

Review Article

Exposure to air pollution and risk of prevalence of childhood allergic rhinitis: A meta-analysis

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ABSTRACT

Objectives: Allergic rhinitis (AR), a common chronic inflammatory disease in the upper airways. The prevalence of AR in children seems to be increasing recently, and the most significant causes of the increase are thought to be changes in environmental factors, especially air pollution. However, we could not find any meta-analysis on the risk of air pollution exposure on the prevalence of AR in childhood. The aim of this research was to carry out a meta-analysis on the results of recent studies (21 st century) to present valid information about exposure to air pollution and risk of prevalence of childhood AR.

Methods: PubMed, Science, Google Scholar, Elsevier and MDPI web database were searched up to January 1, 2000 to February 28, 2018. Including of air pollution and AR in childhood related to the observation of literature. Meta-analysis, study quality assessment, heterogeneity analysis and publication bias test were using Stata-MP 14.1 and Review Manager version 5.3 software.

Results: 13 studies will be included in the meta-analysis (8 cross-sectional studies, 5 cohort studies). Exposure to NO₂ (OR_{Europe} = 1.031, 95%CI [1.002,1.060], P = 0.033; OR_{Asia} = 1.236, 95%CI [1.099,1.390], P = 0.000; OR_{overall} = 1.138, 95%CI [1.052,1.231], P = 0.001); Exposure to SO₂ (OR_{Europe} = 1.148, 95%CI [1.030,1.279], P = 0.012; OR_{Asia} = 1.044, 95%CI [0.954,1.142], P = 0.352; OR_{overall} = 1.085, 95%CI [1.013,1.163], P = 0.020); Exposure to PM₁₀ (OR_{Europe} = 1.190, 95%CI [1.092,1.297], P = 0.000; OR_{Asia} = 1.075, 95%CI [0.995,1.161], P = 0.066; OR_{overall} = 1.125, 95%CI [1.062,1.191], P = 0.000); Exposure to PM_{2.5} (OR_{Europe} = 1.195, 95%CI [1.050,1.360], P = 0.007; OR_{Asia} = 1.163, 95%CI [1.074,1.260], P = 0.000; OR_{overall} = 1.172, 95%CI [1.095,1.254], P = 0.000).

Conclusions: Exposed to air pollution probable is a risk of prevalence of childhood AR. And the prevalence of AR will be increase when exposed to NO₂, SO₂, PM₁₀ and PM_{2.5}, but maybe the relationship between SO₂/PM₁₀ and prevalence of AR are not closely in Asia.

1. Introduction

Allergic rhinitis (AR), a common chronic inflammatory disease in the upper airways, affects about 30–40% of the population worldwide. Also, AR is a common problem for children, which develops based on disruptions in the immune system. The probability of human gene mutation has not changed significantly, but reports that over the past few decades indicated that the prevalence of AR in children seems to be increasing [1–4]. The most significant causes of the increase are thought to be changes in environmental factors, such as air pollution, socioeconomic status, cultural difference, lifestyle changes or exposure to new allergens [5,6]. Among them, air pollution is regarded as the most important one. The existing evidences provides considerable support for the existing literature, if childhood exposure to airborne

pollutants is a considerable predictor of respiratory morbidity in childhood, early [7].

Air pollution, it is a major and rising danger in an environment associated with persistent increases in medical expense and morbidity. Air pollution refers to ozone (O₃), nitrogen dioxide (NO₂), sulfur dioxide (SO₂) and particulate matter (PM), and so on [8]. Their harmful effects on respiratory system have acquired much awareness. It has been reported that exposure to outdoor air pollutants such as NO₂, SO₂, O₃ and PM have adverse effects on immune competent cells and airway responsiveness [9], and there are also different air pollutants in different regions. Recent reports have demonstrated an association between high levels of bad air quality and an increased risk of allergic sensitization and prevalence of airway inflammatory diseases, such as COPD, bronchitis, asthma and AR.

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As we all know, AR has a significant impact on the quality of life of patients by causing uncomfortable symptoms such as nasal congestion, nasal pruritus, sneezing, rhinorrhea and nasal obstruction. Furthermore, AR is a risk factor for asthma, allergic conjunctivitis, rhinosinusitis, nasal polyposis, and secretory otitis media, resulting in important medical and social problems, especially in childhood. Thus, in this study, we focused on the associations between air pollution and children's AR. The aim of this research was to carry out a meta-analysis on the results of all conducted studies to present valid information about the correlations between the concentration of airborne pollutants and the prevalence of AR in childhood. Then, we aimed to assess the impact of specific pollutants exposure on the risk of AR in children.

2. Methods

Two researchers performed a systematic search independently to find the studies on AR and air pollution in childhood. Several web databases including PubMed, Science, Google Scholar, Elsevier and MDPI were searched for relevant articles, and searched up to January 1, 2000 to February 28, 2018.

Relevant studies were identified using four sets of keyword combinations.

1. 'Children/Kids/childhood' and 'air pollution/air pollutants' and 'allergic rhinitis/respiratory allergic diseases';
2. 'Children/Kids/childhood' and 'air quality' and 'allergic rhinitis/respiratory allergic diseases';
3. 'Children/Kids/childhood' and 'environment' and 'allergic rhinitis/respiratory allergic diseases';
4. 'Children/Kids/childhood' and 'nitrogen dioxide (NO₂)/sulfur dioxide (SO₂)/particulate matter (PM)' and 'allergic rhinitis/respiratory allergic diseases'.

We limited the language to English when searched. And we searched manually the reference lists of all included studies.

The inclusion criteria of meta-analysis included three points. The first, only observational studies including cross-sectional, cohort and case-control studies that have examined the association between air pollution exposure in childhood (age:0–18) and AR reported, which all can offer data to calculate the adjusted odds ratio (including gender, age, family history of asthma and allergic diseases, etc.) of AR with corresponding 95% confidence intervals (CI) for exposure to air pollutants (NO₂/SO₂/PM₁₀/PM_{2.5}).

The second explicitly specified the term 'AR' as an outcome for investigation.

The third all documents contain data on air pollutants, including nitrogen dioxide (NO₂), sulfur dioxide (SO₂), Particulate Matter < 10 μm in diameter (PM₁₀) and Particulate Matter diameter < 2.5 μm (PM_{2.5}) in their respective regions and the international evaluation standard for AR.

The exclusion criteria excluded adulthood AR and reviews, comments, incomplete information, governmental reports, letters, experimental studies or abstract.

Two authors independently extracted the parameters of the study design from each article, the age of the participants, and calculated the adjusted effect size and the corresponding 95% CI of the corrected odds ratio of the children after exposure to air pollutants (NO₂, SO₂, PM_{2.5}, PM₁₀). If necessary, resolve differences by discussing, examining, and negotiating with a third author.

Heterogeneity between study results was assessed using the Cochran Q statistic test and sensitivity analysis. I² statistic to determine the percentage of variability due to heterogeneity in the use. Study results were considered consistent when there was less than 50% variation due to heterogeneity, using fixed effects models, on the contrary, using random effects models (I² > 50%). Using random-effect meta-regression to study significant heterogeneity to determine which study-level

factors explained heterogeneity [10]. Sensitivity analysis was used to evaluate the stability of the included literature and subgroup analysis by region. And subgroup analysis by region. All analyses were performed using the software Stata-MP 14.1 (Stata Corporation, College Station, TX) and Review Manager version 5.3.

According to population scale research design, air pollution exposure measurement, contact time measurement method, doctor diagnosis, methodological quality of assessment study, international classification of diseases and questionnaire of ISAAC, confounding controls utilized, and statistical methods used. The quality of the study was evaluated using the Combie [11] for cross-sectional studies and the Newcastle Ottawa Scale (NOS) [12] for cohort studies. The total 7.0 points, 6.0–7.0 points evaluated level A, 4.0–5.5 points evaluated level B, less than 4.0 point was level C when using the Combie. And in cohort studies, full score was 9 points, 5–9 points can be assessed high level by NOS.

