Int J Clin Exp Med 2026;19(4):87-100
www.ijcem.com /ISSN:1940-5901/IJCEM0170559

Review Article

miR-146 rs2910164 and miR-196a2 rs11614913 polymorphisms and risk of ovarian cancer: a system review and meta-analysis

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Received December 6, 2025; Accepted March 11, 2026; Epub April 15, 2026; Published April 30, 2026

Abstract: Objective: Published data on the association between the miR-196a2 rs11614913 and miR-146 rs2910164 polymorphisms and ovarian cancer are controversial. A meta-analysis was performed to assess whether the polymorphisms of miR-196a2 rs11614913 and miR-146 rs2910164 are associated with ovarian cancer risk. Methods: Medline, Embase, China National Knowledge Infrastructure, and Chinese Biomedicine Databases were searched to identify eligible studies. Pooled odds ratios (ORs) and 95% confidence intervals (CIs) for miR-196a2 rs11614913 and miR-146 rs2910164 polymorphisms and ovarian cancer were appropriately derived from fixed-effects or random effects models. Results: A total of 7 studies were enrolled in this meta-analysis. The pooled analyses revealed that miR-196a2 rs11614913 polymorphism increased the risk of ovarian cancer in all models except heterozygote comparison, allele contrast (T vs C): OR, 0.72; 95% CI, 0.63-0.83; homozygote (TT vs CC): OR, 0.51; 95% CI, 0.39-0.68; dominant model (TT + TC vs CC): OR, 0.73; 95% CI, 0.58-0.91; recessive model (TT vs TC + CC): OR, 0.58; 95% CI, 0.47-0.73. Conclusion: The present meta-analysis reveals that miR-196a2 rs11614913 variant may serve as genetic biomarkers of ovarian cancer.

Keywords: miR-146, miR-196a2, ovarian cancer, polymorphisms, meta-analysis

Introduction

Ovarian cancer is the leading cause of death in women with malignant tumors. About 140,000 people die of ovarian cancer every year worldwide [1]. Because the ovary is deep in the pelvic cavity, there are often no obvious symptoms and signs in the early stage of the disease. Approximately 2/3 of ovarian cancer patients are already in advanced cancer stage at initial diagnosis, and the 5-year survival rate for ovarian cancer is only 20%-36% [2, 3]. Therefore, identification of the susceptible population of ovarian cancer is significant for improving disease diagnosis rate, achieving early treatment, and improving prognosis. Epidemiological and biological studies have shown that ovarian cancer is a multi-stage complex disease caused by environmental and genetic factors [4]. Genetic factors play an important role in the occurrence and development of ovarian cancer [5].

MicroRNA (miRNA) is an endogenous non-coding single-stranded RNA with a length of about 22 nucleotides. It can participate in the regulation of gene expression by inducing degradation or inhibiting the translation of target mRNA [6]. The mechanism of miRNAs-mediated regulation of multiple biological functions is constantly being studied. It is currently believed that many miRNAs affect the growth, proliferation, invasion, metastasis, drug resistance and recurrence of different gynecological malignant tumors [7]. A number of studies have shown that the gene polymorphisms of miRNAs are related to the occurrence and development of various cancerous diseases such as lung cancer, breast cancer, bladder cancer, and gastric cancer [8-11]. Single Nucleotide Polymorphisms (SNP) may affect the expression and function of miRNAs, thereby regulating the occurrence and development of cancer. The miR-146

https://doi.org/10.62347/LNXY3168

(rs2910164) polymorphism is a change in nuclease G to C, which causes the C: U mismatch to occur in pre-miR-146. Xu et al. found that compared with pre-miR-146 carrying C, pre-miR-146 carrying G had a higher level of mature miR-146, and individuals carrying the miR-146 GG genotype had a higher risk of liver cancer than those carrying the CC genotype [12]. The miR-196a2 (rs11614913) polymorphism is a change in mononucleotide T to C, and this mutation may also affect the expression of miR-196a2 [13]. Duan et al. found that CC genotype of miR-196a2 had lower mature miR-196a2 content than TT genotype [14]. Feng et al. found that individuals carrying CC homozygous genotypes can increase the risk of cancer [15].

Members of the miR-146 and miR-196 gene families have been reported to play important roles in carcinogenesis by participating in key biological processes, including cell proliferation, apoptosis, invasion, metastasis, and immune regulation [16]. miR-146 functions as a critical regulator of inflammatory and immune signaling pathways, partly through interactions with targets such as IRAK1 and TRAF6, which are involved in tumor-related chronic inflammation and cancer progression [17, 18]. Dysregulated expression of miR-146 has been observed in several malignancies and has also been reported in ovarian cancer, suggesting its potential involvement in ovarian tumor initiation and progression [19]. Similarly, miR-196 family members are implicated in the regulation of genes related to cell differentiation, migration, and oncogenic transformation, including HOX gene clusters that are essential for developmental processes and tumorigenesis [20, 21]. Aberrant expression of miR-196 has been documented in multiple cancer types, and emerging evidence indicates that altered miR-196 expression may be associated with ovarian cancer development and disease aggressiveness [22]. Given the biological relevance of the miR-146/196 gene family in cancer-related pathways and their reported dysregulation in ovarian cancer, genetic polymorphisms affecting their expression or maturation may influence individual susceptibility to ovarian cancer.

Over the past two decades, a number of studies have investigated the association between miR-146 rs2910164 and miR-196a2 rs11614913 polymorphisms and susceptibility to ovarian cancer in different populations. However, the findings have remained inconclusive and sometimes contradictory, possibly due to limited sample sizes, ethnic differences in allele distribution, variations in study design, inconsistent genetic comparison models, and potential methodological biases such as deviation from Hardy-Weinberg equilibrium in certain studies [23-28]. Therefore, an updated and comprehensive meta-analysis is warranted. In the present study, we conducted a systematic meta-analysis by integrating the most recent evidence from both international and Chinese databases, performing ethnicity-stratified analyses, and applying multiple approaches to assess robustness and heterogeneity, including sensitivity analysis, Galbraith plot analysis, and Trial Sequential Analysis. This study aims to provide a more reliable and methodologically rigorous evaluation of the relationship between miR-146 and miR-196a2 polymorphisms and ovarian cancer risk, thereby clarifying the existing inconsistencies in the literature.

Materials and methods

Publication search

A comprehensive literature search was conducted in Embase, PubMed, CNKI (China National Knowledge Infrastructure), and the Chinese Biomedicine Database up to January 10, 2025. To ensure both sensitivity and specificity, we applied a two-level search strategy. The initial search used broad terms related to microRNAs and ovarian cancer ("microRNA" OR "miRNA" AND "ovarian cancer"), followed by a targeted search specifically focused on the polymorphisms of interest using keywords including "miR-146" OR "miR-146 rs2910164" and "miR-196a2" OR "miR-196a2 rs11614913" combined with "polymorphism" or "variant". In addition, the reference lists of relevant articles were manually screened to identify any additional eligible studies. This refined search strategy was designed to minimize the risk of missing relevant studies while ensuring that the final included articles were directly related to miR-146 rs2910164 and miR-196a2 rs11614913 polymorphisms and ovarian cancer susceptibility.

Inclusion and exclusion criteria

To be included in the analysis, studies had to meet specific criteria: (i) they needed to investi-

gate the relationship between the miR-146 or miR-196a2 polymorphism and ovarian cancer risk using case-control designs, regardless of sample size; (ii) they had to provide sufficient data for calculating odds ratios (OR) with a 95% confidence interval (CI). Studies that were conference abstracts, conference reports, reviews, meta-analyses, or lacked adequate data were excluded.

