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Global Incidence and Prevalence of Eosinophilic Esophagitis, 1976–2022: A Systematic Review and Meta-analysis

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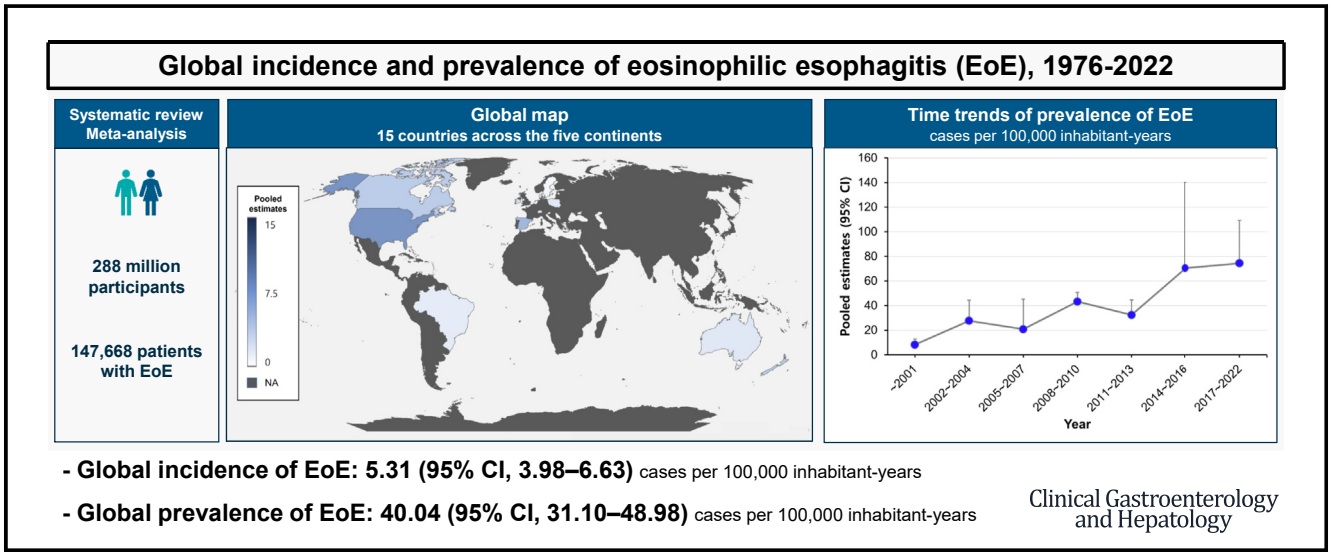

BACKGROUND AND AIMS: **Owing to 2018 expanded diagnostic criteria for eosinophilic esophagitis (EoE) and thus a possible increase in diagnosis, previous studies on the global incidence and prevalence of EoE may need to be updated. We aimed to describe global, regional, and national trends in the**

Abbreviations used in this paper: **CI, confidence interval; EoE, eosinophilic esophagitis; GERD, gastroesophageal reflux disease; PPI, proton pump inhibitor; HPF, high-power field; HICs, high-income countries; LMICs, low- or middle-income countries; OR, odds ratio.**

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incidence and prevalence of EoE from 1976 to 2022 and analyze their associations with geographic, demographic, and social factors through a systematic review.

METHODS: **We searched the PubMed/MEDLINE, Embase, CINAHL, Google Scholar, and Cochrane databases from their inception dates to December 20, 2022, for studies that reported the incidence or prevalence of EoE in the general population. We calculated the global incidence and prevalence of EoE using pooled estimates with 95% confidence intervals (CIs) and performed subgroup analysis based on age, sex, race, geographical area, World Bank income group, and diagnostic criteria of EoE.**