3. Results

Following the development of our search strategy, Totally, 547 relevant articles were resulted from primary research in web databases including PubMed, Science, Google Scholar, Elsevier and MDPI. After deleting duplicate articles and reviews, 389 relatively articles were obtained. Then, 344 articles were excluded due to irrelevance to study the subject after evaluation of titles and abstracts, so 45 articles included in the study for reviewing full-text. Next, 32 articles were excluded after reviewing full-texts due to incomplete information and low-quality studies. Thus, 13 studies that met inclusive criteria were included in the meta-analysis (Fig. 1).

These studies were published from January 1, 2000 to February 28, 2018. Eight of the included articles had been carried out as cross-sectional surveys and five of them had been carried out as cohort studies, including 123266 AR children contributed to the meta-analysis. Of these studies, 12 analyzed the correlations between NO₂; 9 articles related to SO₂; 11 studies related to PM₁₀ concentrations and AR risk, and 4 reported the correlation between PM_{2.5} concentration and AR risk.

The basic information of 13 included studies is summarized in Table 1.

Verification of heterogeneity analysis mainly through sensitivity analysis and the Cochran Q statistic test. For sensitivity analysis, the results were overall more stable in our analyses.

12 studies [13–23,25] (totally, 92607 children with AR) about air pollutants and AR were selected in this research. Because of the heterogeneity $P_{\text{Europe}} = 0.73$, $I^2 = 0\%$; $P_{\text{Asia}} = 0.054$, $I^2 = 49.5\%$; $P_{\text{overall}} = 0.001$, $I^2 = 66.6\%$, so we used the random effect method to evaluate. Our results showed statistical correlations between the concentration of NO₂ and the prevalence of childhood AR ($OR_{\text{Europe}} = 1.031$, 95%CI [1.002,1.060], $P = 0.033$; $OR_{\text{Asia}} = 1.236$, 95%CI [1.099,1.390], $P = 0.000$; $OR_{\text{overall}} = 1.138$, 95%CI [1.052,1.231], $P = 0.001$). The results demonstrated that air pollutant–NO₂ might significantly increase the risk of AR in childhood (Fig. 2).

Nine studies [13,15–17,19–23] (totally, 46392 children with AR) about SO₂ and AR were selected in this research. Based on the results of fixed effect method ($P_{\text{Europe}} = 0.817$, $I^2 = 0\%$; $P_{\text{Asia}} = 0.611$, $I^2 = 0\%$; $P_{\text{overall}} = 0.613$, $I^2 = 0\%$), statistical correlations between the concentration of SO₂ and the prevalence of childhood AR were not been found ($OR_{\text{Europe}} = 1.148$, 95%CI [1.030,1.279], $P = 0.012$; $OR_{\text{Asia}} = 1.044$, 95%CI [0.954,1.142], $P = 0.352$; $OR_{\text{overall}} = 1.085$, 95%CI [1.013,1.163], $P = 0.020$). There is no correlation between SO₂ and AR in Asia, but overall analysis of SO₂ has a risk for AR in childhood (Fig. 3).

Associations between PM₁₀ and AR were reported in eleven studies [13,15–23,25] (totally, 87169 children with AR). Because of low heterogeneity ($P_{\text{Europe}} = 0.623$, $I^2 = 0\%$; $P_{\text{Asia}} = 0.693$, $I^2 = 0\%$; $P_{\text{overall}} = 0.568$, $I^2 = 0\%$), fixed effect method was used. Our results showed that there was an obvious association between exposure to

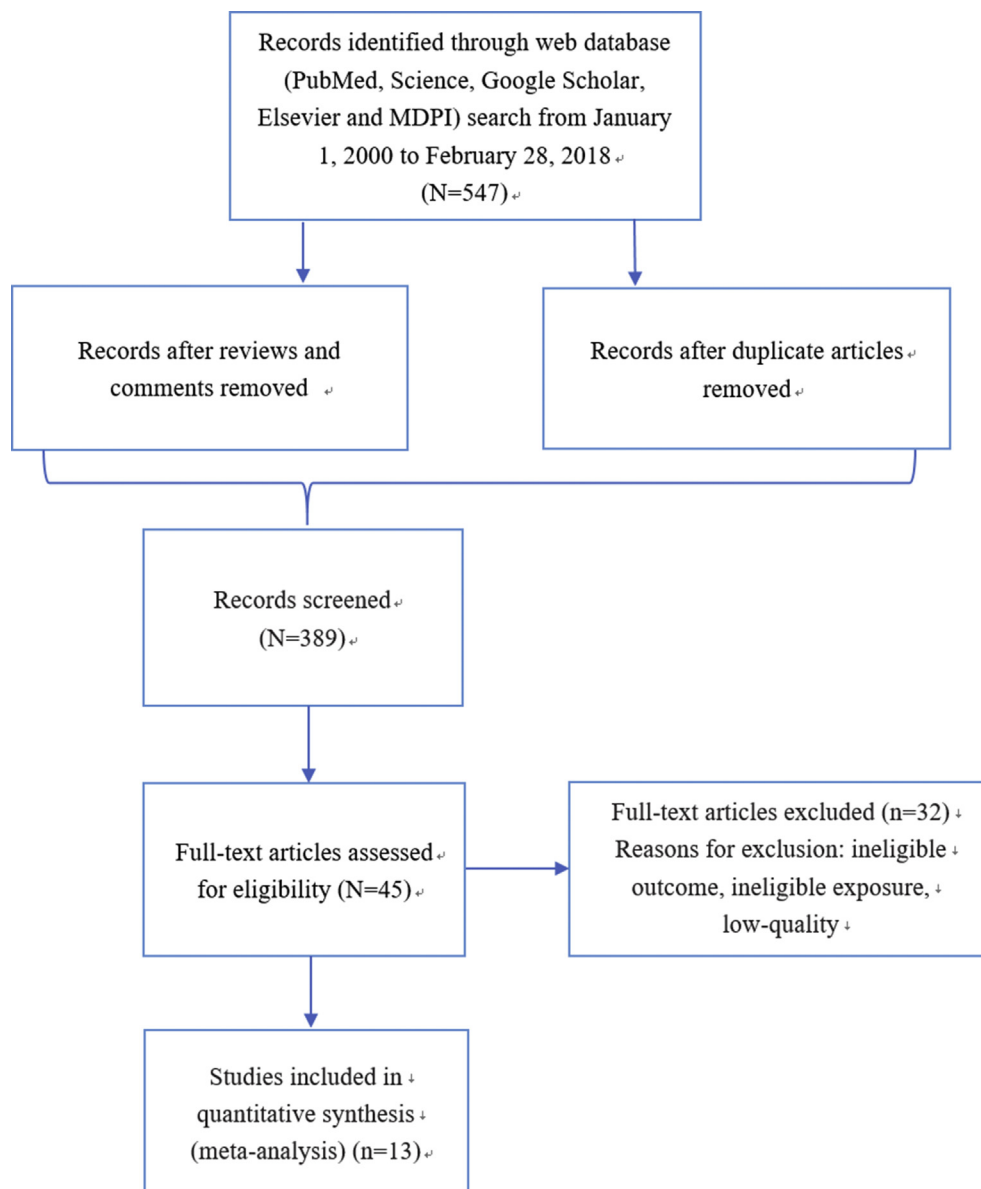


Fig. 1. Flowchart for identification of studies selected.

PM₁₀ and AR children incidence ($OR_{Europe} = 1.190$, 95%CI [1.092,1.297], $P = 0.000$; $OR_{Asia} = 1.075$, 95%CI [0.995,1.161], $P = 0.066$; $OR_{overall} = 1.125$, 95%CI [1.062,1.191], $P = 0.000$). There is no correlation between PM₁₀ and AR in Asia, but overall analysis of PM₁₀ has a risk for AR in childhood (Fig. 4).

4 studies [14,18,23,24] (totally, 39753 children with AR) about PM_{2.5} and AR were selected in this research. Because of heterogeneity ($P_{Europe} = 0.175$, $I^2 = 45.6\%$; $P_{Asia} = 0.163$, $I^2 = 48.6\%$; $P_{overall} = 0.272$, $I^2 = 23.1\%$), fixed effect method was used. Our results showed that the prevalence of AR in childhood statistically associated with exposure to PM_{2.5} ($OR_{Europe} = 1.195$, 95%CI [1.050,1.360], $P = 0.007$; $OR_{Asia} = 1.163$, 95%CI [1.074,1.260], $P = 0.000$; $OR_{overall} = 1.172$, 95%CI [1.095,1.254], $P = 0.000$). These demonstrated that there was a significant association between exposure to PM_{2.5} for AR in childhood (Fig. 5).