The study was designed according to the Population, Comparison, and Outcome (PICO) framework, in which the population consisted of patients with ovarian cancer and cancer-free controls, the comparison involved different genotypes of miR-146 rs2910164 and miR-196a2 rs11614913 polymorphisms, and the outcome of interest was ovarian cancer risk; this systematic review and meta-analysis was prospectively registered in the International Prospective Register of Systematic Reviews (PROSPERO; registration number: CRD42024-484825).

Data extraction

Data extraction was conducted independently by two reviewers (K. Yi and A. Wang), who adhered to predetermined inclusion criteria. Any disagreements were resolved through consultation with an arbitrator (L. Chen). The extracted information included details such as the author's surname, publication year, participant country, sample size, ethnicity, genotyping methods, minor allele frequency (MAF) and Hardy-Weinberg equilibrium (HWE).

Study quality was assessed independently by two reviewers using the Newcastle-Ottawa Scale (NOS) for case-control studies. The NOS evaluates methodological quality across three domains: selection (0-4 stars), comparability (0-2 stars), and exposure (0-3 stars), with a maximum score of 9 stars.

Specifically, the selection domain assessed the adequacy of case definition, representativeness of cases, selection of controls, and definition of controls. The comparability domain evaluated whether cases and controls were matched or adjusted for important confounding factors, such as age or ethnicity. The exposure domain assessed the ascertainment of exposure (genotyping method), consistency of genotyping procedures between cases and controls, and the non-response rate. Discrepancies in quality assessment were resolved by discussion or consultation with a third reviewer. Studies with a NOS score of ≥6 were considered to be of high methodological quality.

Statistical analysis

Statistical analyses were performed using STATA software (version 13.0; StataCorp, College Station, TX, USA). Pooled odds ratios (ORs) with corresponding 95% confidence intervals (CIs) were calculated to assess the association between miR-146 rs2910164 and miR-196a2 rs11614913 polymorphisms and ovarian cancer risk under different genetic models, including allele contrast, homozygote, heterozygote, dominant, and recessive models. Between-study heterogeneity was evaluated using Cochran's Q test and the I^2 statistic. A fixed-effects model (Mantel-Haenszel method) was applied when heterogeneity was not significant ($P > 0.05$ and $I^2 < 50\%$) [29, 30]; otherwise, a random-effects model (DerSimonian and Laird method) was used [31]. Subgroup analyses were conducted according to ethnicity. Sensitivity analyses were performed by sequentially omitting individual studies to assess the stability of the pooled results. Publication bias was assessed using Begg's funnel plot and Egger's regression test, with $P < 0.05$ indicating potential publication bias. All statistical tests were two-sided [32, 33].

Trial sequential analysis

Trial Sequential Analysis (TSA) was conducted to evaluate the required information size (RIS) and the reliability of the results. The RIS was calculated based on a 5% risk of type I error ($\alpha = 5\%$), 80% power of the study ($\beta = 20\%$), and a two-sided boundary type was applied. TSA software from the Copenhagen Trial Unit was utilized for this analysis.

Characteristics of studies

After conducting a comprehensive literature search, 55 articles were initially identified for examination. Following a review of titles and abstracts, 42 articles were excluded. Full texts of 13 articles were obtained and carefully reviewed, resulting in the exclusion of 1 article due to review study [34], and 2 articles not

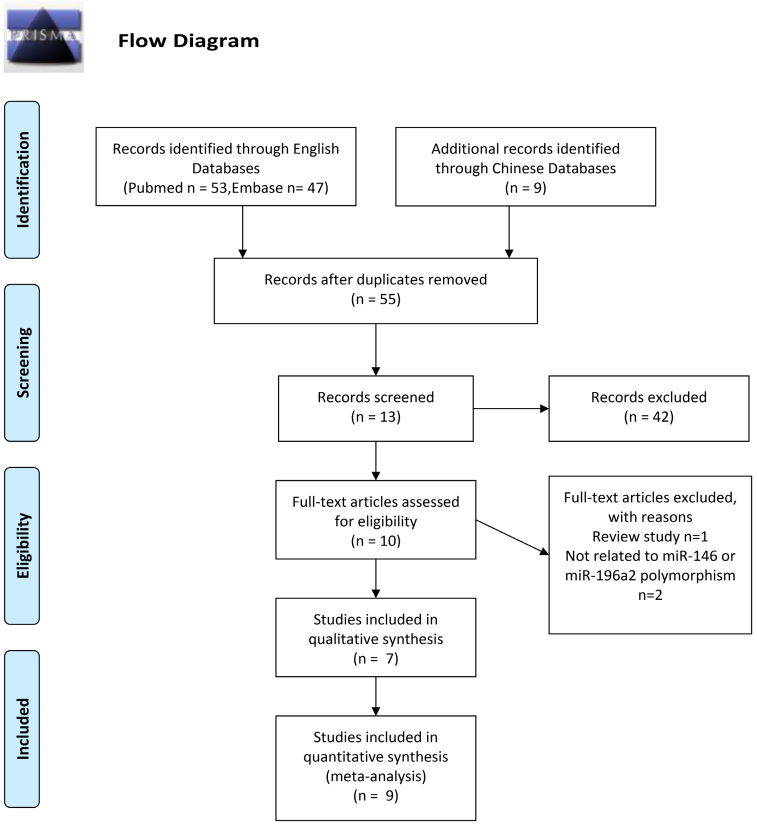

Figure 1. Literature search and study selection procedures used for a meta-analysis of miR-146 and miR-196a2 polymorphisms and ovarian cancer risk.

related to the miR-146 or miR-196a2 polymorphism [35, 36].

Ultimately, seven case-control studies examining miR-146 and miR-196a2 polymorphisms and ovarian cancer risk were included, in accordance with MOOSE guidelines [23-28, 37]. The process of literature search and study selection is illustrated in **Figure 1**.

The features of the included studies are summarized in **Table 1**. Among the included studies, 2 involved subjects of Caucasian descent, and 3 involved subjects of Asian descent.

Quantitative synthesis

Connection between the miR-196a2 rs1161-4913 polymorphism and ovarian cancer susceptibility.

Pooled odds ratios (ORs) and 95% confidence intervals (CIs) for miR-196a2 polymorphism and ovarian cancer were derived from fixed effects models. The meta-analysis revealed a significant increase in the risk of ovarian cancer associated with the miR-196a2 rs1161-4913 polymorphism across all models except heterozygote comparison (**Table 2**). **Figure 2** shows the forest plots illustrating the association between miR-196a2 rs11614913 polymorphism and ovarian cancer risk.

Connections between miR-146 rs2910164 polymorphism and ovarian cancer susceptibility.

Pooled odds ratios (ORs) and 95% confidence intervals (CIs) for miR-146 rs2910164 polymorphism and ovarian cancer were derived from random effects models. The meta-analysis revealed a lack of significant correlation between miR-146 rs2910164 polymorphism and ovarian cancer across all models (**Table 3**). Figure S1 shows the forest plots illustrating the association between miR-146 rs2910164 polymorphism and ovarian cancer risk.

The Newcastle-Ottawa Scale (NOS) scores, reflecting the quality of the included studies, are summarized in **Table 4**.

Heterogeneity analysis

No substantial heterogeneity was detected in meta-analysis of miR-196a2 rs11614913 polymorphism. For miR-146 rs2910164 polymorphism, a substantial heterogeneity was detected among studies in all models. Galbraith plot analyses were conducted to investigate potential sources of heterogeneity across the studies. It was observed that one study [37] contributed to the heterogeneity for miR-146 rs2910164 polymorphism, as shown in **Figure 3**. Upon removal of the outlier study, a significant decrease in heterogeneity was noted.