RESULTS: **Forty studies met the eligibility criteria, including over 288 million participants and 147,668 patients with EoE from 15 countries across the five continents. The global pooled incidence and prevalence of EoE were 5.31 cases per 100,000 inhabitant-years (95% CI, 3.98–6.63; number of studies, 27; sample population, 42,191,506) and 40.04 cases per 100,000 inhabitant-years (95% CI, 31.10–48.98; number of studies, 20; sample population, 30,467,177), respectively. The pooled incidence of EoE was higher in high-income countries (vs low- or middle-income countries), males, and North America (vs Europe and Asia). The global prevalence of EoE followed a similar pattern. The pooled prevalence of EoE gradually increased from 1976 to 2022 (1976–2001; 8.18; 95% CI, 3.67–12.69 vs 2017–2022; 74.42; 95% CI, 39.66–109.19 cases per 100,000 inhabitant-years).**

CONCLUSIONS: **The incidence and prevalence of EoE have increased substantially and vary widely across the world. Further research is needed to evaluate the incidence and prevalence of EoE in Asia, South America, and Africa.**

Keywords: Eosinophilic Esophagitis; Global Trend; Incidence; Prevalence; Systematic Review and Meta-analysis.

Eosinophilic esophagitis (EoE) is a chronic allergen/immune-mediated disease characterized by symptoms of esophageal dysfunction and eosinophilic infiltration of the esophageal mucosa in the absence of secondary causes of eosinophilia.[1] Typical symptoms vary according to the patient's age,[1] and current guidelines suggest that EoE should be diagnosed when symptoms of esophageal dysfunction are concurrent with $\geq$15 eosinophils/high-power field (HPF) on endoscopic biopsy. However, there is a lack of awareness regarding the disease, and many patients have already reported complications, mainly associated with esophageal dysfunction or fibrosis, in their first medical evaluation.[2]

Previous studies have found that the incidence of EoE is increasing faster than the increase in biopsy or disease awareness.[3,4] Although the most recent systematic review was published in 2019, including 29 studies on EoE,[5] it did not investigate national and regional differences. Furthermore, as the diagnostic criteria have been updated recently, the results of this study may not reflect the real-world incidence and prevalence of EoE according to the new consensus.

In the context of the increasing incidence and prevalence of EoE and consequently increasing social burden worldwide, a systematic review and meta-analysis that provides accurate estimates of the incidence and prevalence of EoE is needed. Therefore, this study aimed to identify global, regional, and national trends in the incidence and prevalence of EoE from 1976 to 2022. We conducted a systematic review and meta-analysis of the incidence and prevalence of EoE in the general population and performed a subgroup analysis based on age, sex, race, geographical area, and diagnostic criteria for EoE.

Materials and Methods

We performed a systematic review and meta-analysis of previous literature to investigate global and national trends in the incidence and prevalence of EoE in different countries and subgroup analysis by age, sex, race, geographical area, and diagnostic criteria of EoE. This systematic review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines,[6] and the protocol was registered with PROSPERO (registration no. CRD42022342812).

Search Strategy and Study Selection

We searched PubMed, MEDLINE, Embase, CINAHL, Google Scholar, and Cochrane databases from their inception dates to December 20, 2022, for studies that reported the incidence or prevalence of EoE in all age groups according to the appropriate diagnostic guidelines for EoE. Studies that did not meet the inclusion criteria were also excluded. Studies were required to include participants from the general population or from community-based datasets.

We excluded studies from which it was not possible to calculate the prevalence or incidence accurately. First, biased samples were excluded, such as individuals

attending screening clinic health checkups, employees at an institution, or university students. Second, studies with fewer than 50 participants were excluded. Thus, because there were no interventional studies, we only included general population-based observational studies with larger samples published in English.

The databases were searched using the terms "*EoE*" or "*eosinophilic esophagitis,*" which were combined using the set operator "AND" with studies identified using the terms "*incidence,*" "*prevalence,*" or "*trend*" as free text terms. A total of 2987 studies were screened, and the titles and abstracts of all selected studies were rescreened for potential suitability. Studies that appeared irrelevant were excluded (Supplementary Table 1 and Supplementary Figure 1). A recursive search was performed using the bibliographies of all eligible papers. Two investigators (JWH and DKY) independently assessed the eligibility of the study, and disagreements were resolved through discussion with a third investigator (SWL).

