (MAF). The Newcastle-Ottawa scale was used to evaluate the quality of individual studies.

2.4. Statistical analysis

Hardy–Weinberg equilibrium (HWE) in the control group of each study was examined. The association between SNP and gastric cancer risk was assessed by odds ratio (OR) and 95% confidence interval (CI) in 5 genetic models, including allelic model, recessive model, dominant model, additive model, and heterozygous comparison model. We pooled these ORs using fixed or random effect model according to heterogeneity. The Chi-square-based Q test and I^2 index were used to assess the presence of statistical heterogeneity. If $P<.10$ for the Q test or $I^2>50\%$, significant heterogeneity between studies existed and the random-effect model was conducted. Otherwise, the fixed-effect model was applied. To validate the stability of the pooled results and identify the sources of heterogeneity, sensitive analysis was carried out. Moreover, the publication bias among studies was evaluated by both Begg test and Egger test. The false-positive report probability (FPRP) analysis and trial sequential analysis (TSA) are performed to confirm the results in this meta-analysis. All statistical tests were performed using STATA software, version 11.0 (STATA Corp., College Station, TX).

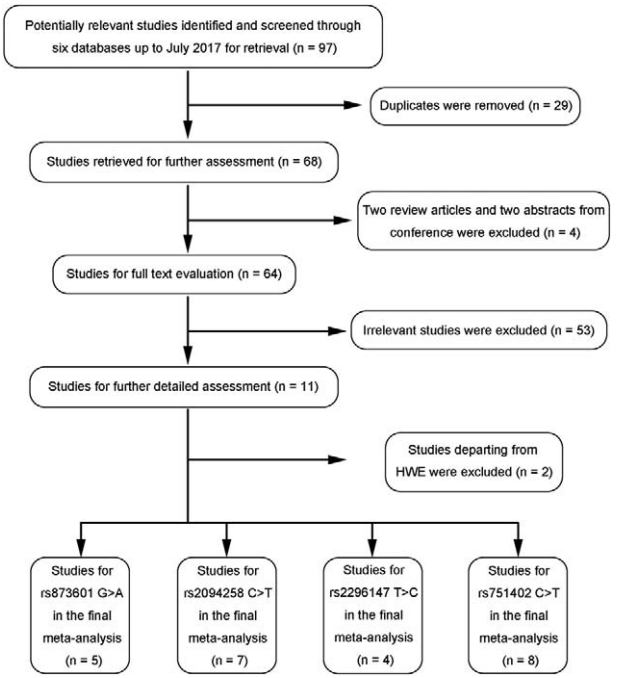

Figure 1. Flow diagram of study search and selection in the current meta-analysis for the association between *XPG* gene polymorphisms and gastric cancer susceptibility.

Table 1

Characteristics of 11 studies included in this meta-analysis.

Refs.	Region	Ethnicity	Sample size		SNPs				
			Case	Control	rs873601 G>A	rs2094258 C>T	rs2296147 T>C	rs751402 C>T	Score
Chen et al[23]	Zhejiang	Asian	692	771	+	+	+	+	5
Duan et al[16]	Liaoning	Asian	478	724			+	+	6
Feng et al[22]	Shanxi	Asian	177	237		+		+	7
Guo et al[21]	Hebei	Asian	142	274				+	6
He et al[24]	Shanghai and Jiangsu	Asian	1125	1196	+	+	+		6
Hua et al[26]	Guangdong, Guangxi and Hainan	Asian	1142	1173	+	+	+	+	5
Li et al[20]	Henan	Asian	216	216				+	6
Lu et al[19]	Gansu	Asian	184	206		+		+	6
Yang et al[18]	Shanxi	Asian	155	246		+		+	5
Yang et al[25]	Henan	Asian	337	347	+	+	+		6
Zhou et al[17]	Hebei	Asian	431	432	+			+	7

SNPs = single nucleotide polymorphisms.

Table 2

Genotype and allele frequencies distribution of *XPG* polymorphism in eleven studies included in this meta-analysis.

	Case			Control			MAF		
Refs.	BB	Bb	bb	BB	Bb	bb	Case	Control	HWE
rs873601 G>A									
Chen et al[23]	172	333	187	205	396	170	0.511	0.477	0.415
He et al[24]	274	560	291	327	605	264	0.508	0.474	0.616
Hua et al[26]	311	557	274	323	598	252	0.484	0.470	0.424
Yang et al[25]	96	163	78	91	164	91	0.473	0.500	0.333
Zhou et al[17]	115	215	101	132	200	100	0.484	0.463	0.152
rs2094258 C>T									
Chen et al[23]	287	304	101	291	368	112	0.366	0.384	0.803
Feng et al[22]	15	75	87	15	96	127	0.703	0.735	0.577
He et al[24]	457	518	150	457	560	179	0.364	0.384	0.728
Hua et al[26]	499	508	135	527	524	122	0.341	0.327	0.623
Lu et al[19]	17	67	100	13	72	121	0.726	0.762	0.605
Yang et al[18]	71	74	10	121	111	14	0.303	0.283	0.076
Yang et al[25]	131	149	57	145	166	36	0.390	0.343	0.252
rs2296147 T>C									
Chen et al[23]	442	217	33	475	264	32	0.204	0.213	0.535
Duan et al[16]	257	122	24	260	132	11	0.211	0.191	0.232
He et al[24]	700	371	54	742	398	56	0.213	0.213	0.779
Hua et al[26]	725	364	53	746	388	39	0.206	0.199	0.182
Yang et al[25]	208	105	24	196	110	41	0.227	0.277	<0.001*
rs751402 C>T									
Chen et al[23]	286	313	93	351	331	89	0.361	0.330	0.416
Duan et al[16]	172	181	47	206	165	29	0.344	0.279	0.605
Feng et al[22]	70	83	24	101	107	28	0.370	0.345	0.967
Guo et al[21]	47	73	22	117	136	21	0.412	0.325	0.029*
Hua et al[26]	426	555	161	433	551	189	0.384	0.396	0.537
Li et al[20]	88	106	22	95	103	18	0.347	0.322	0.174
Lu et al[19]	69	91	24	87	97	22	0.378	0.342	0.510
Yang et al[18]	49	73	33	103	111	32	0.448	0.356	0.807
Zhou et al[17]	174	196	61	193	193	46	0.369	0.330	0.827

HWE = Hardy–Weinberg equilibrium, MAF = minor allele frequency.
* $P < .05$.

Table 3

Meta-analysis of *XPG* polymorphism and the risk of gastric cancer in Chinese populations.