4. Discussion

AR is caused by inappropriate immunological response to airborne antigens. This meta-analysis presented a comprehensive report that is

the first quantitative summary of the prevalence of AR in childhood and air pollution. Our results showed a major correlation between the concentrations of main pollutants and the prevalence of AR in children. These results demonstrated that in childhood, exposure to NO₂, SO₂, PM₁₀ and PM_{2.5} significantly all increased the risk of suffering from AR. NO₂, SO₂, PM₁₀ and PM_{2.5} presented risk factors for AR in childhood. However, these associations were not found in SO₂ and PM₁₀ in Asia region.

Air pollution refers to nitrogen dioxide (NO₂), sulfur dioxide (SO₂), particulate matter (PM) and ozone (O₃) and so on. Their harmful effects on respiratory system have acquired much awareness. Recent studies have demonstrated an association between high levels of air quality and an increased risk of allergic diseases. (Air Pollution and Allergic Disease) Exposure to environmental pollutants especially in the air, has in fact been identified as a major cause of many common diseases and allergies. Joanna et al. reported that outdoor air contaminants were major environmental factors responsible for adverse respiratory health effects in children [26]. Epidemiological investigation provided evidence that exposure to outdoor air pollutants such as NO₂, SO₂, PM and O₃ have adverse effects on immune cells and airway

Table 1
 Characteristics of included studies for air pollution with AR on children. (NO₂: nitrogen dioxide; SO₂: sulfur dioxide; PM₁₀: particulate matter with aerodynamic diameter less than 10 mm; PM_{2.5}: particulate matter with aerodynamic diameter less than 2.5 mm; ETS: environment tobacco smoke).

Study and quality	Country	Age(years)	Participants	Study design	Exposure factors	Exposure assessment	Outcome assessment	Adjustment variables	Research result
C. Pe´nard-Morand 2005(A)	France (Western Europe)	9 to 11	9615	Cross-sectional	NO ₂ , SO ₂ , PM ₁₀	Air pollution assessed from fixed monitoring sites	ISAAC questionnaire	age, sex, family history of allergy, passive smoking and parental education	NO ₂ OR = 1.00 (95%CI = 0.90–1.10) SO ₂ OR = 1.16 (95%CI = 1.01–1.32) PM ₁₀ OR = 1.32 (95%CI = 1.04–1.68) NO ₂ OR = 1.06 (95%CI = 0.91–1.23)
Annest-Maesano 2007(A)	France (Western Europe)	1.5 to 6	5338	Cross-sectional	NO ₂ , PM _{2.5}	Air pollution assessed from fixed monitoring sites	ISAAC questionnaire	age, sex, family history of allergy and passive smoking	PM _{2.5} OR = 1.13 (95%CI = 0.97–1.33) NO ₂ OR = 1.14 (95%CI = 0.92–1.36)
C. Pe´nard-Morand 2010(A)	France (Western Europe)	9 to 11	4907	Cross-sectional	NO ₂ , SO ₂ , PM ₁₀	Air pollution assessed from fixed monitoring sites	ISAAC questionnaire	age, sex, older siblings, family history of allergy, parental education, mother's ethnic origin, smoking at home, mould or dampness at home, natural gas used for heating, cooking or for water-heater at home, and pets at home, with an exchangeable working correlation structure using the community as a stratum	SO ₂ OR = 1.13 (95%CI = 0.95–1.34) PM ₁₀ OR = 1.20 (95%CI = 1.01–1.44) NO ₂ OR = 1.083 (95%CI = 0.875–1.340)
LU Chan 2013(B)	China (East Asia)	3 to 6	2159	Cross-sectional	NO ₂ , SO ₂ , PM ₁₀	Air pollution assessed from fixed monitoring sites	ISAAC questionnaire	age, parental atopy, breast-feeding, cockroaches noted and flooding or water damage	SO ₂ OR = 0.997 (95%CI = 0.843–1.179) PM ₁₀ OR = 1.074 (95%CI = 0.710–1.625) NO ₂ OR = 1.55 (95%CI = 1.17–2.05)
Miao-Miao Liu 2013(A)	China (East Asia)	3 to 7	6730	Cross-sectional	NO ₂ , SO ₂ , PM ₁₀	Air pollution assessed from fixed monitoring sites	ISAAC questionnaire	Age, Sex, Breast feeding, Parental education, Family history of allergy, Family history of asthma, House near main road, House near factory or chimney, Home coal use, Ventilation device, House pets, Home decoration, ETS	SO ₂ OR = 1.29 (95%CI = 0.96–1.73) PM ₁₀ OR = 0.97 (95%CI = 0.76–1.25) NO ₂ OR = 1.03 (95%CI = 1.00–1.06) PM _{2.5} OR = 1.38 (95%CI = 1.08–1.78) PM ₁₀ OR = 1.16 (95%CI = 1.04–1.29) NO ₂ OR = 1.10 (95%CI = 0.87–1.39)
Wood HE 2015(A)	Britain (Northwest Europe)	8 to 9	995	Cross-sectional	NO, PM _{2.5} , PM ₁₀	Air pollution modelling and data collection	ISAAC questionnaire	Age, Sex, BMI, ETS, Ethnicity, Study year	SO ₂ OR = 1.01 (95%CI = 0.85–1.20) PM ₁₀ OR = 1.07 (95%CI = 0.86–1.33)
Ho Hyun Kim 2015(A)	Korea (East Asia)	7 to 12	4404	Cross-sectional	NO ₂ , SO ₂ , PM ₁₀	Air pollution assessed from fixed monitoring sites	ISAAC questionnaire	age, gender, exposure to secondhand smoking, household income, type of residence, built year of residence, and indoor leak status	

(continued on next page)

Table 1 (continued)

Study and quality	Country	Age(years)	Participants	Study design	Exposure factors	Exposure assessment	Outcome assessment	Adjustment variables	Research result
Hui-YingChung 2016(High)	Taiwan, China (South East Asia)	0 to 6	9960	Cohort	NO ₂ , SO ₂ , PM ₁₀	Air pollution assessed from fixed monitoring sites	ICD-9	Age and gender	NO ₂ OR = 1.47 (95%CI = 1.14-1.84) SO ₂ OR = 1.05 (95%CI = 0.67-1.33) PM ₁₀ OR = 1.12 (95%CI = 0.79-1.45) NO ₂ OR = 1.81 (95%CI = 1.10-2.95) SO ₂ OR = 0.88 (95%CI = 0.60-1.30) PM ₁₀ OR = 0.97 (95%CI = 0.35-2.67) NO ₂ OR = 1.41 (95%CI = 1.01-1.97)
Wei Liu 2016(High)	China (East Asia)	4 to 6	3358	Cohort	NO ₂ , SO ₂ , PM ₁₀	Air pollution assessed from fixed monitoring sites	ISAAC questionnaire	age, sex, family history of atopy, ownership of residence, breastfeeding, home dampness, distance of residence from the nearest main traffic road, usage of heating during winter, renovating the residence or buying new large furniture during early lifetime and household ETS	
Qihong Deng 2016(High)	China (East Asia)	3 to 6	2598	Cohort	NO ₂ , SO ₂ , PM ₁₀	Air pollution assessed from fixed monitoring sites	ISAAC questionnaire	sex, age, birth season, breast-feeding, and parental atopy, SES, ETS, new furniture, visible mold/damp stains, window condensation, cockroach and household dogs	
I-Jen Wang 2016(High)	Taiwan, China (South East Asia)	4 to 7	2661	Cohort	NO ₂ , SO ₂ , PM ₁₀ , PM _{2.5}	Air pollution assessed from fixed monitoring sites	ISAAC questionnaire	age, gender, body mass index, environmental tobacco smoke, maternal history of atopy, maternal education and nationality, duration of breast feeding, duration of sleep, number of siblings, temperature, relative humidity, and distance from the home to the air monitoring station	SO ₂ OR = 1.21 (95%CI = 0.93-1.59) PM ₁₀ OR = 1.58 (95%CI = 1.07-2.33) NO ₂ OR = 0.95 (95%CI = 0.74-1.20)
Fei'er Chen 2017(A)	China (East Asia)	4 to 6	30759	Cross-sectional	PM _{2.5}	Air pollution modelling and database of Global Burden of Disease	ISAAC questionnaire	age, family history of asthma and allergic diseases, breastfeeding, parental smoking, indoor dampness, interior decoration, and household annual income/capita and annual average temperature	SO ₂ OR = 1.00 (95%CI = 0.78-1.29) PM ₁₀ OR = 1.15 (95%CI = 0.79-1.66) PM _{2.5} OR = 1.54 (95%CI = 1.03-2.32) PM _{2.5} OR = 1.15 (95%CI = 1.06-1.23)
Dan Norbäck 2018(High)	China (East Asia)	3 to 6	39782	Cohort	NO ₂ , PM ₁₀	National Bureau of Statistics of the People's Republic of China	ISAAC questionnaire	sex, age, birth season, birth weight, breast-feeding, parental atopy, lifetime passive smoking, lifetime mould/dampness, living near traffic, lifetime outdoor T, socioeconomic status	NO ₂ OR = 1.20 (95%CI = 1.09-1.32) PM ₁₀ OR = 1.06 (95%CI = 0.96-1.18)

