

**Supplementary Table S1.** Clinical and demographic characteristics of CRC patients and healthy control subjects

Characteristics	CRC patients	Healthy control subjects	P
Age (years, mean $\pm$ SD)	59.3 $\pm$ 6.7	59.9 $\pm$ 6.3	0.13
Gender, n (%)			
Male	421 (59.6)	431 (55.6)	0.12
Female	285 (40.4)	344 (44.4)	
Tumour stage, n (%)			
I + II	403 (57.1)		
III + IV	303 (42.9)		

**Note.** CRC, colorectal cancer.

**Supplementary Table S2.** Characteristics of the case-control studies included in the current meta-analysis

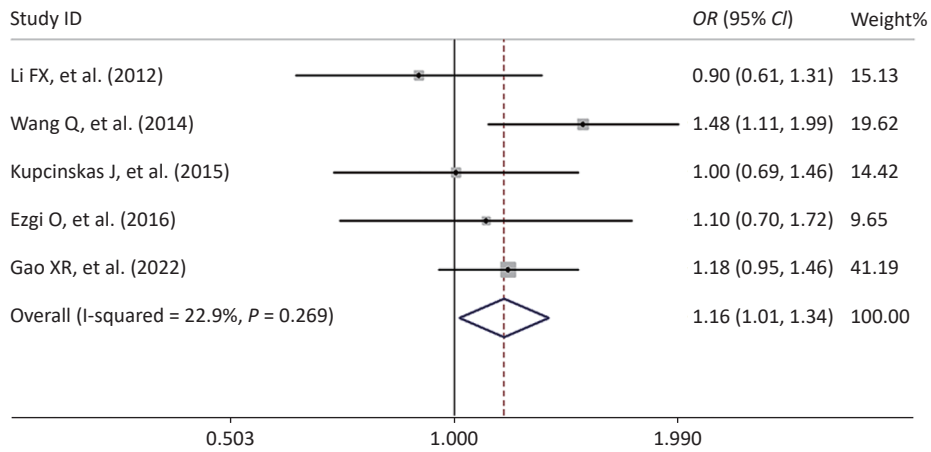
Author	Year of publication	Country	Cancer type	Genotyping method	Case group			Control group			$P_{HWE}$ value
					AA	AG	GG	AA	AG	GG	
Li FX, et al. <sup>[9]</sup>	2012	China	Colorectal cancer	MassARRAY	155	71	5	180	92	20	0.09
Wang Q, et al. <sup>[6]</sup>	2014	China	Colorectal cancer	TaqMan	228	161	28	269	128	19	0.45
Kupcinskis J, et al. <sup>[10]</sup>	2015	Lithuania,Latvia	Colorectal cancer	TaqMan	77	91	24	147	173	56	0.66
Ezgi O, et al. <sup>[8]</sup>	2016	Turkey	Colorectal cancer	PCR-RFLP	142	48	10	176	54	0	0.04
Gao XR, et al.	2022	China	Colorectal cancer	Sequencing	362	292	52	439	300	36	0.09

**Note.** PCR-RFLP: Polymerase Chain Reaction-Restriction Fragment Length Polymorphism.

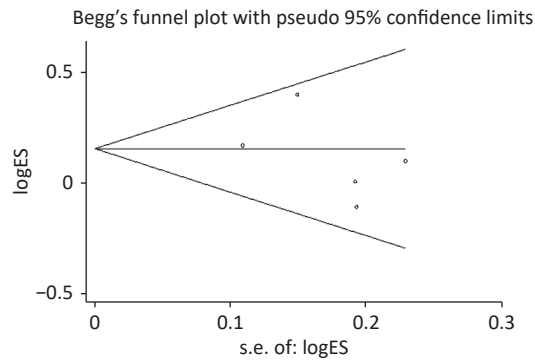
**Supplementary Table S3.** Publication bias analysis of the relationship between the rs2274223 genetic polymorphism and CRC risk

Comparison	P	
	Begg's test	Egger's test
GG vs. AA	1	0.75
AG vs. AA	0.46	0.45
(AG + GG) vs. AA	1	0.35
GG vs. (AA + AG)	1	0.88
G vs. A	0.81	0.76