Genetic comparison	P_Q	I^2, %	95% CI	P_Z	Model
rs873601 G>A					
G vs A	.336	12.30	1.09 (1.02–1.16)	.010*	Fixed
GG + AG vs AA	.263	23.70	1.16 (1.04–1.28)	.007*	Fixed
GG vs AG + AA	.578	0.00	1.08 (0.98–1.20)	.121	Fixed
GG vs AA	.333	12.60	1.18 (1.04–1.34)	.009*	Fixed
GG vs AG	.663	0.00	1.04 (0.93–1.16)	.478	Fixed
rs2094258 C>T					
C vs T	.133	38.90	0.98 (0.92–1.05)	.618	Fixed
CC + CT vs TT	.119	40.80	1.01 (0.89–1.14)	.881	Fixed
CC vs CT + TT	.409	2.10	0.96 (0.88–1.06)	.413	Fixed
CC vs TT	.083	46.40	1.00 (0.80–1.25)	.974	Random
CC vs CT	.734	0.00	0.95 (0.86–1.05)	.286	Fixed
rs2296147 T>C					
T vs C	.687	0.00	1.02 (0.94–1.10)	.678	Fixed
TT + CT vs CC	.264	24.50	1.27 (1.01–1.60)	.045*	Fixed
TT vs CT + CC	.866	0.00	0.98 (0.89–1.08)	.721	Fixed
TT vs CC	.281	21.50	1.25 (0.99–1.58)	.065	Fixed
TT vs CT	.885	0.00	0.95 (0.86–1.05)	.337	Fixed
rs751402 C>T					
C vs T	.045	51.20	1.16 (1.04–1.29)	.008*	Random
CC + CT vs TT	.079	45.10	1.23 (1.00–1.52)	.047*	Random
CC vs CT + TT	.375	7.20	1.15 (1.05–1.27)	.003*	Fixed
CC vs TT	.035	53.70	1.35 (1.06–1.72)	.016*	Random
CC vs CT	.878	0.00	1.13 (1.02–1.25)	.015*	Fixed

CI = confidence interval.
* $P < .05$.

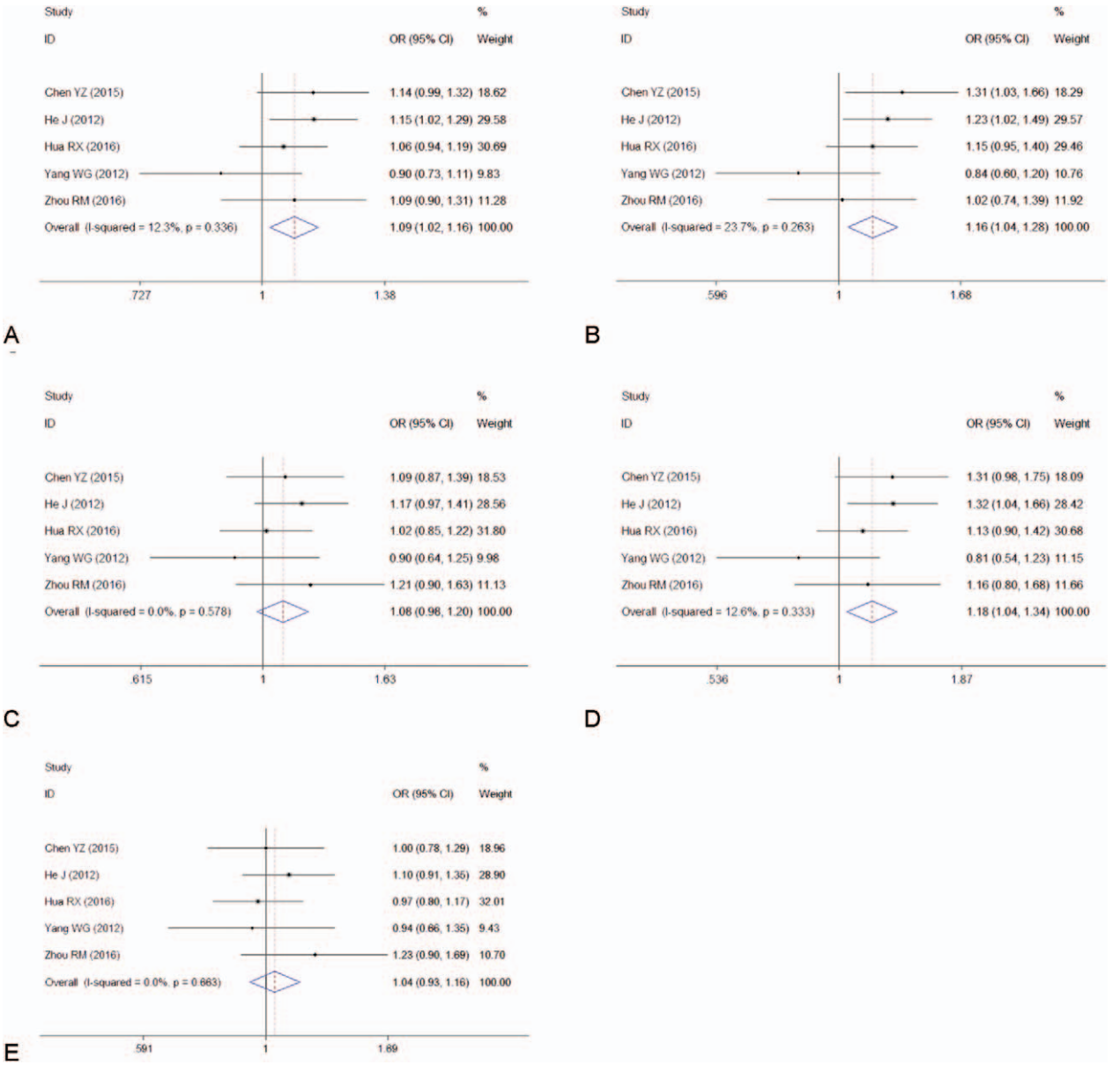

Figure 2. Forest plots for meta-analysis of rs873601 polymorphism and the risk of gastric cancer in Chinese populations. (A) Allelic model (G vs A). (B) Recessive genetic model (GG + AG vs AA). (C) Dominant genetic model (GG vs AG + AA). (D) Addictive genetic model (GG vs AA). (E) Heterozygous comparison model (GG vs AG).

2.5. Ethical review

The current meta-analysis was performed on the base of previous studies. Thus, the ethical approval was not required.