Sensitivity analysis and cumulative analysis

For miR-196a2 rs11614913 polymorphism, the sensitivity analyses (**Figure 4**) and cumulative meta-analysis (**Figure 5**) demonstrated that the results are stable. Figure S2 shows

Table 1. Characteristics of studies included in this meta-analysis

Author	Year	Country	Ethnicity	SNPs studied	Sample Case/control	Genotyping Methods	MAF in Controls	HWE
Pastrello	2010	Italy	Caucasian	miR-146	101/155	PCR-DS	0.22	0.33
Yue	2011	China	Asian	miR-146	131/227	PCR-RFLP	0.45	0.45
Liu	2015	China	Asian	miR-146, miR-196a2	141/100	PCR-RFLP	0.39, 0.47	0.13, 0.86
Song	2016	China	Asian	miR-196a2	479/431	PCR-RFLP	0.43	0.38
Sun	2016	China	Asian	miR-146, miR-196a2	134/227	PCR-RFLP	0.31, 0.40	0.37, 0.36
Lukács	2019	Hungary	Caucasian	miR-146, miR-196a2	75/75	PCR-RFLP	0.27, 0.40	0.81, 0.44
Hussein	2022	Ejypt	Caucasian	miR-196	50/50	PCR-RFLP	0.34	<0.01

Abbreviations: PCR-DS, polymerase chain reaction-direct sequencing; PCR-RFLP, polymerase chain reaction-restriction fragment length polymorphism; MAF, minor allele frequency. HWE, Hardy-Weinberg equilibrium.

the sensitivity analyses for miR-146 rs2910164 polymorphism.

Publication bias

We applied Begg's & Egger's tests to check the literature for publishing bias. For miR-196a2 rs11614913 polymorphism, the Begg's funnel-plot curves did not reveal any asymmetric trends (**Figure 6**). Besides, the statistical outcomes showed no bias in publication. Results of Begg's and Egger's test: allele contrast 0.18 and 0.43, homozygote 0.35 and 0.44, heterozygote 0.18 and 0.65, dominant model 1.00 and 0.66, recessive model 0.35 and 0.37.

For miR-146 rs2910164 polymorphism, Egger's test showed publication bias in the recessive model. Results of Begg's and Egger's test: allele contrast 0.80 and 0.36, homozygote 0.81 and 0.57, heterozygote 1.00 and 0.66, dominant model 0.80 and 0.73, recessive model 0.08 and 0.02 (Figure S3).

Trial sequential analysis

TSA was used to further investigate the relationship between miR-196a2 rs11614913 polymorphism and ovarian cancer risk. The results indicated that the cumulative Z value (Z-curve) did not cross the TSA boundary, suggesting that the cumulative amount of information did not reach the required information size (**Figure 7**). This indicates that the traditional meta-analysis may provide a false positive conclusion, and further trials are needed to confirm the association.

Discussion

This meta-analysis examined the association between miR-146 rs2910164 and miR-196a2 rs11614913 polymorphisms and the risk of ovarian cancer based on seven case-control studies. To our knowledge, it is the first meta-analysis to investigate this association. The overall results demonstrated a significant increased risk of ovarian cancer associated with the miR-196a2 rs11614913 polymorphism in all models except heterozygote comparison. Subgroup analysis based on ethnicity revealed a significant increased risk among Asian populations in all models except heterozygote comparison. However, among Caucasian populations, a significant increased risk was found only in the allele contrast, homozygote comparison and recessive model. The reason for this discrepancy is not clear. One possible explanation is that the genotype distribution of miR-196a2 rs11614913 T differs between Caucasian and Asian populations. The study found that the distribution of miR-196a2 rs11614913 T alleles in the 3'untranslated region was 38.0% (95/250) among Caucasian patients, while among Asian patients, it was 48.8% (672/1,376). This difference in genotype distribution may contribute to the varying associations between miR-196a2 rs11614913 polymorphism and ovarian cancer risk in different ethnic groups. Another explanation could be the limited sample size of Caucasian patients included in the meta-analysis. The small number of Caucasian patients may have resulted in insufficient statistical power to investigate the true associations.

For miR-146 rs2910164 polymorphism, this meta-analysis reveals no significant associations between miR-146 polymorphism and ovarian cancer in all models.

From our perspective, the observed association between the miR-196a2 rs11614913 poly-

Table 2. Quantitative analyses of the miR-196a2 rs11614913 polymorphism on the ovarian cancer risk

Variables	Genetic model		Allele contrast		Homozygote		Heterozygote		Dominant Model		Recessive Model	
	Sample size		T vs. C		TT vs. CC		TC vs. CC		TT + TC vs. CC		TT vs. TC + CC	
	N[a]	Case/control	OR (95% CI)	P_{value}[b]	OR (95% CI)	P_{value}[b]	OR (95% CI)	P_{value}[b]	OR (95% CI)	P_{value}[b]	OR (95% CI)	P_{value}[b]
Total	5	879/883	0.72 (0.63, 0.83)	0.503	0.51 (0.39, 0.68)	0.682	0.87 (0.68, 1.11)	0.637	0.73 (0.58, 0.91)	0.925	0.58 (0.47, 0.73)	0.087
Caucasian	2	125/125	0.58 (0.41, 0.84)	0.206	0.39 (0.19, 0.81)	0.401	0.90 (0.50, 1.60)	0.374	0.67 (0.39, 1.14)	0.921	0.37 (0.20, 0.69)	0.144
Asia	3	754/758	0.75 (0.64, 0.87)	0.910	0.54 (0.40, 0.73)	0.630	0.86 (0.66, 1.13)	0.420	0.74 (0.58, 0.95)	0.681	0.62 (0.49, 0.79)	0.168

[a]Number of comparisons. [b]*P* value of Q-test for heterogeneity test. Random-effects model was used when *P* value for heterogeneity test <0.05; otherwise, fixed-effects model was used.