Data Extraction and Statistical Analysis

Data were extracted independently by 2 investigators (JWH and DKY) using Microsoft Excel (version 2013). The following data were collected for each study: first author, publication year, country, diagnosis criteria used to define EoE, study design (retrospective and prospective), study duration, total number of subjects providing data, number of subjects with EoE, age group (children and adults), sex, and race of subjects. All studies were evaluated for risk of bias, as assessed by Hoy et al.[7] Nine risk items were evaluated, and a study was considered to have a low risk of bias if 3 or fewer items were applicable, and a high risk of bias when seven or more items were applicable. Five studies were evaluated as having a high overall risk of bias and excluded from the analysis.

We considered all studies using the diagnostic criteria for EoE without researcher validation, such as code-based studies ($k = 40$), and strict studies using the diagnostic criteria for EoE with researcher validation ($k = 30$). We performed extensive subgroup analyses stratified by country, sex, age group, geographical area, diagnostic criteria of EoE (ie, those provided by either the 2007,[8] 2011,[9] or 2018[1] guidelines), and data source. Furthermore, we compared subgroup differences in EoE incidence and prevalence using the mean difference with 95% confidence intervals (CIs).

High-income countries (HICs) and low- or middle-income countries (LMICs) were divided based on the World Bank 2020.[10] In this study, the HICs included Australia, Canada, Denmark, Ireland, the Netherlands, New Zealand, Poland, Slovenia, Spain, Sweden, Switzerland, and the United States, whereas the LMICs included Brazil, China, and Serbia. The diagnostic criteria for EoE have changed over time (the 2007,[8] 2011,[9] and 2018[1] guidelines). The 2007 consensus definition of EoE is based on its clinical symptoms of esophageal dysfunction, biopsy findings (≥15 eosinophils/HPF), and exclusion of other disorders associated with similar clinical, histological, or endoscopic features, especially pathologic gastroesophageal reflux disease (GERD).[8] The 2011 consensus of EoE is the inclusion of the word chronic, the term immune or antigen-driven, and the term proton pump inhibitor-responsive esophageal eosinophilia.[9] The 2018 guidelines for the definition of EoE include symptoms of esophageal dysfunction, biopsy findings (≥15 eosinophils/HPF), and no other significant causes of symptoms or esophageal eosinophilia with the removal of proton pump inhibitor (PPI) trial requirement.[1]

A random-effects model was used to combine the proportion of subjects with EoE in each study to determine the global pooled incidence and prevalence of EoE. Heterogeneity was assessed using the I^2 statistic,[11] which describes the degree of inconsistency among studies. A value of 0% indicated that there was no observed heterogeneity, and higher values indicated increasing heterogeneity. The global incidence and prevalence of EoE were compared using pooled estimates with 95% CIs. The Egger test and funnel plots were used to assess the publication bias. The 95% prediction interval was used to make our main results robust for the summary of estimates and to assess the

What You Need to Know

Background

Although the most recent systematic review on the prevalence of eosinophilic esophagitis (EoE) was published in 2019, including 29 studies on EoE, it did not investigate national and regional differences. In addition, diagnostic criteria for EoE have been updated recently. The real-world incidence and prevalence of EoE according to a new consensus are not known.

Findings

The global pooled incidence and prevalence of EoE were 5.31 cases per 100,000 inhabitant-years (95% confidence interval, 3.98–6.63) and 40.04 cases per 100,000 inhabitant-years (95% confidence interval, 31.10–48.98), respectively. The pooled prevalence and incidence of EoE were higher in high-income countries, males, and North America. The pooled prevalence and incidence of EoE have increased from 1976 to 2022.

Implications for patient care

This emphasizes the need to increase the diagnostic method's sensitivity and develop well-established EoE treatment guidelines. The significant variation in the incidence and prevalence of EoE worldwide underscores the importance of the genetic, ethnic, and cultural differences in EoE.