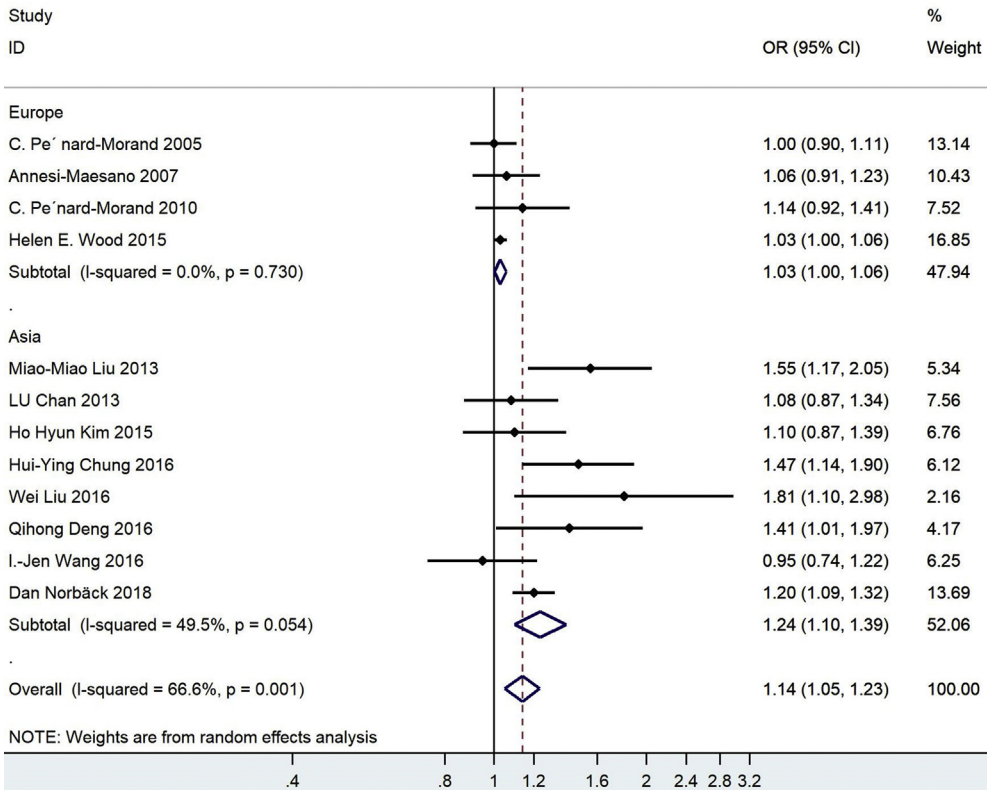


Fig. 2. Forest plot of the risk of NO₂ with AR on children.

hyperresponsiveness [27]. Mostly consistent with these research, our meta-analysis showed meaningful correlations between the concentrations of NO₂, SO₂, PM₁₀ and PM_{2.5} and the prevalence of AR in childhood, but maybe SO₂ and PM₁₀ are less impact on AR in Asia.

To explore the impact of NO₂ on children with AR, our meta-analysis included 12 related studies and the results indicated that NO₂ was a risk factor for AR in childhood. Recently, Kuo-Ying Wang et al. [28] also reported that NO and NO₂ were two main air pollutants that were

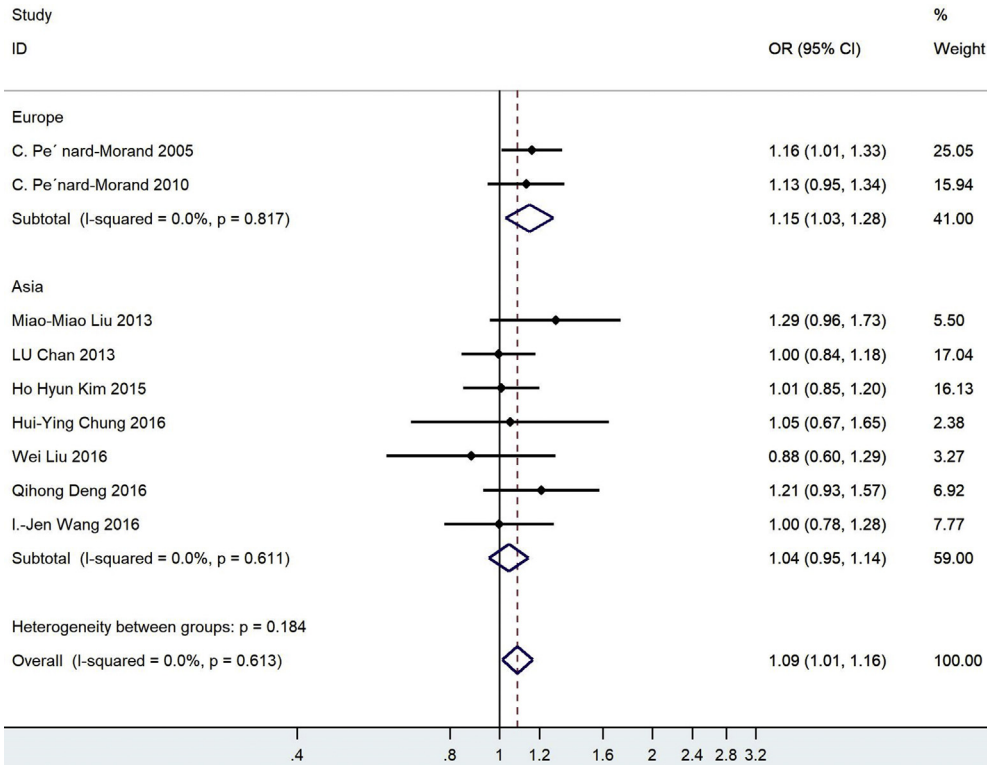


Fig. 3. Forest plot of the risk of SO₂ with AR on children.