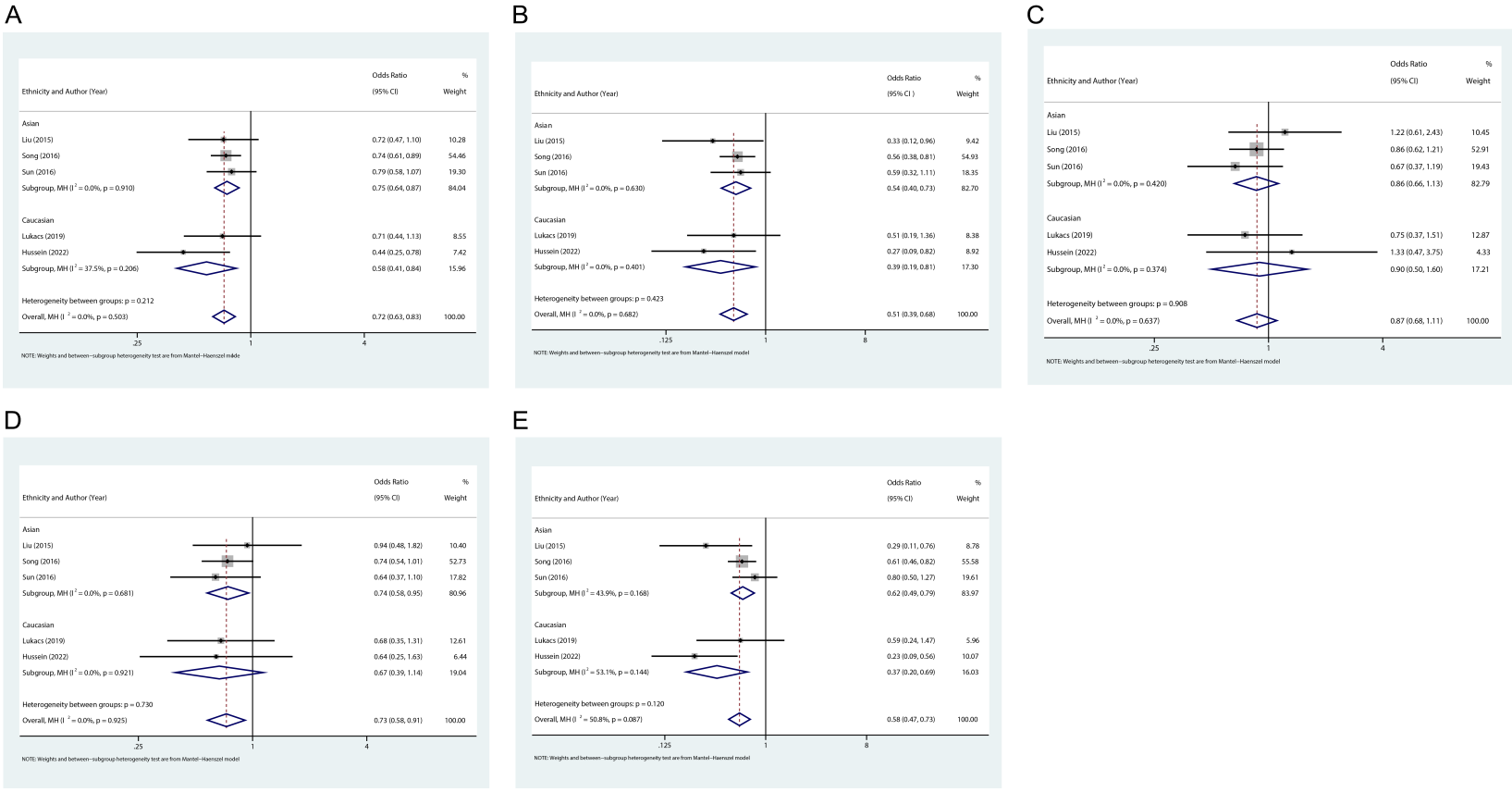

Figure 2. Forest plots of ORs with 95% CIs for miR-196a2 rs11614913 polymorphism and ovarian cancer risk. A-E. These images show allelic, homozygous, heterozygous, dominant model and recessive models, respectively.

Table 3. Quantitative analyses of miR-146 rs2910164 polymorphism on ovarian cancer risk

Variables	Genetic model		Allele contrast		Homozygote		Heterozygote		Dominant Model		Recessive Model	
	Sample size		G vs. C		GG vs. CC		GC vs. CC		GG + GC vs. CC		GG vs. GC + CC	
	N[a]	Case/control	OR (95% CI)	P_{value}[b]	OR (95% CI)	P_{value}[b]	OR (95% CI)	P_{value}[b]	OR (95% CI)	P_{value}[b]	OR (95% CI)	P_{value}[b]
Total	5	582/784	1.13 (0.71, 1.82)	0.000	1.27 (0.42, 3.90)	0.000	0.75 (0.43, 1.32)	0.047	0.91 (0.47, 1.77)	0.005	1.35 (0.67, 2.72)	0.000
Caucasian	2	176/230	1.27 (0.76, 2.14)	0.133	2.02 (0.24, 17.2)	0.080	1.57 (0.24, 10.2)	0.128	1.84 (0.24, 14.2)	0.092	1.26 (0.82, 1.92)	0.294
Asia	3	406/554	1.05 (0.51, 2.13)	0.000	1.04 (0.24, 3.90)	0.000	0.66 (0.36, 1.22)	0.038	0.78 (0.36, 1.67)	0.003	1.40 (0.41, 4.84)	0.000

[a]Number of comparisons. [b]*P* value of Q-test for heterogeneity test. Random-effects model was used when *P* value for heterogeneity test <0.05; otherwise, fixed-effects model was used.

Table 4. Quality assessment of case-control studies included in this meta-analysis[a]

Study	Adequate definition of cases	Representativeness of cases	Selection of control	Definition of control	Control for important factor or additional factor[b]	Exposure assessment	Same method of ascertainment for cases and controls	Nonresponse rate[c]	Total quality scores[d]
Pastrello	★	★	★	★	★	-	★	★	7
Yue	★	★	★	★	★	-	★	★	7
Liu	★	★	★	★	★	-	★	★	7
Song	★	★	★	★	★	-	★	★	7
Sun	★	★	★	★	★★	-	★	★	8
Lukács	★	★	★	★	★	-	★	★	7
Hussein	★	★	–	★	★	-	★	★	6

[a]A study can be awarded a maximum of one star for each numbered item except for the item Control for most important factor or second important factor. [b]A maximum of two stars can be awarded for Control for most important factor or second important factor. Studies that controlled for maternal age received one star, whereas studies that controlled for high risk factors (tobacco smoking or body mass index or family history of cancer) received one additional star. [c]One star was awarded if there was no significant difference in the response rate between control subjects and cases in the chi-square test (P > 0.05). [d]The studies are considered to be low-quality, when the scores were lower than six stars in quality assessment.

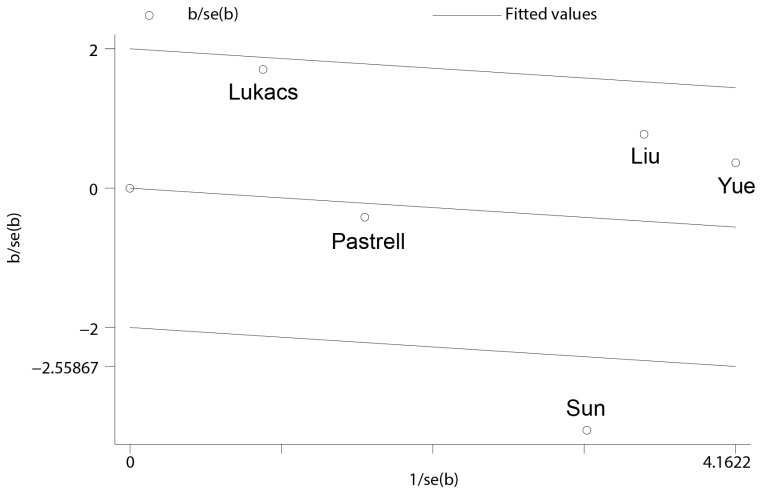

Figure 3. Galbraith plots for heterogeneity test of miR-146 rs2910164 polymorphism.

morphism and ovarian cancer susceptibility should be interpreted with caution. Although statistically significant associations were identified across multiple genetic models, the Trial Sequential Analysis indicated that the cumulative evidence has not yet reached the required information size, suggesting that the current findings may be influenced by random error. Therefore, we consider the present results to provide suggestive rather than definitive evidence for an association. We believe that the inconsistencies among previous studies and across ethnic subgroups may be partly explained by differences in allele frequency distributions, limited sample sizes, and heterogeneity in study design. In particular, the relatively small number of studies involving Caucasian populations may have restricted statistical power, whereas the more consistent findings observed in Asian populations may reflect both larger sample sizes and distinct genetic backgrounds.