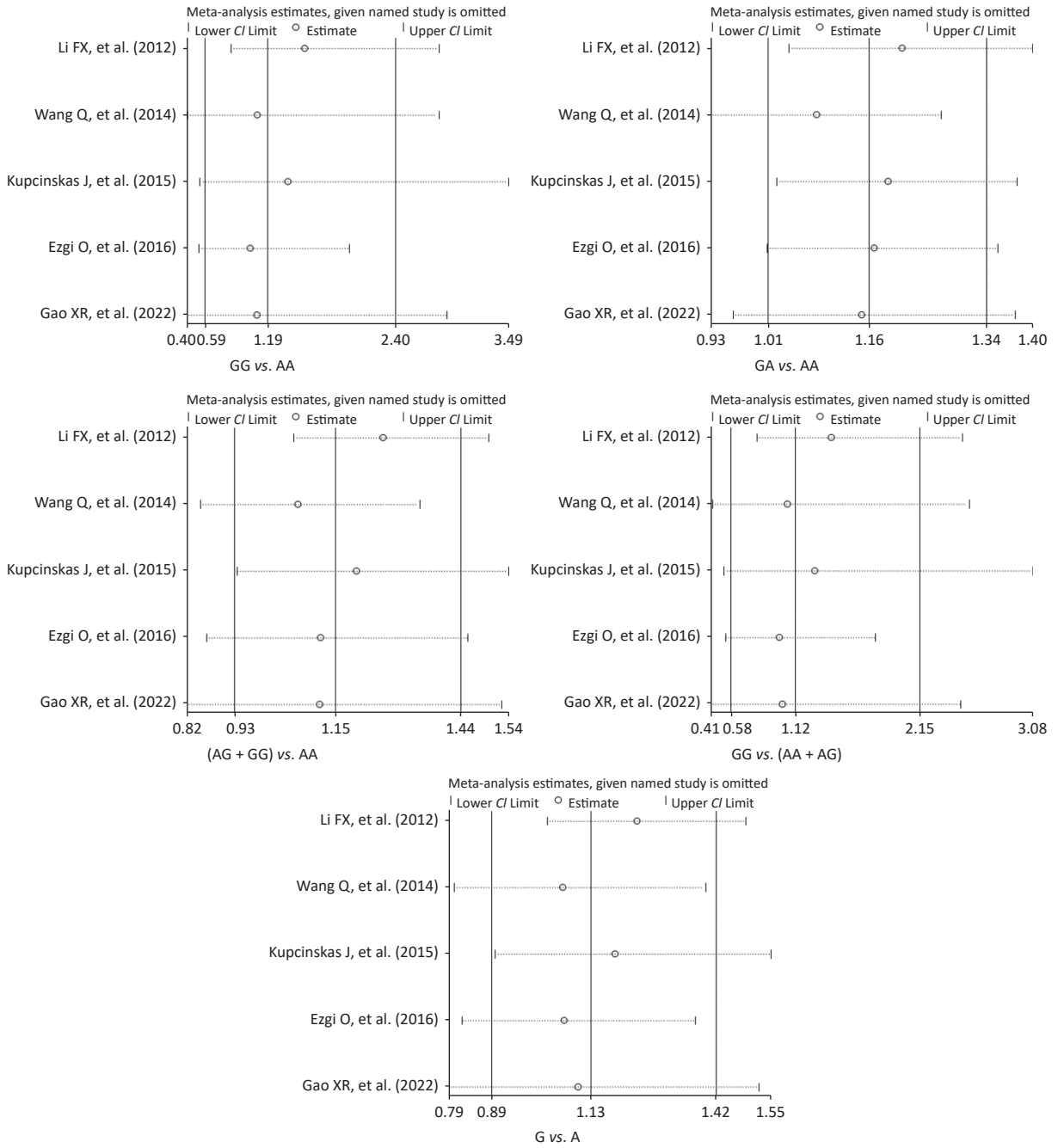
**Note.** CRC, colorectal cancer.



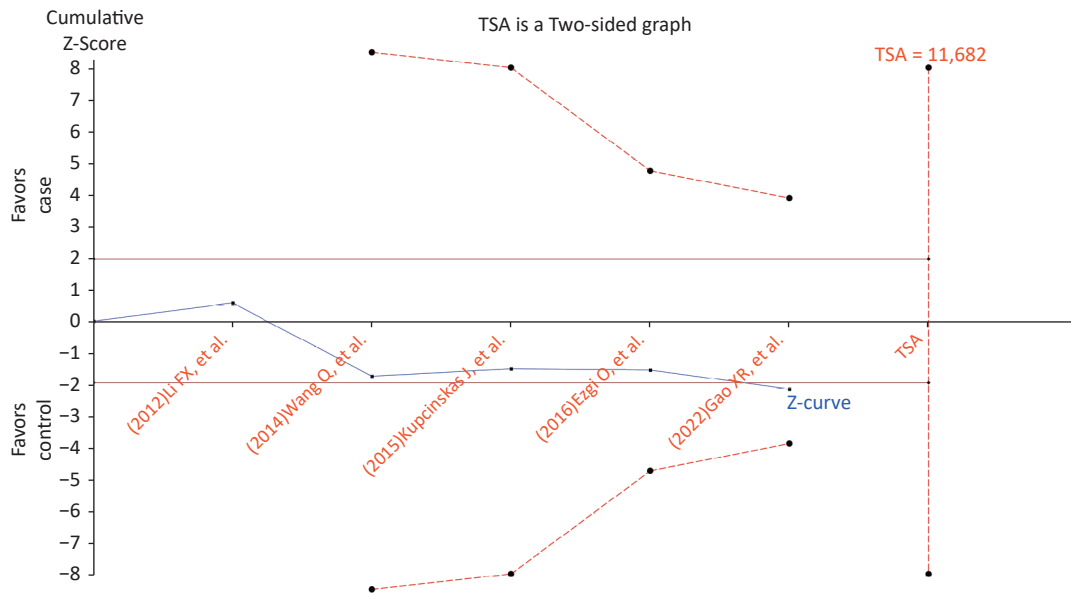
**Supplementary Figure S1.** Forest plot of the relationship between the rs2274223 genetic polymorphism and CRC risk under AG vs. AA.



**Supplementary Figure S2.** Begg's funnel plot of the relationship between the rs2274223 genetic polymorphism and CRC risk under AG vs. AA.



**Supplementary Figure S3.** Sensitivity analysis of the relationship between the rs2274223 genetic polymorphism and CRC risk. CRC, colorectal cancer.



**Supplementary Figure S4.** Trial sequential analysis for the relationship between the rs2274223 genetic polymorphism and CRC risk under AG vs. AA (The needed sample size is 11,682 samples, and the cumulative z-curve did not cross the trial sequential monitoring boundary before reaching the required sample size, indicating that our findings need to be confirmed further). CRC, colorectal cancer.