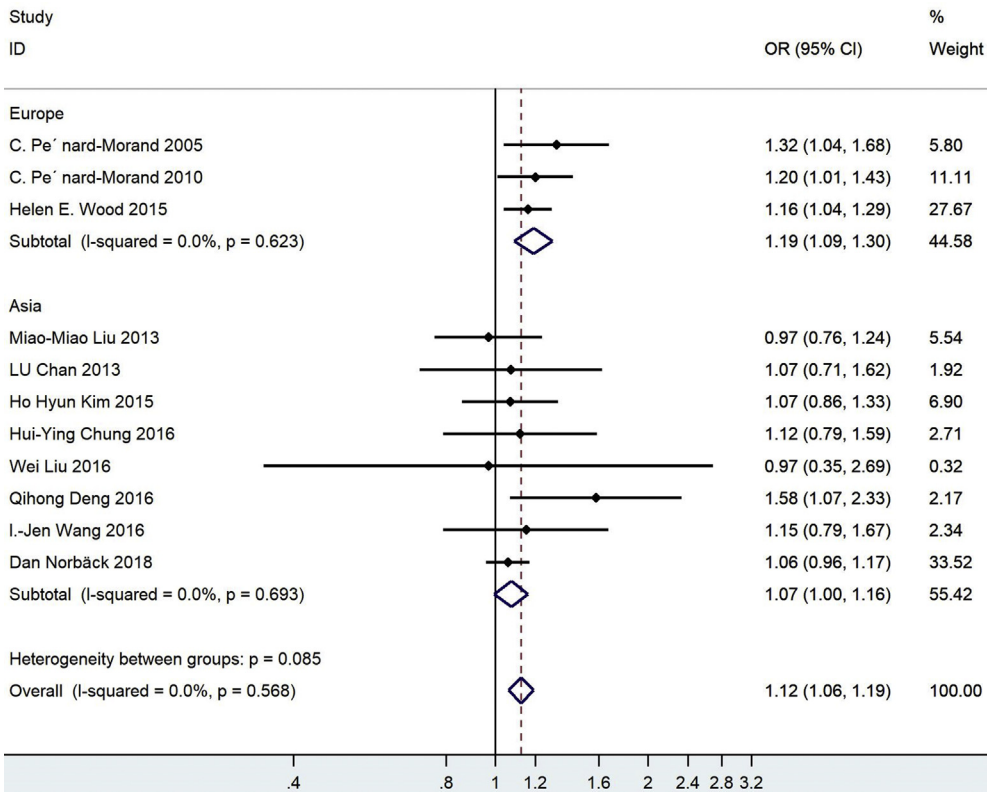


Fig. 4. Forest plot of the risk of PM₁₀ with AR on children.

positively associated with respiratory diseases; Young outpatients (age 0–15 years) were most sensitive to changes air pollution and meteorology factors, followed by the eldest (age ≥ 66 years) and age 16–65 years of outpatients. Furthermore, Katrin et al. [29] found that low ozone concentrations and NO₂ caused the inflammation of the human nasal mucosa in vitro. Initiation factors such as atopy or pre-existing

inflammation did increase the sensitivity to O₃ and NO₂. However, the association between SO₂ and children with AR is controversial. On the one hand, our analysis demonstrated that there were no statistical correlations between the concentration of SO₂ and the prevalence of childhood AR in Asia. An expected cohort study [30] evaluated the relationship between individual-based exposure to traffic-

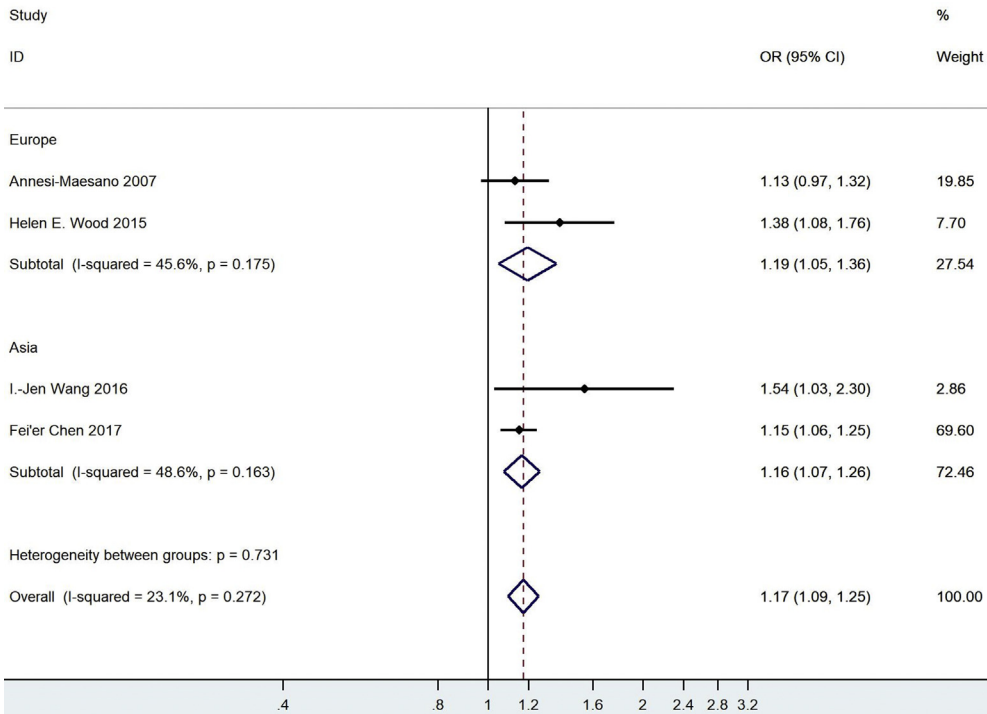


Fig. 5. Forest plot of the risk of PM_{2.5} with AR on children.

related air pollution (TRAP) and allergic diseases outcomes during the first 6 years of life, and they also found no association between SO₂ exposure and allergic sensitization. Meanwhile et al. [31] found the relationship between TRAP and AR in middle-school students in Taiwan, China, and found significant associations for TRAP (e.g. CO, NO_x and O₃) in both sexes but none for SO₂. On the other hand, some new literature have found that SO₂ concentrations were closely associated with the prevalence of AR. We think these differences may mostly ascribe to disparity in region, race, ethnicity, and so on, for example, China's major air pollutants have been transformed from SO₂ to PM, which requires more research to illustrate.

Experimental exposure of PM leads to oxidative stress, airway hyperresponsiveness, and airway remodeling, either alone or in combination with allergic sensitization [32]. Children are more affected than adults, and boys more affected than girls [33]. Our meta-analysis demonstrated that PM₁₀ and PM_{2.5} were risk factors for AR. PM can act as allergen carriers, aggravating allergic reactions, and smaller particles can enter the respiratory tract, breaking the mucosa [34]. However, it should be noted that in addition to the size of PM, the chemical compositions are very significant for understanding the health effects of PM. And Individuals also have different susceptibility to air pollutants, which requires us to further explore.

5. Conclusion

All in all, our meta-analysis demonstrates an association between exposure to air pollution and the risk of AR in childhood. The air pollution exposure is a risk factor for AR among children, and the prevalence of AR will be increase when exposed to NO₂, SO₂, PM₁₀ and PM_{2.5}, but maybe the relationship between SO₂/PM₁₀ and prevalence of AR are not closely in Asia. The findings highlight the need for more comprehensive atmospheric control policies by government departments to protect sensitive kids and the importance of continuously modifying existing regulations considering recent discoveries. So, it is of great significance to continue to explore the correlation between air pollution and AR for improving the prevention and treatment of it.

Declarations

Ethics approval and consent to participate (not applicable)

The authors declare no financial or other conflicts of interest regarding the content of this article.

Consent for publication

Not applicable.

Availability of data and material

We guarantee that all data are true and reliable, all from our research group.

A total of 13 articles were included in the full text for meta-analysis, and we manually searched from the web database including PubMed, Science, Google Scholar, Elsevier and MDPI. By reading the full text, we can find OR related to air pollution from the results (original, table or figure).

All data generated or analyzed during this study are included in this published article and its [supplementary information files](#).

Competing interests

The authors Qi-Yuan Zou and Yang Shen are contributed equally who are the first author.

The authors disclose no conflict of interest regarding this work.

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Authors' contributions

QyZ was an independent reviewer who a major contributor in writing the manuscript.

YS was the second reviewer who a major contributor in writing and modified the manuscript.

XK provided a lot of help in the literature search.

SLH and HyK guided and reviewed the entire Meta-analysis.

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List of abbreviations

AR	Allergic rhinitis
NO ₂	Nitrogen dioxide
SO ₂	sulfur dioxide
PM	particulate matter
O ₃	Ozone
OR	Odds Ratio
CI	confidence intervals
NOS	The Newcastle Ottawa Scale
TRAP	Traffic-related air pollution

Appendix A. Supplementary data

Supplementary data related to this article can be found at <http://dx.doi.org/10.1016/j.ijporl.2018.06.039>.