Table 1. Characteristics of Previous Studies Assessing Incidence and/or Prevalence for EoE Included in Our Systematic Review

First author, publication year	Country	Setting	Diagnosis criteria[b]	Study design	Period	Age of patients	Total sample	Patients with EoE
Noel RJ et al, 2004	US	Population	Before 2007 consensus	Retrospective	2000–2003	Children	2,397,589[a]	103
Straumann A et al, 2005	Switzerland	Population	Before 2007 consensus	Retrospective	1989–2004	Adults	100,000	23
Cherian S et al, 2006	Australia	Population	Before 2007 consensus	Retrospective	1995–2004	Children	3,198,653[a]	285
Gill R, et al, 2007	US	Population	Before 2007 consensus	Retrospective	1995–2004	Children	600,000	44
Prasad GA et al, 2009	US	Population	After 2007 consensus	Retrospective	1976–2005	Adults and children	120,000	55 adults and 23 children
Dalby K et al, 2010	Denmark	Population	After 2007 consensus	Prospective	2005–2007	Children	256,164	6
Hruz P et al, 2011	Switzerland	Population	After updated consensus 2011	Prospective	1989–2009	Adults and children	90,000	43 adults and 3 children
O'Donnell S et al, 2011	Ireland	Population	After 2007 consensus	Retrospective	2000–2008	Adults and children	350,000	7 adults and 6 children
Van Rhijn BD et al, 2013	Netherlands	Population	After updated consensus 2011	Retrospective	1996–2010	Adults and children	16,615,394	538 adults and 136 children
Syed AA et al, 2012/Stewart MJ et al, 2013	Canada	Population	After updated consensus 2011	Retrospective	2004–2008	Adults and children	1,250,000	338 adults and 83 children
Arias A et al, 2013	Spain	Population	After updated consensus 2011	Retrospective	2005–2011	Adults (>16 years)	89,642	40
Prakash R et al, 2013	US	Population	NA	Retrospective	2010–2013	Adults and children	14,360,300	4680
Dellon ES et al, 2014	US	Population	After updated consensus 2011	Retrospective	2009–2011	Adults and children	11,569,217	4700 adults and 1813 children
Ally MR et al, 2014	US (military)	Military	After updated consensus 2011	Retrospective (ICD code)	2008–2009	Adults (>20 years) and children (<20 years)	10,180,515	987
Ma X et al, 2015	China	Population	After updated consensus 2011	Prospective	NA	Adults (>18 years)	3600	4
Dellon ES et al, 2015	Denmark	Population	After updated consensus 2011	Retrospective	1997–2012	Adults and children	5,528,985[a]	844
Maradey-Romero C et al, 2015	US	Population	After updated consensus 2011	Retrospective	2011–2014	Adults (18-65 years), children (<18 years), and elderly (>65 years)	9,559,570	3360 adults, 1120 children, and 360 elderly
Homan M et al, 2015	Slovenia	Population	After updated consensus 2011	Retrospective	2005–2012	Children (<18 years)	NA	25
Kim S et al, 2015	USA	Population	After updated consensus 2011	Retrospective (ICD code)	2008–2013	Adults (>18 years) and children (<18 years)	3,486,069	1344 adults and 217 children