3. Results

3.1. Study selection and characteristics

The study selection process in this meta-analysis is shown in Fig. 1. A total of 97 studies were found in the initial search (PubMed: 40, Embase: 18, Web of Science: 19, CNKI: 16, and Wan fang: 4). Of these, 29 studies were duplicated. Therefore, 68 articles were retrieved based on the search criteria. Among these studies, 2 review articles, 2 abstracts from conferences, and 53 irrelevant studies were excluded. Finally, the remaining eleven studies were selected and the data in them were extracted.[16–26] Of them, 3 studies were medium quality and the other studies were high quality (Table 1). The genotype and allele frequencies distribution of *XPG* gene polymorphisms in all studies are listed in Table 2. However, phenotype distribution of rs2296147 in Yang et al's study[25] and rs751402 in Guo et al's study[21] departed from HWE (Table 2). Their data were excluded and not used for further meta-analysis. Therefore, 5 studies for rs873601, 7 studies for rs2094258, 4 studies for rs2296147, and 8 studies for rs751402 were used for the final meta-analysis.

3.2. Meta-analysis results

For rs873601 and rs2296147, no significant heterogeneity was observed in 5 genetic models, and the fixed-effect model was used to calculate the ORs and 95% CIs (Table 3). We found that rs873601 was significantly associated with the increased gastric cancer risk in

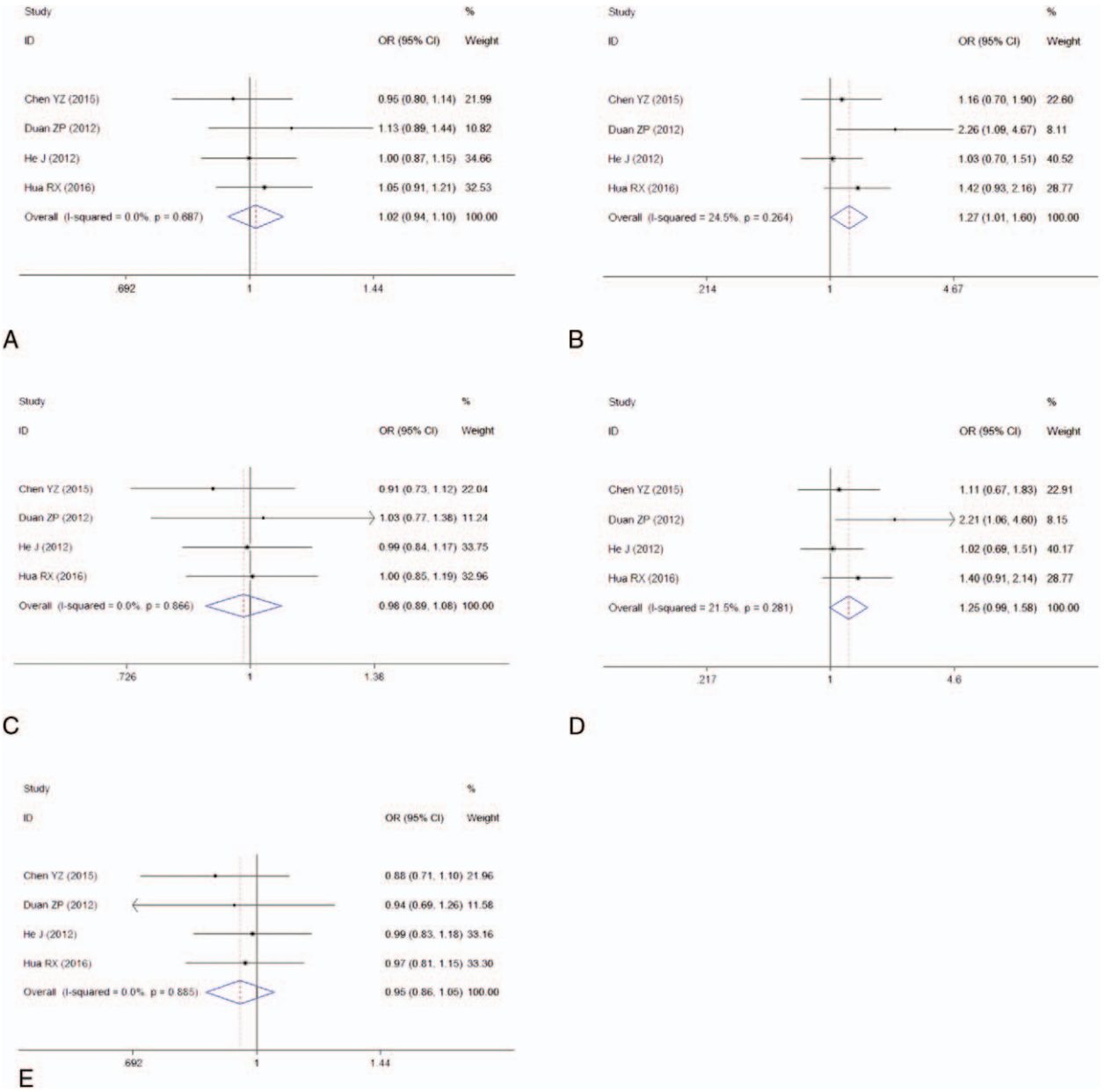

Figure 3. Forest plots for meta-analysis of rs2296147 polymorphism and the risk of gastric cancer in Chinese populations. (A) Allelic model (T vs C). (B) Recessive genetic model (TT + CT vs CC). (C) Dominant genetic model (TT vs CT + CC). (D) Addictive genetic model (TT vs CC). (E) Heterozygous comparison model (TT vs CT).

allelic, recessive, and additive models. However, no obvious association between rs873601 and gastric cancer susceptibility was detected in dominant model or heterozygous model (Table 3 and Fig. 2). Furthermore, our data indicated that rs2296147 was significantly associated with the elevated risk of gastric cancer in recessive model, but not in other models (Table 3 and Fig. 3).

For rs2094258, the significant heterogeneity was present in additive model. Therefore, the random-effect model was used in this genetic model and the fixed-effect model was used for other genetic models. No association between rs2094258 and gastric cancer susceptibility was found using the 5 genetic models in this meta-analysis (Table 3 and Fig. 4).

For rs751402, the heterogeneity in dominant and heterozygous models was not statistically significant, and the fixed-effect model was selected. Meanwhile, the random-effect model was used for other genetic models. Our data showed that rs751402 was associated with the increased susceptibility to gastric cancer in all genetic models (Table 3 and Fig. 5).

3.3. Heterogeneity and sensitivity analyses

Meta-regression was performed for rs2094258 and rs751402 to explore the source of heterogeneity. The publication year was considered as possible covariate. However, the result indicated that publication year was not the main factor responsible for the heterogeneity in any genetic model (Table 4).