With regard to miR-146 rs2910164, our findings support the viewpoint that this polymorphism is unlikely to play a major role in ovarian cancer susceptibility. No significant associations were observed across any genetic model, even after heterogeneity exploration and sensitivity analyses. From an interpretative standpoint, we suggest that miR-196a2 rs11614913 may represent a potential genetic marker for ovarian cancer risk, whereas the contribution of miR-146 rs2910164 appears to be limited. Nevertheless, given the methodological limitations and the incomplete cumulative evidence, future large-scale, well-designed studies with standardized methodologies are warranted to validate and refine these conclusions.

Heterogeneity among the included studies is a critical issue in meta-analyses, as it can impact the dependability of the findings. In this study, heterogeneity was detected among the studies in miR-146 rs2910164 polymorphism, and a Galbraith plot analysis identified one studies as major source of heterogeneity. After excluding this outlier study, a significant decrease in heterogeneity was observed, and the null results remained.

Publication bias, which arises from the selective publication of studies, is another concern in meta-analyses. To address this issue, Begg's and Egger's tests were performed, and funnel plots were examined. Based on the outcomes of these examinations and the graphical representations of the data, it can be inferred that there is no indication of any publication bias in miR-196a2 rs11614913 polymorphism. For miR-146 rs2910164 polymorphism, Egger's test found a publication bias in the recessive model.

Despite the significant findings, there are some limitations to this study. First, the limited number of samples and the inclusion of a small number of studies may have limited the statistical power to examine the associations comprehensively. Second, the analysis was based on unadjusted odds ratios (ORs) as not all studies provided adjusted ORs. Additionally, when adjusted ORs were available, they were adjusted for different factors, such as race, age, or body mass index (BMI), which could introduce confounding effects. Lastly, there was significant heterogeneity among the included studies, and one study was not in Hardy-Weinberg equilibrium (HWE).

Conclusion

In conclusion, this meta-analysis provides evidence that the miR-196a2 rs11614913 variant

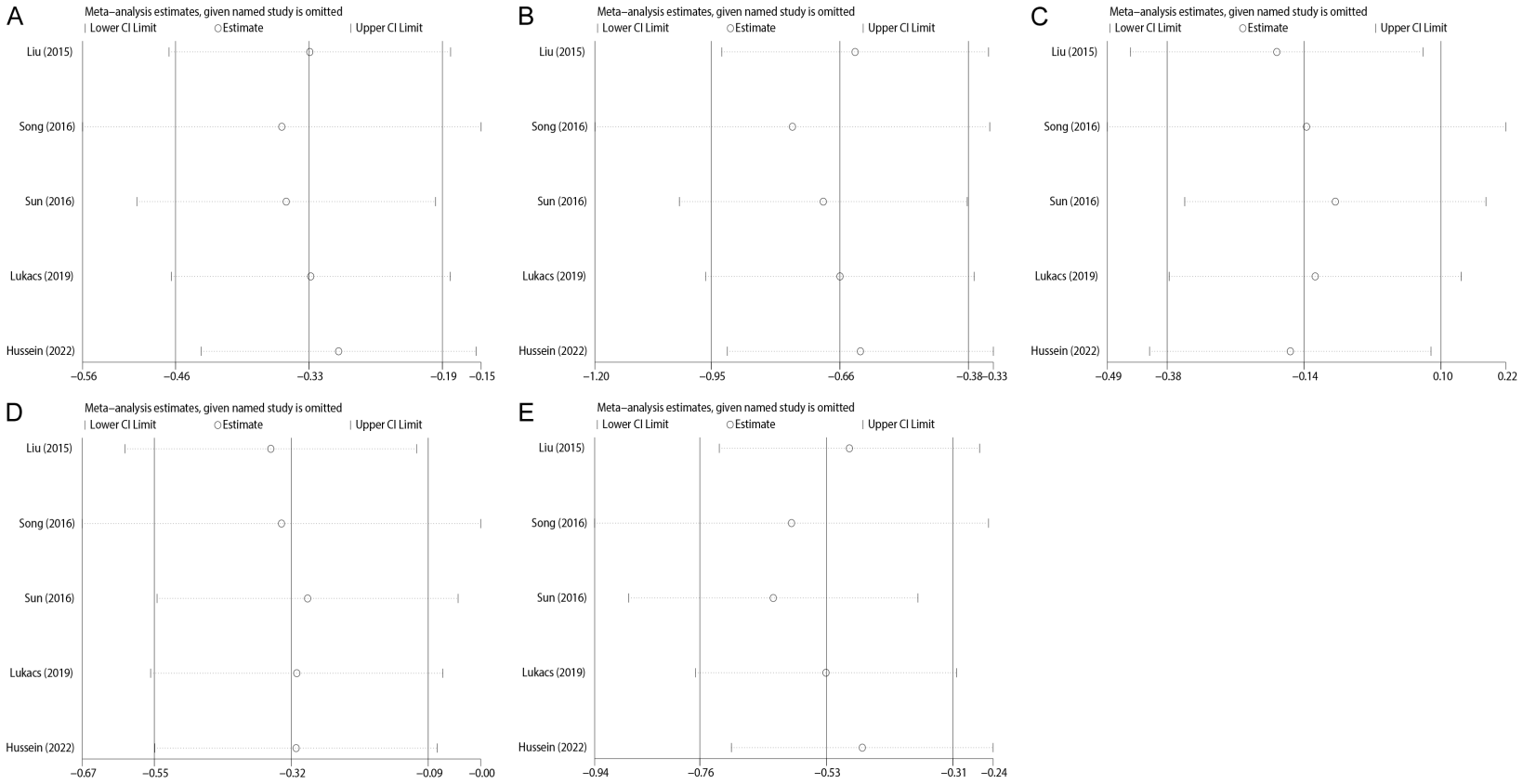

Figure 4. Sensitivity analysis of associations between miR-196a2 rs11614913 polymorphism and ovarian cancer risk. A-E. These images show allelic, homozygous, heterozygous, dominant model and recessive models, respectively.