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Study	ES	[95% Conf. Interval]		% Weight
-----+-----				
Europe				
C. Pe´nard-Morand	1.000	0.900	1.111	13.14
Annesi-Maesano 2007	1.060	0.910	1.235	10.43
C. Pe´nard-Morand 2	1.140	0.920	1.413	7.52
Helen E. Wood 2015	1.030	1.000	1.061	16.85
Sub-total				
D+L pooled ES	1.031	1.002	1.060	47.94
-----+-----				
Asia				
Miao-Miao Liu 2013	1.551	1.171	2.055	5.34
LU Chan 2013	1.083	0.875	1.340	7.56
Ho Hyun Kim 2015	1.100	0.870	1.391	6.76
Hui-Ying Chung 2016	1.470	1.140	1.896	6.12
Wei Liu 2016	1.810	1.100	2.978	2.16
Qihong Deng 2016	1.410	1.010	1.968	4.17
I.-Jen Wang 2016	0.950	0.740	1.220	6.25
Dan Norbäck 2018	1.200	1.090	1.321	13.69
Sub-total				
D+L pooled ES	1.236	1.099	1.390	52.06
-----+-----				
Overall				
D+L pooled ES	1.138	1.052	1.231	100.00
-----+-----				

Test(s) of heterogeneity:					
	Heterogeneity statistic	degrees of freedom	P	I-squared**	Tau-squared
Europe	1.30	3	0.730	0.0%	0.0000
Asia	13.86	7	0.054	49.5%	0.0127
Overall	32.90	11	0.001	66.6%	0.0092

** I-squared: the variation in ES attributable to heterogeneity)

Note: between group heterogeneity not calculated;
only valid with inverse variance method

Significance test(s) of ES=1

Europe	z=	2.13	p =	0.033
Asia	z=	3.54	p =	0.000
Overall	z=	3.24	p =	0.001

Study	ES	[95% Conf. Interval]		% Weight
Europe				
C. Pe´nard-Morand	1.320	1.040	1.675	5.80
C. Pe´nard-Morand	1.200	1.010	1.426	11.11
Helen E. Wood 2015	1.160	1.040	1.294	27.67
Sub-total				
I-V pooled ES	1.190	1.092	1.297	44.58
Asia				
Miao-Miao Liu 2013	0.970	0.760	1.238	5.54
LU Chan 2013	1.074	0.710	1.625	1.92
Ho Hyun Kim 2015	1.070	0.860	1.331	6.90
Hui-Ying Chung 2016	1.120	0.790	1.588	2.71
Wei Liu 2016	0.970	0.350	2.688	0.32
Qihong Deng 2016	1.580	1.070	2.333	2.17
I.-Jen Wang 2016	1.150	0.790	1.674	2.34
Dan Norbäck 2018	1.060	0.960	1.171	33.52
Sub-total				
I-V pooled ES	1.075	0.995	1.161	55.42
Overall				
I-V pooled ES	1.125	1.062	1.191	100.00

Test(s) of heterogeneity:

	Heterogeneity statistic	degrees of freedom	P	I-squared**
Europe	0.95	2	0.623	0.0%
Asia	4.72	7	0.693	0.0%
Overall	8.63	10	0.568	0.0%
Overall Test for heterogeneity between sub-groups:				
	2.96	1	0.085	

** I-squared: the variation in ES attributable to heterogeneity)

Significance test(s) of ES=1

Europe	z=	3.96	p =	0.000
Asia	z=	1.84	p =	0.066
Overall	z=	4.01	p =	0.000

Study	ES	[95% Conf. Interval]		% Weight
-----+-----				
Europe				
C. Pe´nard-Morand	1.160	1.010	1.332	25.05
C. Pe´nard-Morand 2	1.130	0.950	1.344	15.94
Sub-total				
I-V pooled ES	1.148	1.030	1.279	41.00
-----+-----				
Asia				
Miao-Miao Liu 2013	1.290	0.960	1.733	5.50
LU Chan 2013	0.997	0.843	1.179	17.04
Ho Hyun Kim 2015	1.010	0.850	1.200	16.13
Hui-Ying Chung 2016	1.050	0.670	1.645	2.38
Wei Liu 2016	0.880	0.600	1.291	3.27
Qihong Deng 2016	1.210	0.930	1.574	6.92
I.-Jen Wang 2016	1.000	0.780	1.282	7.77
Sub-total				
I-V pooled ES	1.044	0.954	1.142	59.00
-----+-----				
Overall				
I-V pooled ES	1.085	1.013	1.163	100.00
-----+-----				

Test(s) of heterogeneity:

	Heterogeneity statistic	degrees of freedom	P	I-squared**
Europe	0.05	1	0.817	0.0%
Asia	4.49	6	0.611	0.0%
Overall	6.30	8	0.613	0.0%
Overall Test for heterogeneity between sub-groups:				
	1.76	1	0.184	

** I-squared: the variation in ES attributable to heterogeneity)

Significance test(s) of ES=1

Europe	z=	2.50	p =	0.012
Asia	z=	0.93	p =	0.352
Overall	z=	2.32	p =	0.020

Study		ES	[95% Conf. Interval]		% Weight
-----+-----					
Europe					
Annesi-Maesano 2007		1.130	0.970	1.316	19.85
Helen E. Wood 2015		1.380	1.080	1.763	7.70
Sub-total					
I-V pooled ES		1.195	1.050	1.360	27.54
-----+-----					
Asia					
I.-Jen Wang 2016		1.540	1.030	2.302	2.86
Fei'er Chen 2017		1.150	1.060	1.248	69.60
Sub-total					
I-V pooled ES		1.163	1.074	1.260	72.46
-----+-----					
Overall					
I-V pooled ES		1.172	1.095	1.254	100.00
-----+-----					

Test(s) of heterogeneity:

	Heterogeneity statistic	degrees of freedom	P	I-squared**
Europe	1.84	1	0.175	45.6%
Asia	1.94	1	0.163	48.6%
Overall	3.90	3	0.272	23.1%
Overall Test for heterogeneity between sub-groups:				
	0.12	1	0.731	