Sensitivity analysis showed that the pooled ORs for rs2094258 were not considerably affected by omitting any single study in the 5 genetic models (Table 5). However, for rs873601 and rs2296147, certain study included in this meta-analysis might influence the whole results (Table 5). More than that, after omitting any single study for rs751402, the result of the SNP was

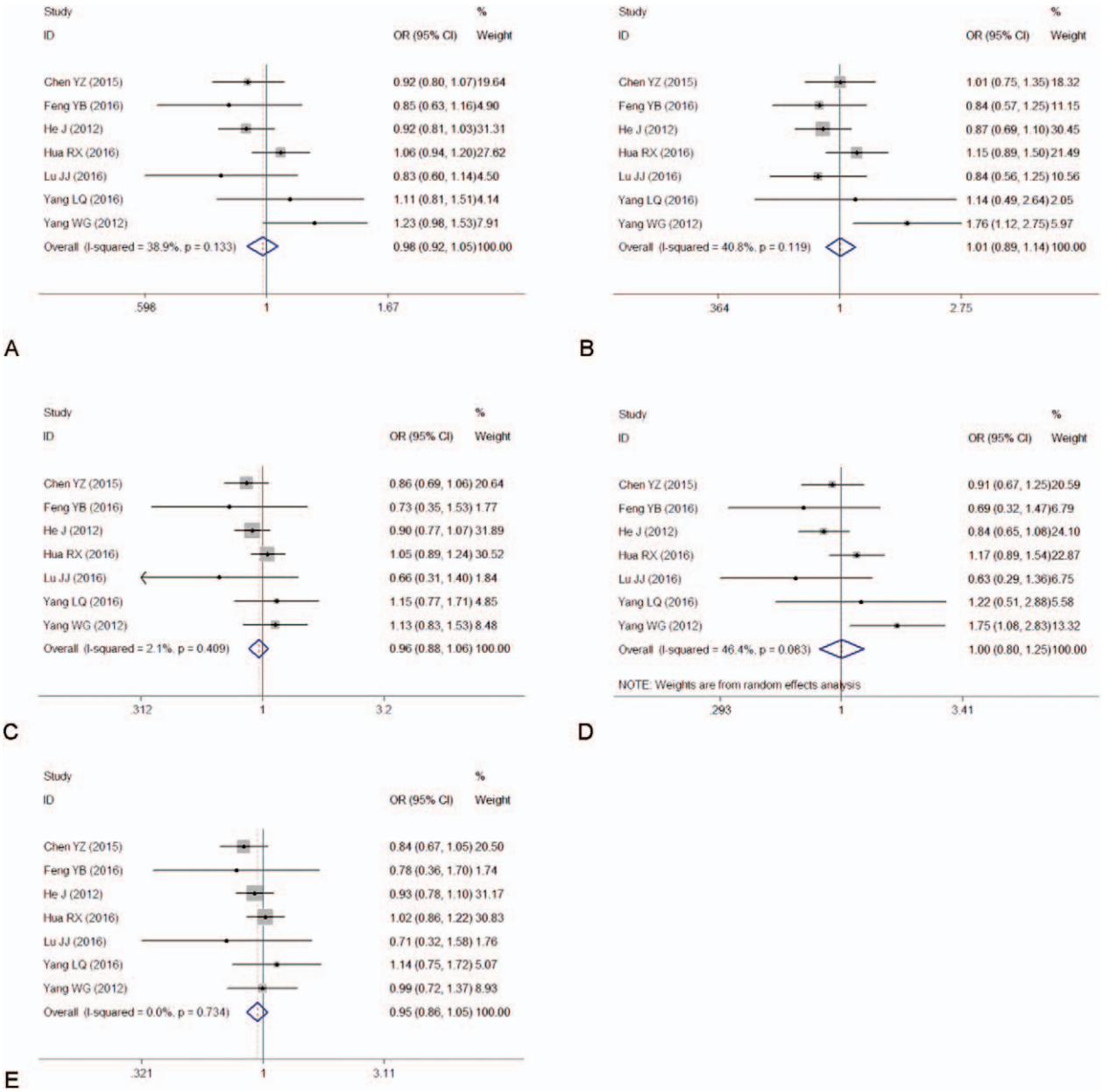

Figure 4. Forest plots for meta-analysis of rs2094258 polymorphism and the risk of gastric cancer in Chinese populations. (A) Allelic model (C vs T). (B) Recessive genetic model (CC + CT vs TT). (C) Dominant genetic model (CC vs CT + TT). (D) Addictive genetic model (CC vs TT). (E) Heterozygous comparison model (CC vs CT).

stable in allelic and dominant models, but not in other genetic models (Table 5).

3.4. Publication bias

For rs751402, the publication bias existed in recessive and additive models, but not in other genetic models. No obvious publication bias was obtained in any genetic model for the other 3 SNPs (Table 6).

3.5. False-positive report probability analysis and trial sequential analysis

The false-positive report probability analysis and trial sequential analysis were performed for the results of rs751402. All significant findings remained significant at a prior probability of .1 and the FPRP values were less than .20 with the exception of the recessive genetic model of rs751402 C>T (Table 7). More than that, our data indicated that the cumulative *Z*-curve crossed the trial sequential monitoring boundary, suggesting that the sample size was sufficient and no further analysis was required to confirm the results of rs751402 in allelic, dominant, addictive, and heterozygous models (Fig. 6). In recessive genetic model, the cumulative *Z*-curve crossed the conventional threshold value, but it did not cross the trial sequential monitoring boundary or the required information size line.

4. Discussion

As we all known, stomach is always exposed to various endogenous and exogenous mutagens. If the capability of DNA