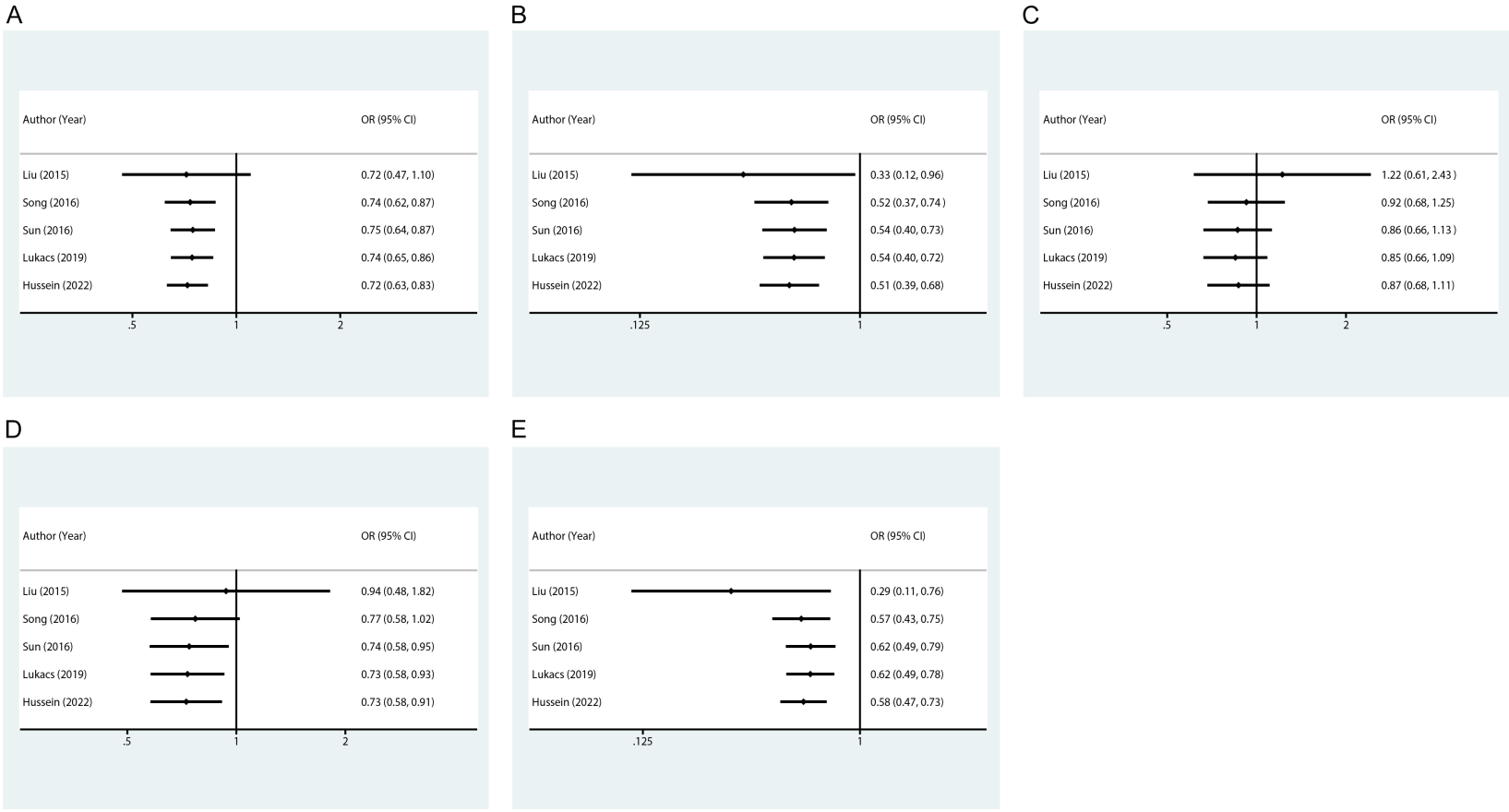

Figure 5. Cumulative meta-analysis of associations between miR-196a2 rs11614913 polymorphism and ovarian cancer risk. A-E. These images show allelic, homozygous, heterozygous, dominant model and recessive models, respectively.

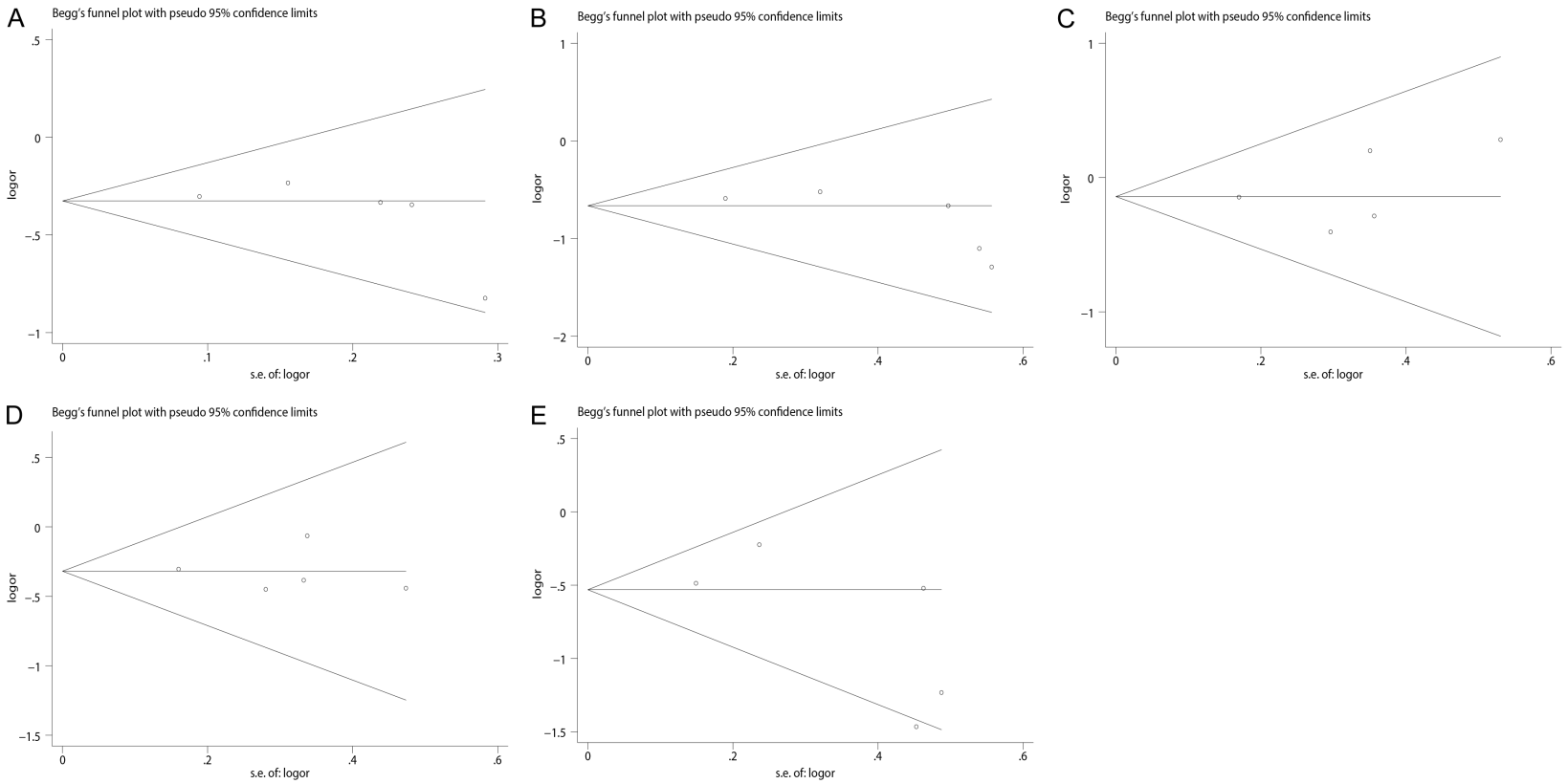

Figure 6. Begg's funnel plot for miR-196a2 rs11614913 polymorphism and ovarian cancer risk. A-E. These images show allelic, homozygous, heterozygous, dominant model and recessive models, respectively.