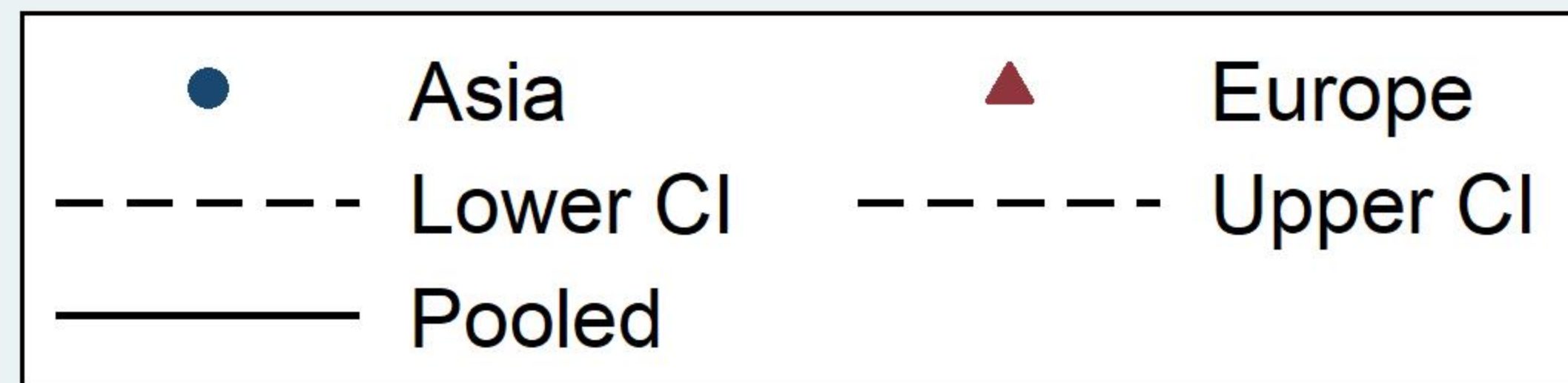
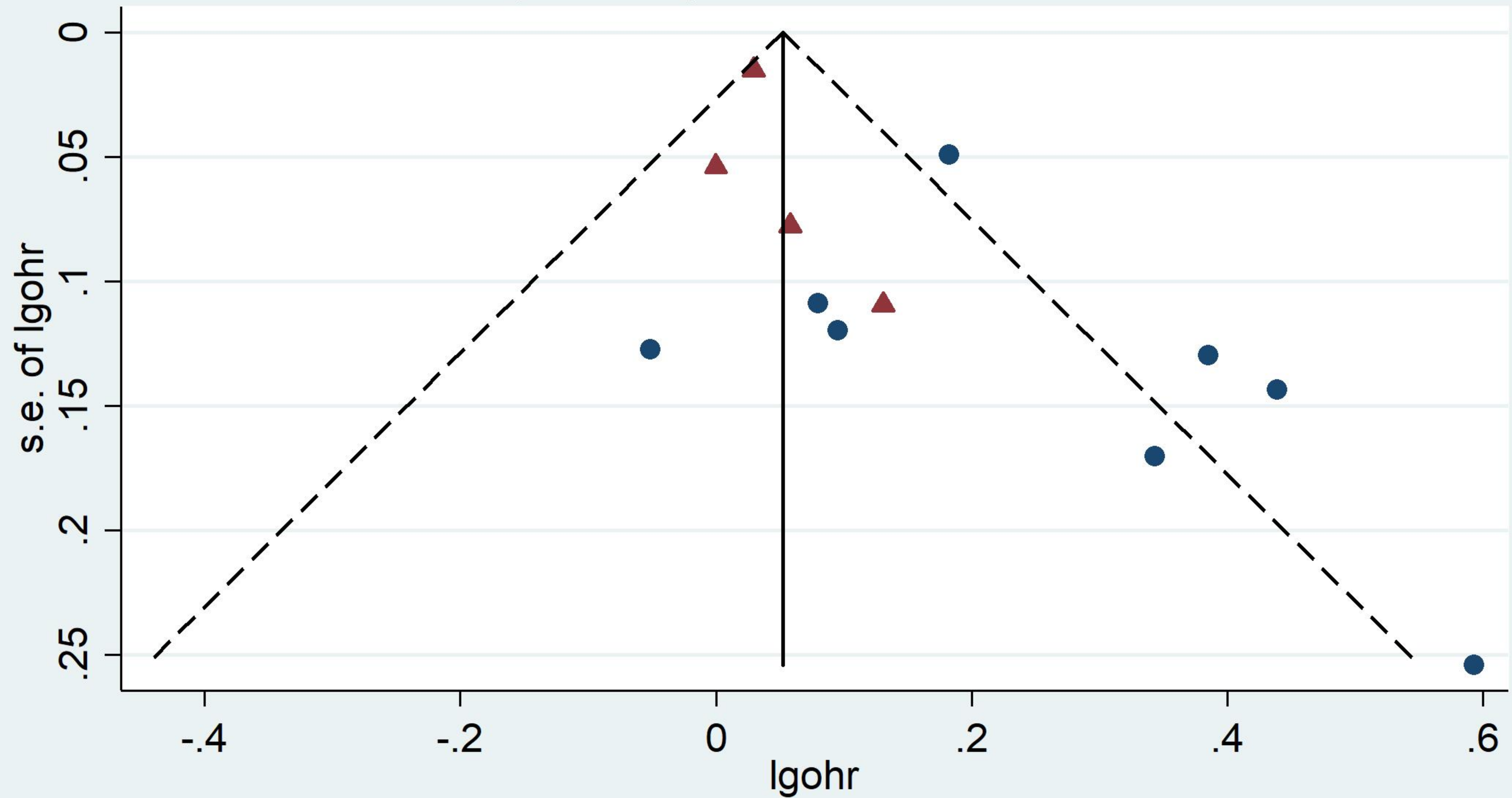
** I-squared: the variation in ES attributable to heterogeneity)

Some heterogeneity observed (up to 48.6%) in one or more sub-groups,
Test for heterogeneity between sub-groups may be invalid

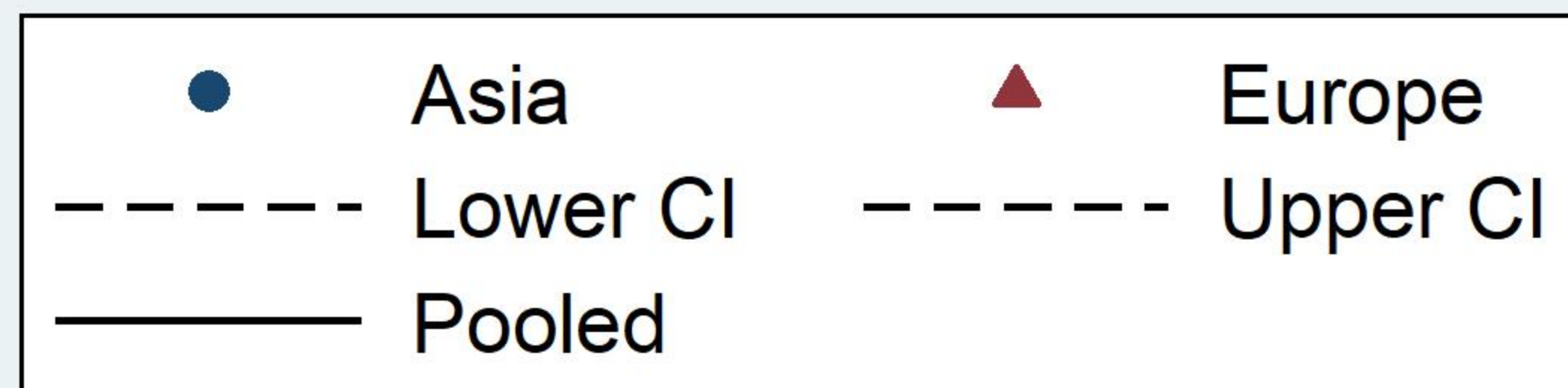
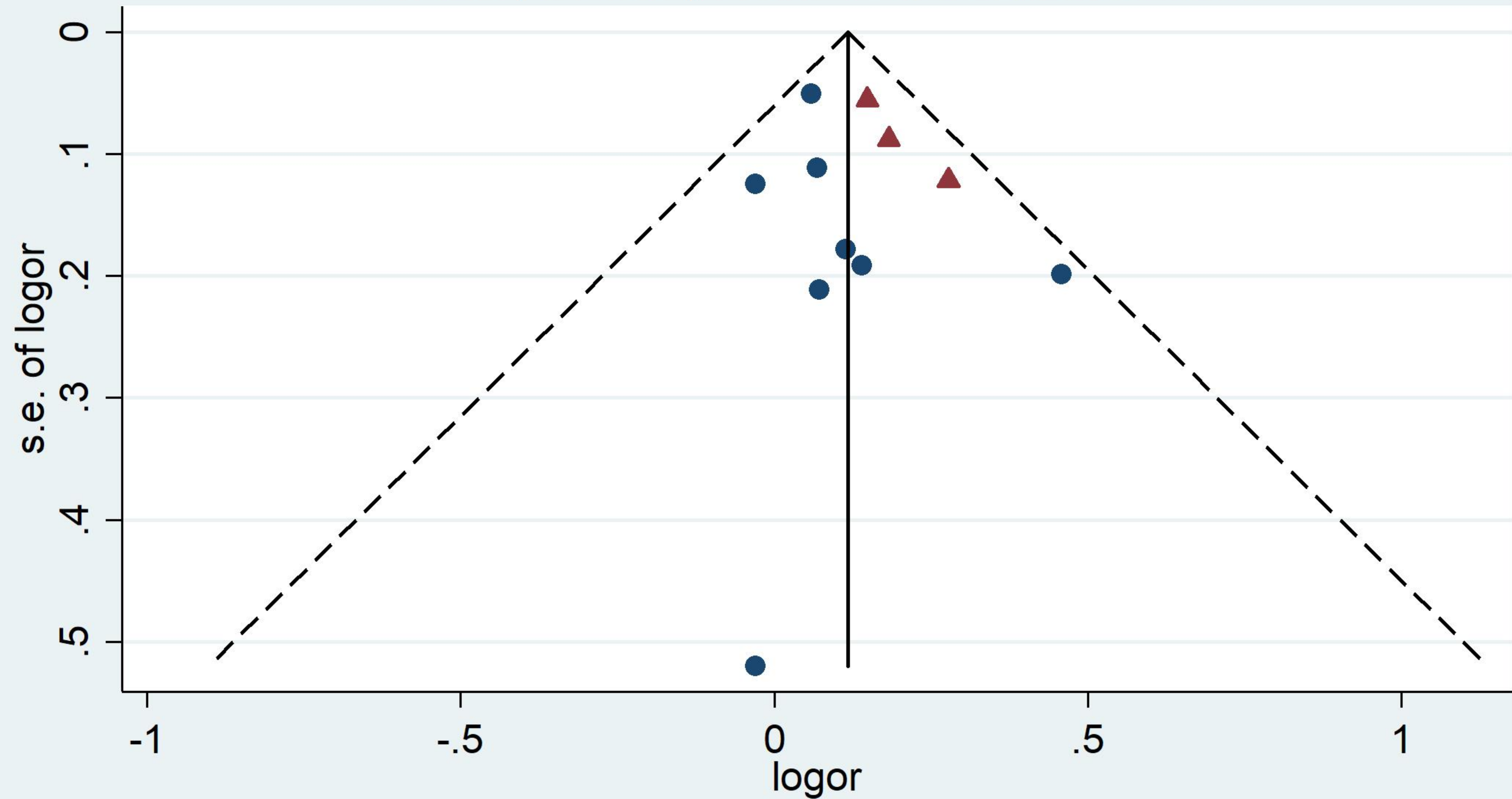
Significance test(s) of ES=1