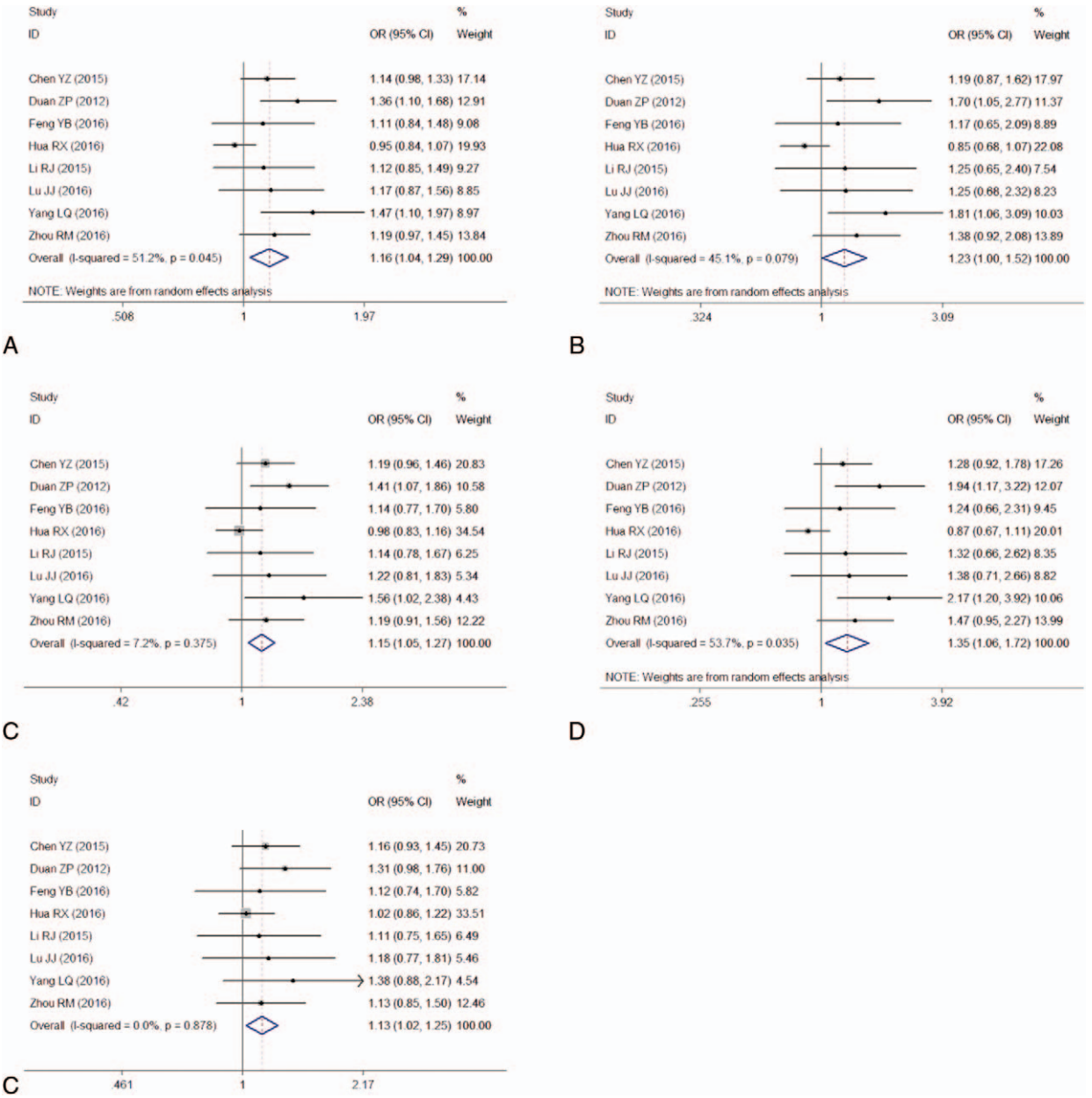

Figure 5. Forest plots for meta-analysis of rs751402 polymorphism and the risk of gastric cancer in Chinese populations. (A) Allelic model (C vs T). (B) Recessive genetic model (CC + CT vs TT). (C) Dominant genetic model (CC vs CT + TT). (D) Addictive genetic model (CC vs TT). (E) Heterozygous comparison model (CC vs CT).

Table 4

Meta-regression of *XPG* polymorphism and the risk of gastric cancer in Chinese populations.

Genetic comparison	Heterogeneity	*t*	*P* > |*t*|	95% CI
rs2094258 C>T				
C vs T	–			
CC + CT vs TT	–			
CC vs CT + TT	–			
CC vs TT	+	−0.61	.570	−0.24, 0.15
CC vs CT	–			
rs751402 C>T				
C vs T	+	−1.24	.263	−0.14, 0.05
CC + CT vs TT	+	−1.12	.304	−0.29, 0.11
CC vs CT + TT	–			
CC vs TT	+	−1.17	.288	−0.33, 0.12
CC vs CT	–			

CI = confidence interval.

repair is insufficient during the process, stomach cells will fail to repair the acquired DNA damage. DNA mutations will accumulate, and eventually gastric cancer is more likely to occur.[16] Therefore, DNA repair system plays a critical role in maintaining genome stability, which prevents gastric carcinogenesis.[12]

XPG has been demonstrated to play an important role in DNA repair system.[13,14] The 1186 amino-acid protein encoded by *XPG* gene functions as a structure-specific endonuclease involved in 2 incision steps, which are critical to correct the excision repair deficiency.[27,28] During the process of DNA repair, the DNA at the 3′ terminus could be cut by the endonuclease via the amino acids located at the N-terminus of XPG protein.[15,29] Therefore, the protein is critical to elimination of the damaged DNA.[30]

Genetic variations of *XPG* may lead to emergence of the corresponding mutated protein, resulting in alteration of DNA

Table 5

Sensitivity analysis of the meta-analysis.