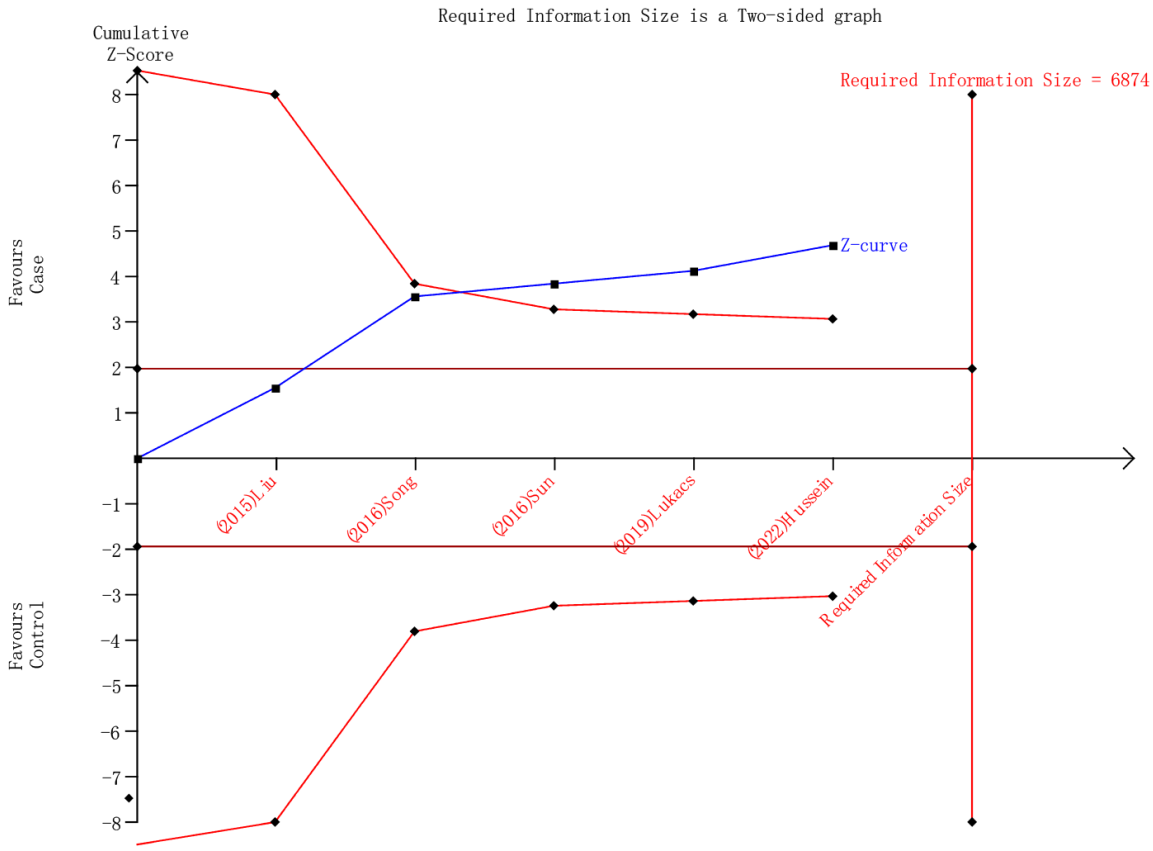

Figure 7. Trial sequential analyses for miR-196a2 rs11614913 polymorphism and ovarian cancer risk.

may serve as a genetic biomarker for ovarian cancer. However, further research is necessary to validate these findings and establish a more comprehensive understanding of the relationship between this polymorphism and ovarian cancer.

Disclosure of conflict of interest

None.

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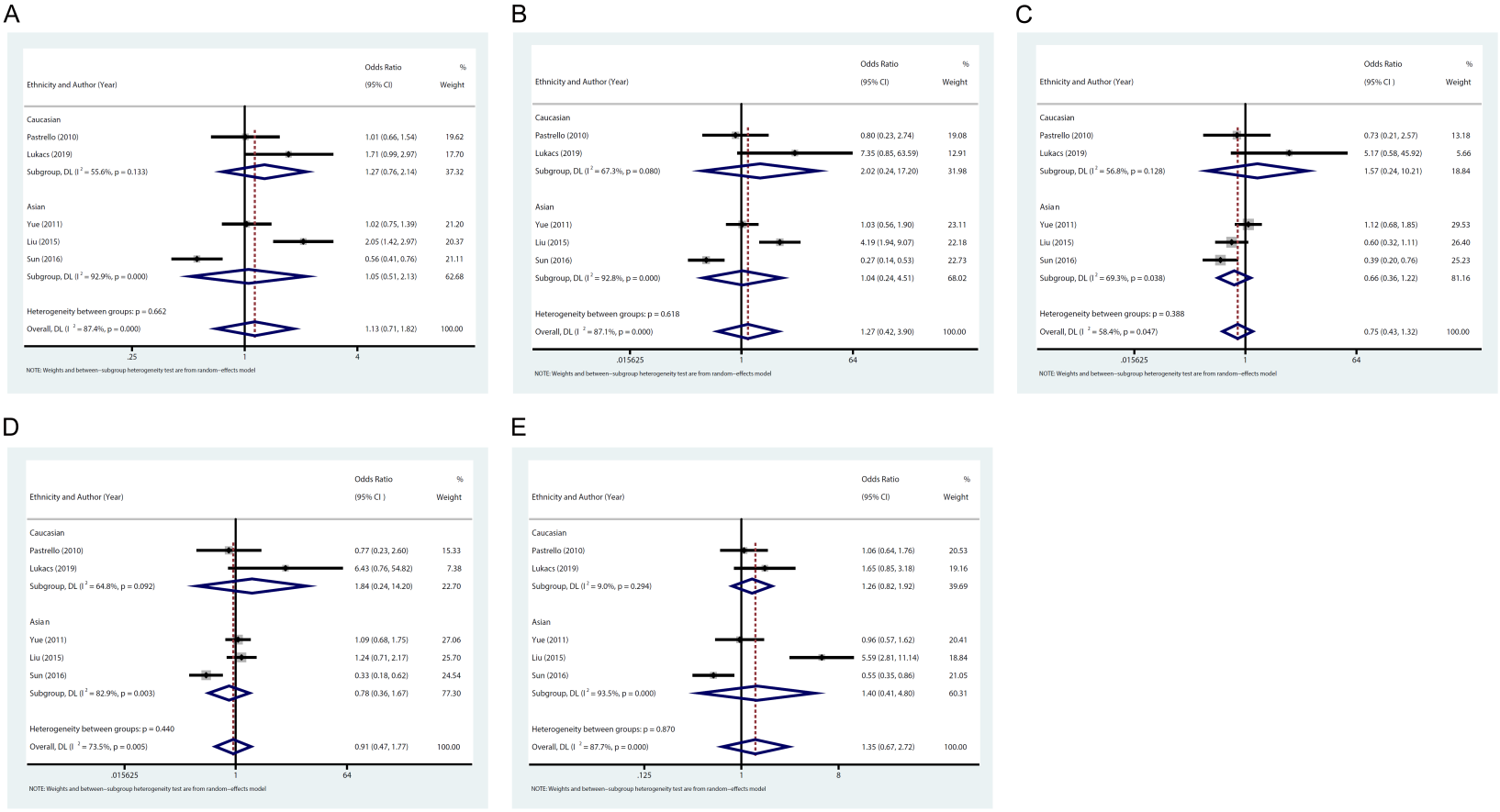

Figure S1. Forest plots of ORs with 95% CIs for miR-146 rs2910164 polymorphism and ovarian cancer risk. A-E. These images show allelic, homozygous, heterozygous, dominant model and recessive models, respectively.