Table 1. Continued

First author, publication year	Country	Setting	Diagnosis criteria[b]	Study design	Period	Age of patients	Total sample	Patients with EoE
Giriens B et al, 2015	Switzerland	Population	After updated consensus 2011	Retrospective	1993–2013	Adults and children	743,317	167 adult and 12 children
Mansoor E et al, 2016	US	Population	After updated consensus 2011	Retrospective	2010–2015	Adults (18-65 years), children (<18 years), and elderly (>65 years)	30,301,440	5840 adult, 1250 children, and 750 elderly
Warner MJ et al, 2017	Netherlands	Population	After updated consensus 2011	Retrospective	1996–2016	Adults (>18 years) and children (<18 years)	16,291,146	1796 adult and 365 children
Molina-Infante J et al, 2018	Spain	Population	After 2018 guidelines	Prospective	2007–2016	Adults (>16 years)	169,403	137
Goncalves LO et al, 2018	Brazil	Population	After 2018 guidelines	Retrospective	2004–2014	Children (0-14 years)	253,706	63
La Orden Izquierdo E et al, 2018	Spain	Population	After 2018 guidelines	Retrospective	2002–2013	Children (<15 years)	485,355	254
Robson J et al, 2018	US	Population	After 2018 guidelines	Retrospective	2011–2016	Children (<18 years)	895,205	1060
Hommeida S et al, 2018	US	Population	After updated consensus 2011	Retrospective	2005–2015	Children (<18 years)	NA	73
Syed A et al, 2017	US	Population	After updated consensus 2011	Retrospective (ICD code)	2009–2013	Adults	27,183,310	5370
Arias A et al, 2019	Spain	Population	After 2018 guidelines	Prospective	2006–2017	Adults and children	104,737	98 adult and 19 children
Ristic N et al, 2019	Serbia	Population	After 2018 guidelines	Retrospective	2010–2017	Children (<18 years)	410,095	35
Limketkai BN et al, 2019	US	Population	After 2018 guidelines	Prospective	2009–2016	Adults (>18 years) and children (<18 years)	134,013,536	102,048
Weerasekera K et al, 2019	New Zealand	Population	After updated consensus 2011	Retrospective	2011–2015	Adults (>16 years) and children (<16 years)	471,315	152
McGowan EC et al, 2020	US	Population	After updated consensus 2011	Retrospective (ICD code)	2012	Children (<17 years)	18,452,886	4836
Zdanowicz K et al, 2020	Poland	Population	After 2018 guidelines	Retrospective	2013–2018	Children (<18 years)	NA	36
RooiJ WE et al, 2020	Netherlands	Population	After 2018 guidelines	Retrospective	1995–2019	Adults (>18 years) and children (<18 years)	16,390,837	3422 adult and 639 children
La Orden Izquierdo E et al, 2021	Spain	Population	After 2018 guidelines	Prospective	2014–2016	Children (<15 years)	NA	148
Melgaard D et al, 2021[3]	Denmark	Population	After 2018 guidelines	Retrospective	2008–2017	Adults	580,000	236

Table 1. Continued

First author, publication year	Country	Setting	Diagnosis criteria[b]	Study design	Period	Age of patients	Total sample	Patients with EoE
Garber et al, 2022	Sweden	Population	After 2018 guidelines	Retrospective	2004–2015	Adults (>18 years) and children (<18 years)	9,672,131	1422
Allin et al, 2022	Denmark	Population	After 2018 guidelines	Retrospective	2008–2018	Adults (>18 years) and children (<18 years)	5,606,705	4011

EoE, Eosinophilic esophagitis; NA, not available; US, United States.
[a]Calculated and estimated from the original data provided in the study.
[b]Guideline definition: The 2007 consensus definition is considered by its related symptoms, biopsy findings (≥15 eosinophils/high-power field), and exclusion of other disorders associated with similar clinical, histological, or endoscopic features; updated 2011 consensus of EoE is inclusion of the word chronic, the term immune or antigen-driven, and the term proton pump inhibitor-responsive esophageal eosinophilia; and 2018 guidelines definition of EoE includes symptoms of esophageal dysfunction, biopsy findings (≥15 eosinophils/high-power field), and no significant other causes of symptoms or esophageal eosinophilia with removal of proton pump inhibitor trial requirements.

uncertainty of our findings using Bayesian statistics.[12] To investigate the impact of time trends, the *P* for the trends was calculated. Microsoft Excel (version 2013) and R software (version 3.1.1; R Foundation) were used to calculate the main results and generate all tables. A 2-sided *P*-value of $< .05$, was considered significant.