Refs.	Genetic comparison	P_Q	I^2, %	95% CI	P_Z	Model
rs873601 G>A						
Chen et al[23]	G vs A	.263	24.70	1.07 (1.00–1.15)	.046	Fixed
	GG+AG vs AA	.268	23.90	1.12 (1.00–1.26)	.057	Fixed
	GG vs AG+AA	.412	0.00	1.08 (0.97–1.21)	.175	Fixed
	GG vs AA	.263	24.80	1.16 (1.00–1.33)	.045	Fixed
	GG vs AG	.514	0.00	1.05 (0.93–1.18)	.436	Fixed
He et al[24]	G vs A	.329	12.80	1.06 (0.99–1.15)	.115	Fixed
	GG+AG vs AA	.201	35.10	1.12 (0.99–1.28)	.072	Fixed
	GG vs AG+AA	.577	0.00	1.05 (0.93–1.18)	.433	Fixed
	GG vs AA	.330	12.60	1.13 (0.97–1.32)	.112	Fixed
	GG vs AG	.597	0.00	1.01 (0.89–1.15)	.839	Fixed
Hua et al[26]	G vs A	.236	29.40	1.10 (1.02–1.19)	.014	Fixed
	GG+AG vs AA	.155	42.80	1.16 (1.02–1.31)	.024	Fixed
	GG vs AG+AA	.536	0.00	1.12 (0.99–1.26)	.079	Fixed
	GG vs AA	.226	31.10	1.21 (1.04–1.40)	.015	Fixed
	GG vs AG	.653	0.00	1.07 (0.94–1.22)	.281	Fixed
Yang et al[25]	G vs A	.764	0.00	1.11 (1.04–1.18)	.003	Fixed
	GG+AG vs AA	.616	0.00	1.19 (1.07–1.33)	.002	Fixed
	GG vs AG+AA	.675	0.00	1.10 (0.99–1.23)	.067	Fixed
	GG vs AA	.770	0.00	1.23 (1.08–1.40)	.002	Fixed
	GG vs AG	.556	0.00	1.05 (0.94–1.18)	.397	Fixed
Zhou et al[17]	G vs A	.207	34.20	1.09 (1.02–1.16)	.015	Fixed
	GG+AG vs AA	.210	33.70	1.17 (1.05–1.31)	.005	Fixed
	GG vs AG+AA	.516	0.00	1.07 (0.96–1.19)	.233	Fixed
	GG vs AA	.207	34.30	1.19 (1.04–1.36)	.013	Fixed
	GG vs AG	.773	0.00	1.02 (0.91–1.14)	.779	Fixed
rs2094258 C>T						
Chen et al[23]	C vs T	.108	44.50	1.00 (0.93–1.07)	.953	Fixed
	CC+CT vs TT	.072	50.60	1.03 (0.83–1.28)	.782	Random
	CC vs CT+TT	.462	0.00	0.99 (0.89–1.10)	.845	Fixed
	CC vs TT	.054	53.90	1.03 (0.77–1.36)	.860	Random
	CC vs CT	.835	0.00	0.98 (0.88–1.09)	.671	Fixed
Feng et al[22]	C vs T	.111	44.10	0.99 (0.93–1.06)	.772	Fixed
	CC+CT vs TT	.100	45.90	1.03 (0.90–1.17)	.656	Fixed
	CC vs CT+TT	.350	10.30	0.97 (0.88–1.06)	.472	Fixed
	CC vs TT	.068	51.20	1.03 (0.82–1.31)	.788	Random
	CC vs CT	.649	0.00	0.95 (0.86–1.05)	.319	Fixed
He et al[24]	C vs T	.161	36.90	1.01 (0.94–1.10)	.734	Fixed
	CC+CT vs TT	.149	38.50	1.07 (0.92–1.24)	.374	Fixed
	CC vs CT+TT	.375	6.60	0.99 (0.88–1.11)	.850	Fixed
	CC vs TT	.126	41.90	1.08 (0.91–1.29)	.390	Fixed
	CC vs CT	.629	0.00	0.96 (0.85–1.08)	.481	Fixed
Hua et al[26]	C vs T	.173	35.10	0.95 (0.88–1.03)	.231	Fixed
	CC+CT vs TT	.119	43.00	0.97 (0.84–1.12)	.672	Fixed
	CC vs CT+TT	.482	0.00	0.92 (0.82–1.03)	.161	Fixed
	CC vs TT	.097	46.40	0.96 (0.73–1.26)	.770	Random
	CC vs CT	.783	0.00	0.91 (0.81–1.03)	.139	Fixed
Lu et al[19]	C vs T	.125	42.00	0.99 (0.93–1.06)	.790	Fixed
	CC+CT vs TT	.101	45.70	1.03 (0.90–1.17)	.658	Fixed
	CC vs CT+TT	.396	3.10	0.97 (0.88–1.06)	.491	Fixed
	CC vs TT	.081	49.10	1.04 (0.83–1.30)	.752	Random
	CC vs CT	.690	0.00	0.95 (0.86–1.05)	.332	Fixed
Yang et al[18]	C vs T	.099	45.90	0.98 (0.88–1.08)	.639	Random
	CC+CT vs TT	.074	50.20	1.02 (0.85–1.23)	.842	Random
	CC vs CT+TT	.372	6.90	0.95 (0.87–1.05)	.319	Fixed
	CC vs TT	.052	54.40	0.99 (0.78–1.26)	.943	Random
	CC vs CT	.731	0.00	0.94 (0.85–1.04)	.213	Fixed
Yang et al[25]	C vs T	.348	10.60	0.96 (0.90–1.03)	.277	Fixed
	CC+CT vs TT	.594	0.00	0.96 (0.84–1.10)	.559	Fixed
	CC vs CT+TT	.419	0.00	0.95 (0.86–1.04)	.269	Fixed
	CC vs TT	.383	5.30	0.94 (0.81–1.09)	.414	Fixed
	CC vs CT	.626	0.00	0.94 (0.85–1.05)	.268	Fixed

(*continued*)

Table 5

(continued).

Refs.	Genetic comparison	P_Q	I^2, %	95% CI	P_Z	Model
rs2296147 T>C						
Chen et al[23]	T vs C	.674	0.00	1.04 (0.94–1.14)	.452	Fixed
	TT+CT vs CC	.148	47.70	1.30 (1.00–1.69)	.050	Fixed
	TT vs CT+CC	.972	0.00	1.00 (0.90–1.12)	.951	Fixed
	TT vs CC	.167	44.10	1.29 (0.99–1.68)	.061	Fixed
	TT vs CT	.950	0.00	0.97 (0.87–1.09)	.609	Fixed
Duan et al[16]	T vs C	.719	0.00	1.00 (0.92–1.10)	.933	Fixed
	TT+CT vs CC	.541	0.00	1.18 (0.92–1.51)	.187	Fixed
	TT vs CT+CC	.741	0.00	0.98 (0.88–1.08)	.646	Fixed
	TT vs CC	.554	0.00	1.16 (0.91–1.49)	.238	Fixed
	TT vs CT	.728	0.00	0.95 (0.86–1.06)	.388	Fixed
He et al[24]	T vs C	.504	0.00	1.03 (0.93–1.14)	.595	Fixed
	TT+CT vs CC	.331	9.60	1.43 (1.07–1.92)	.016	Fixed
	TT vs CT+CC	.701	0.00	0.98 (0.87–1.10)	.708	Fixed
	TT vs CC	.316	13.20	1.40 (1.04–1.88)	.026	Fixed
	TT vs CT	.827	0.00	0.93 (0.82–1.06)	.278	Fixed
Hua et al[26]	T vs C	.527	0.00	1.00 (0.91–1.11)	.934	Fixed
	TT+CT vs CC	.169	43.80	1.21 (0.92–1.59)	.183	Fixed
	TT vs CT+CC	.730	0.00	0.97 (0.86–1.09)	.633	Fixed
	TT vs CC	.184	40.90	1.19 (0.90–1.57)	.235	Fixed
	TT vs CT	.737	0.00	0.94 (0.83–1.07)	.369	Fixed
rs751402 C>T						
Chen et al[23]	C vs T	.028	57.70	1.16 (1.02–1.33)	.022	Random
	CC+CT vs TT	.049	52.50	1.26 (0.98–1.63)	.074	Random
	CC vs CT+TT	.281	19.50	1.14 (1.03–1.27)	.014	Fixed
	CC vs TT	.020	59.90	1.38 (1.02–1.86)	.035	Random
	CC vs CT	.807	0.00	1.13 (1.01–1.26)	.040	Fixed
Duan et al[16]	C vs T	.100	43.60	1.09 (1.01–1.17)	.025	Fixed
	CC+CT vs TT	.131	39.10	1.10 (0.95–1.27)	.215	Fixed
	CC vs CT+TT	.504	0.00	1.12 (1.01–1.24)	.025	Fixed
	CC vs TT	.074	47.80	1.27 (1.00–1.62)	.053	Random
	CC vs CT	.924	0.00	1.11 (1.00–1.24)	.055	Fixed
Feng et al[22]	C vs T	.026	58.20	1.16 (1.03–1.31)	.013	Random
	CC+CT vs TT	.047	52.90	1.25 (0.99–1.58)	.058	Random
	CC vs CT+TT	.274	20.40	1.15 (1.05–1.27)	.004	Fixed
	CC vs TT	.019	60.30	1.37 (1.04–1.79)	.023	Random
	CC vs CT	.800	0.00	1.13 (1.02–1.26)	.018	Fixed
Hua et al[26]	C vs T	.669	0.00	1.21 (1.11–1.31)	<.001	Fixed
	CC+CT vs TT	.804	0.00	1.35 (1.13–1.61)	.001	Fixed
	CC vs CT+TT	.867	0.00	1.24 (1.11–1.40)	<.001	Fixed
	CC vs TT	.691	0.00	1.48 (1.22–1.78)	<.001	Fixed
	CC vs CT	.974	0.00	1.19 (1.05–1.34)	.006	Fixed
Li et al[20]	C vs T	.026	58.20	1.16 (1.03–1.31)	.013	Random
	CC+CT vs TT	.049	52.60	1.24 (0.99–1.56)	.063	Random
	CC vs CT+TT	.274	20.40	1.15 (1.05–1.27)	.004	Fixed
	CC vs TT	.020	60.10	1.36 (1.04–1.77)	.025	Random
	CC vs CT	.801	0.00	1.13 (1.02–1.26)	.017	Fixed
Lu et al[19]	C vs T	.027	57.90	1.16 (1.03–1.30)	.015	Random
	CC+CT vs TT	.049	52.50	1.24 (0.99–1.56)	.065	Random
	CC vs CT+TT	.280	19.60	1.15 (1.04–1.27)	.005	Fixed
	CC vs TT	.021	59.90	1.35 (1.03–1.77)	.027	Random
	CC vs CT	.805	0.00	1.13 (1.02–1.25)	.021	Fixed
Yang et al[18]	C vs T	.103	43.10	1.09 (1.02–1.17)	.013	Fixed
	CC+CT vs TT	.141	37.80	1.10 (0.95–1.27)	.190	Fixed
	CC vs CT+TT	.483	0.00	1.13 (1.03–1.25)	.011	Fixed
	CC vs TT	.082	46.50	1.26 (1.00–1.60)	.049	Random
	CC vs CT	.892	0.00	1.12 (1.01–1.24)	.030	Fixed
Zhou et al[17]	C vs T	.031	56.80	1.15 (1.02–1.31)	.022	Random
	CC+CT vs TT	.068	48.90	1.22 (0.97–1.54)	.096	Random
	CC vs CT+TT	.279	19.70	1.15 (1.04–1.27)	.008	Fixed
	CC vs TT	.027	57.90	1.34 (1.01–1.76)	.040	Random
	CC vs CT	.800	0.00	1.13 (1.02–1.26)	.022	Fixed