Europe	z=	2.69	p =	0.007
Asia	z=	3.71	p =	0.000
Overall	z=	4.57	p =	0.000

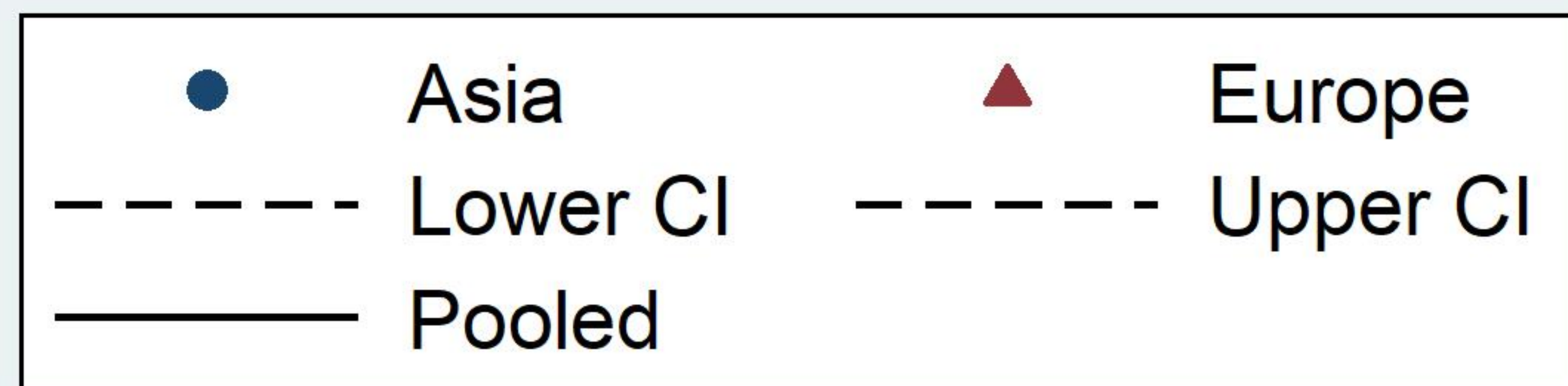
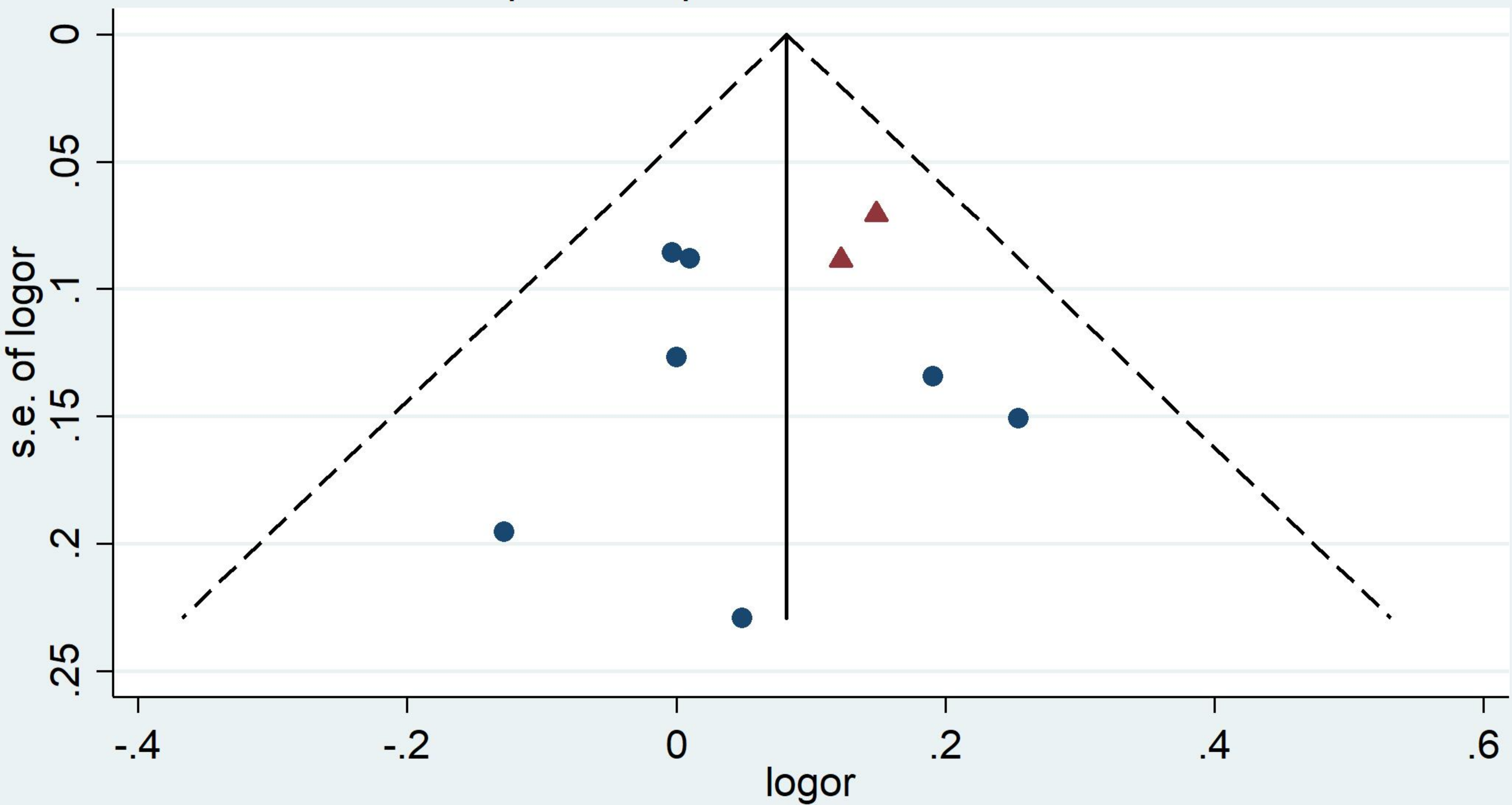
Funnel plot with pseudo 95% confidence limits



Funnel plot with pseudo 95% confidence limits



Funnel plot with pseudo 95% confidence limits



Funnel plot with pseudo 95% confidence limits