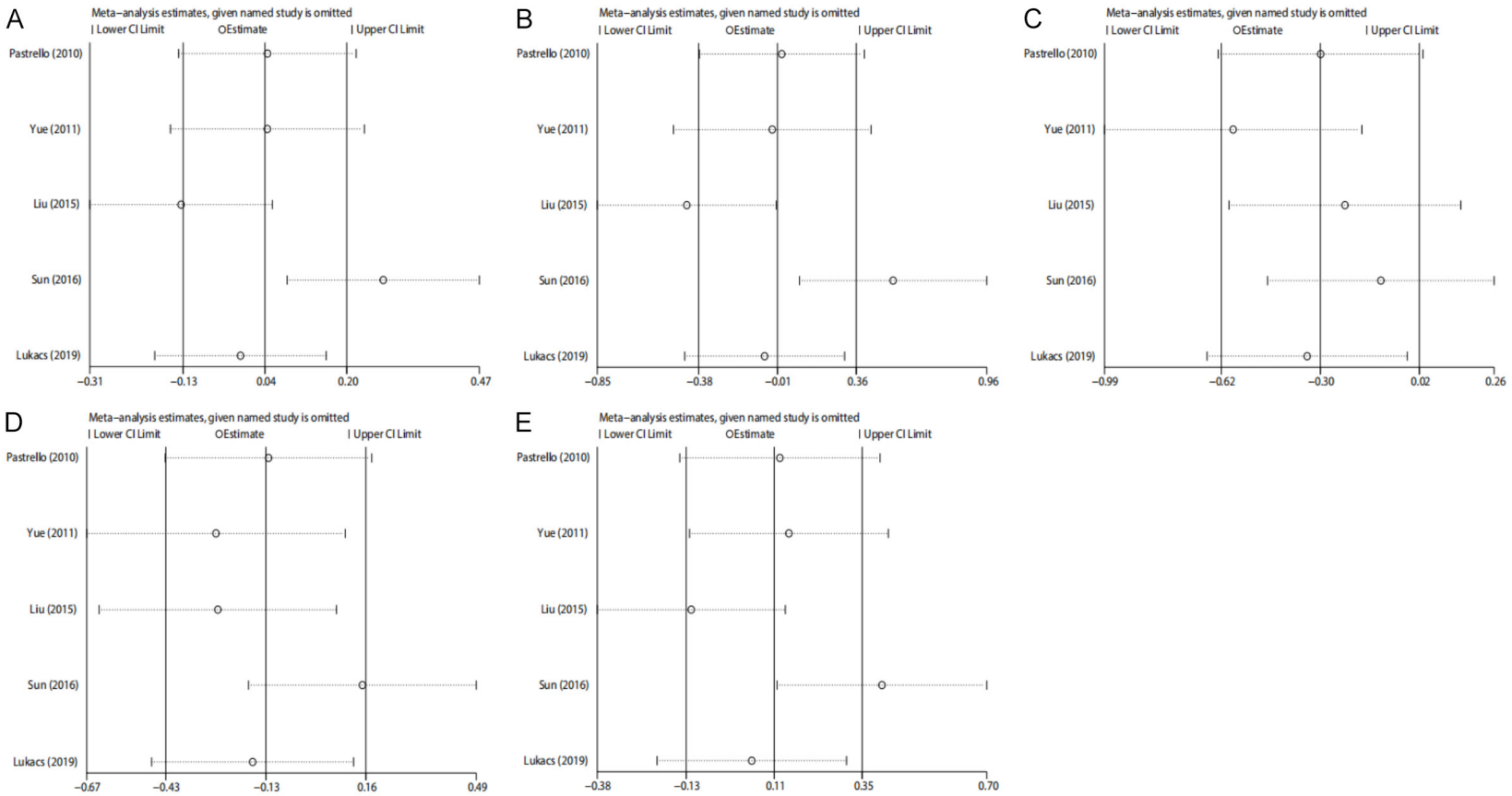

Figure S2. Sensitivity analysis of associations between miR-146 rs2910164 polymorphism and ovarian cancer risk. A-E. These images show allelic, homozygous, heterozygous, dominant model and recessive models, respectively.

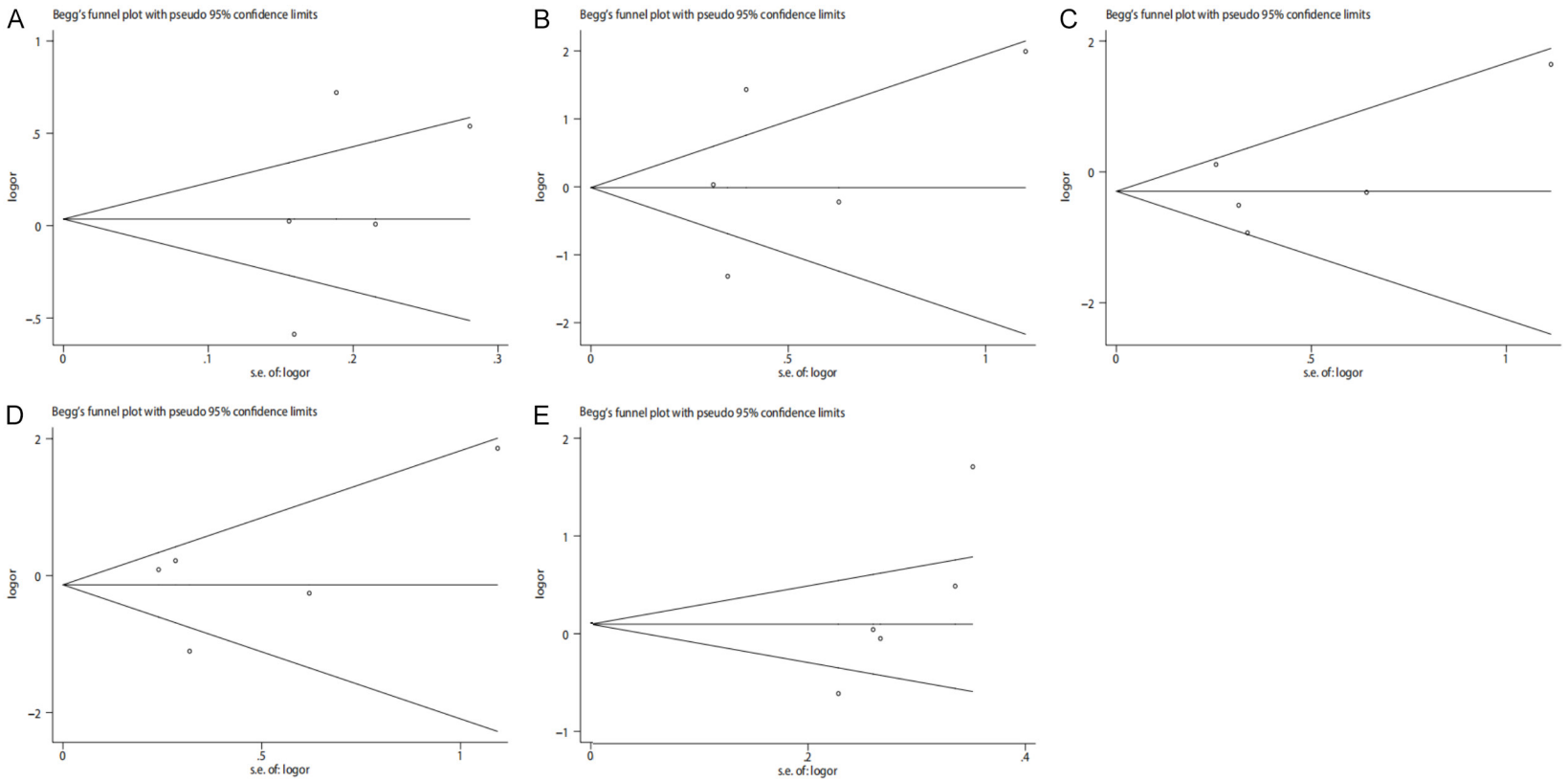

Figure S3. Begg's funnel plot for miR-146 rs2910164 polymorphism and ovarian cancer risk. A-E. These images show allelic, homozygous, heterozygous, dominant model and recessive models, respectively.