CI = confidence interval.

Table 6

Publication bias analysis of the meta-analysis.

Genetic comparison	Begg test	Egger test		
		t	*P*	95% CI
rs873601 G>A				
G vs A	0.221	−1.28	.290	−8.43, 3.59
GG+AG vs AA	0.221	−2.10	.127	−8.62, 1.77
GG vs AG+AA	0.806	−0.39	.719	−6.65, 5.19
GG vs AA	0.462	−1.41	.252	−8.65, 3.33
GG vs AG	0.806	0.24	.828	−5.02, 5.83
rs2094258 C>T				
C vs T	1.000	0.00	.996	−3.59, 3.57
CC+CT vs TT	0.548	0.63	.559	−3.12, 5.12
CC vs CT+TT	0.368	−0.46	.664	−2.68, 1.87
CC vs TT	1.000	0.00	.999	−3.43, 3.43
CC vs CT	0.368	−0.55	.604	−2.10, 1.36
rs2296147 T>C				
T vs C	0.734	0.68	.568	−7.00, 9.62
TT+CT vs CC	0.308	2.06	.176	−4.13, 11.68
TT vs CT+CC	0.734	−0.04	.975	−6.58, 6.47
TT vs CC	0.308	1.86	.203	−4.70, 11.89
TT vs CT	0.308	−0.98	.430	−6.18, 3.89
rs751402 C>T				
C vs T	0.536	2.38	.055	−0.08, 5.64
CC+CT vs TT	0.711	2.75	.033	−0.28, 4.88
CC vs CT+TT	0.386	2.06	.085	−0.36, 4.17
CC vs TT	0.711	2.63	.039	0.19, 5.42
CC vs CT	0.386	1.83	.117	−0.39, 2.66

CI = confidence interval.

repair capacity. Therefore, compared with others, certain individuals carrying more *XPG* variations have the increased susceptibility to gastric cancer.[16]

Several studies have showed that *XPG* gene polymorphism is significantly associated with not only the risk of cancer but also the efficacy of chemotherapy in cancer patients. For example, platinum-based chemotherapeutics is the most common regimens for various cancers. To today, *XPG* gene polymorphism has been demonstrated to influence the efficacy of chemotherapy in many types of cancers, such as, nonsmall cell lung cancer,[31,32] osteosarcoma cancer,[33–35] and ovarian cancer.[36] Additionally, certain leukemia subline is resistant to F11782, a novel dual catalytic inhibitor of topoisomerases with DNA repair-inhibitory properties. Further research indicated that NER activity was decreased 3-fold in these cells companied with a decreased (67%) level of XPG.[37]

Thus far, several published studies have focused on the association between *XPG* gene polymorphisms (including rs873601, rs2094258, rs2296147, and rs751402) and gastric cancer susceptibility in Chinese populations.[16–26] However, the conclusions in these literatures were not consistent or even contradictory, which might be due to the relatively small sample size in a single study. To resolve this controversy, we performed the current meta-analysis.

Our results indicated that no association between rs2094258 and gastric cancer risk was observed. Although rs873601 and rs2296147 were associated with high gastric cancer risk in certain genetic models, these results should nonetheless be applied cautiously due to the instability. Additionally, our data showed that rs751402 was associated with increased susceptibility to gastric cancer in allelic and dominant models. The results of rs751402 in allelic and dominant models were robust. And no evidence indicated that obvious asymmetry for the 2 models existed. The false-positive report probability analysis and trial sequential analysis of the results of rs751402 suggested that the sample size was sufficient and most of these results are reliable. Therefore, no

Table 7

False-positive report probability values for significant results.

Genotype	Crude OR (95% CI)	Power*	*P*†	Prior probability				
				.25	.1	.01	.001	.0001
rs751402 C>T								
C vs T	1.16 (1.04–1.29)	1.000	.006	.018	.053	.379	.860	.984
CC+CT vs TT	1.23 (1.00–1.52)	.967	.055	.146	.340	.850	.983	.998
CC vs CT+TT	1.15 (1.05–1.27)	1.000	.006	.017	.049	.364	.852	.983
CC vs TT	1.35 (1.06–1.72)	.803	.015	.054	.145	.652	.950	.995
CC vs CT	1.13 (1.02–1.25)	1.000	.018	.050	.137	.636	.946	.994

CI = confidence interval, OR = odds ratio.

* Statistical power was calculated using the number of observations in the subgroup and the OR and *P* values in this table.

† Chi-square test was adopted to calculate the genotype frequency distributions.

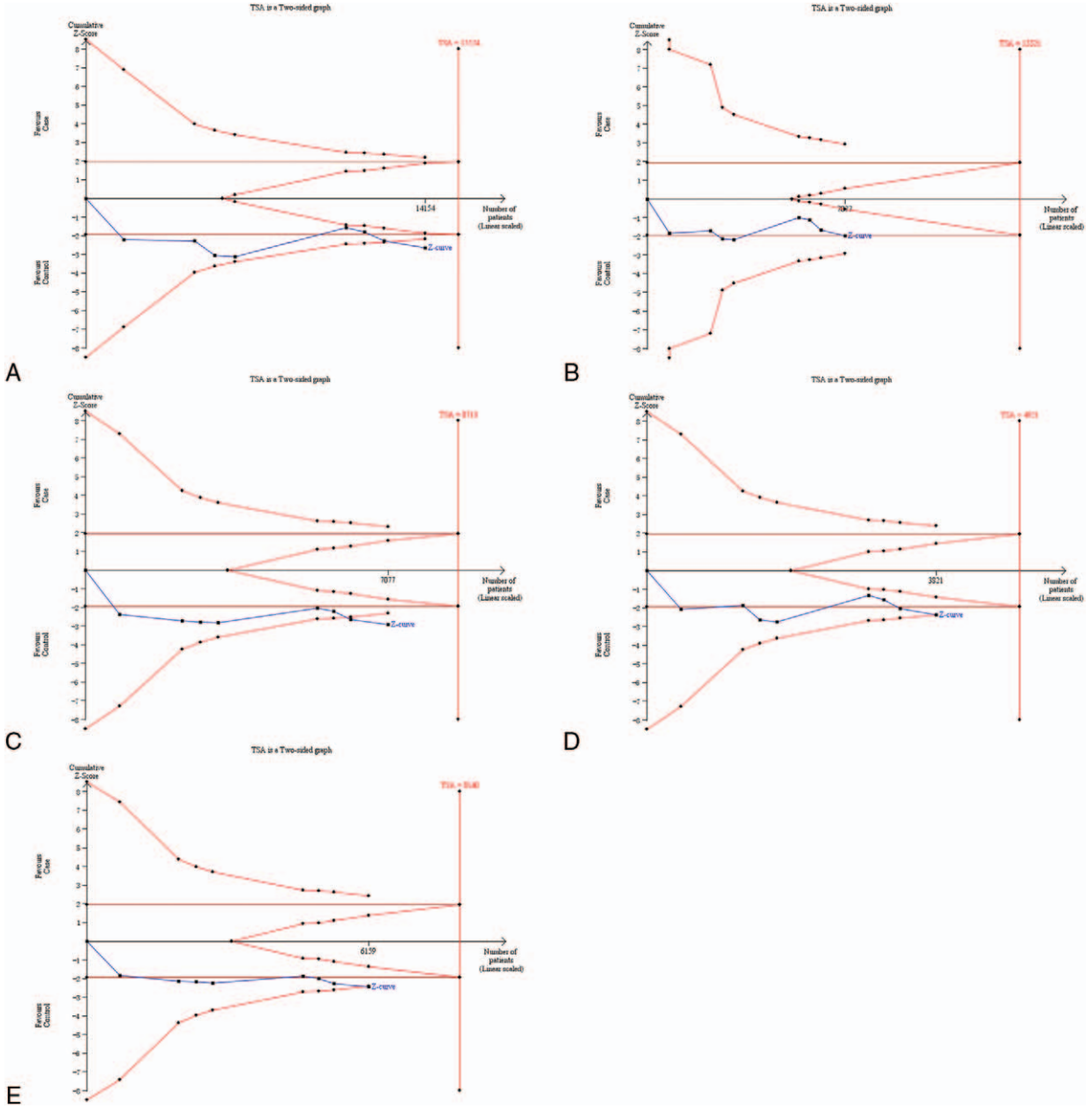

Figure 6. Trial sequential analysis of rs751402 polymorphism and the risk of gastric cancer in Chinese populations. (A) Allelic model (C vs T). (B) Recessive genetic model (CC + CT vs TT). (C) Dominant genetic model (CC vs CT + TT). (D) Addictive genetic model (CC vs TT). (E) Heterozygous comparison model (CC vs CT).

further analysis was required to confirm the results of rs751402 with the exception of the results in recessive genetic model.

The data in our study showed that the rs751402 C>T was associated with high risk of gastric cancer in Chinese populations. On the one hand, it suggests the clinicians that the individuals with T allele of rs751402 may have a high susceptibility to gastric cancer in Chinese populations. Therefore, the screening for gastric cancer in these individuals may be more important. And it is good for the early detection and treatment of gastric cancer. On the other hand, it suggests researchers that the cells with T allele of rs751402 may be more likely to lead to cancer. The underlying mechanism needs further research and the relevant study may provide a clue for gastric cancer prevention.

All of the studies included in this meta-analysis met our inclusion criteria. In spite of these, several limitations that exist in the current meta-analysis have to be acknowledged. First, some valuable information, involved in gastric carcinogenesis, from individual participants was missing in our study, such as occupation, physical activity, local environmental factor, and *Helicobacter pylori* infection. Second, our analysis was performed with only Chinese populations. Therefore, it is unknown whether the results will extend to other populations. Third, we carried out meta-regression considering only publication year without other factors. Last, certain obvious publication bias was detected.

Despite these limitations, the meta-analysis still provides new insights into the relationship of *XPG* gene and the occurrence of gastric cancer. A part of the research results from the previous studies included in the current meta-analysis were in accordance with our results. However, the numbers of studies and subjects

were relatively small in this meta-analysis, which might reduce the statistical power for identifying the potential association between these *XPG* gene polymorphisms and gastric cancer susceptibility. A larger study should be performed to confirm the present negative results.

In conclusion, our meta-analysis demonstrates that rs751402, but not rs873601, rs2094258, or rs2296147, was associated with gastric cancer risk. These results suggest that the SNP has the potential to be the biomarker for susceptibility to gastric cancer. However, large-scale studies among different ethnic groups with more detailed individual information are needed to validate our conclusion.

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