Results

The search strategy identified 2987 studies. Of these, 180 studies were evaluated, and 136 were excluded due to inappropriate study design, a lack of population-based studies, or a lack of focus on the outcome of EoE. A total of 40 studies met the eligibility criteria (total studies, k = 40; researcher-validated studies, k = 30) and included a total of 287,974,384 participants and 147,668 patients from 15 countries (Australia, Brazil, Canada, China, Denmark, Ireland, the Netherlands, New Zealand, Poland, Serbia, Slovenia, Spain, Sweden, Switzerland, and the United States).[3,13-51] The 30 researcher-validated studies included a total sample of 41,791,440 participants and 12,983 patients from 15 countries (Australia, Brazil, Canada, China, Denmark, Ireland, the Netherlands, New Zealand, Poland, Serbia, Slovenia, Spain, Sweden, Switzerland, and the United States).[13-22,24,25,28,29,31,35-40,42-44,46-51] Supplementary Figure 1 summarizes the results of the search strategy. All studies were performed in a single country. The EoE data of patients from 1976 to 2022 were included; all were population-based studies. Twenty-one studies included both children and adults[3,17,19-21,23-28,30,32,33,38,39,41,44,47,50,51]; 6 studies included only adults[14,22,31,34,37,49]; and 13 studies included only children.[13,15,16,18,29,35,36,40,42,43,45,46,48] The detailed characteristics of all included studies are shown in Table 1.

Global Pooled Incidence of EoE

The global pooled incidence of EoE in the 27 included studies was 5.31 cases per 100,000 inhabitant-years (95% CI, 3.98–6.63; I^2 = 99.7%) with a 95% PI of −1.72 to 12.34[13-22,24,28,29,35-37,39,40,42-44,46-51] (Table 2). The pooled incidence of EoE was higher in the HIC group[13-22,24,28,29,36,37,39,40,43,44,46-51] than in the LMIC group[35,42] (5.63; 95% CI, 4.24–7.03 vs 1.64; 95% CI, 0.04–3.24 cases per 100,000 inhabitant-years). The incidence studies included Serbia and Brazil as LMICs. The pooled incidence of EoE was higher in males[17,22,25,37-39,47,48,50] than in females[17,22,25,37-39,47,48,50] (9.38; 95% CI, 7.49–11.28 vs 2.83; 95% CI, 2.05–3.62 per 100,000 inhabitant-years). The odds ratio (OR) for EoE in male compared with female was 3.94 (95% CI, 2.78–5.59). The pooled incidence of EoE was higher in adults[14,22,37,39,44,47,49,50] compared with children[13,15,16,18,29,35,36,39,40,42-44,46-48,50] (7.20; 95% CI, 4.84–9.56 vs 4.95; 95% CI, 3.91–5.98 cases per 100,000 inhabitant-years) (Supplementary Tables 12 and 13). The

OR for EoE in adults compared with children was 1.45 (95% CI, 0.97–2.17). However, when sorted by sex and age group, the pooled incidence of EoE was highest in male children[39,40] (18.88; 95% CI, 15.31–22.44), followed by male adults[22,37,39] (13.36; 95% CI, 10.90–15.81), and lowest in female adults[22,37,39] (2.22; 95% CI, 0.17–4.26). The pooled incidence of EoE was higher in North America[13,16,17,21,24,36,43] than in Europe[14,18-20,22,28,29,37,39,40,42,46-51] or Oceania[15,44] (10.02; 95% CI, 6.53–13.52 vs 4.16; 95% CI, 2.47–5.86 or 4.99; 95% CI, 1.22–8.76 cases per 100,000 inhabitant-years, respectively). In addition, the pooled incidence of EoE was lower in researcher validation cases studies[13-22,24,28,29,35-37,39,40,42-44,46-51] compared with code-based studies[3,23,26,27,30,32-34,41] (5.31; 95% CI, 3.98–6.63 vs 9.53; 95% CI, 6.69–12.38 per 100,000 inhabitant-years) (Supplementary Table 2).

The national pooled incidence of EoE in individual countries is shown in Supplementary Tables 4, 5, and Figure 1 (*A*). The incidence of EoE tends to increase with time. The incidence was 0.31 (95% CI, 0.19–0.42) cases per 100,000 inhabitant-years before the year 2001,[13-15,17,19,25,47] 0.79 (95% CI, 0.55–1.03) during the years 2002 to 2004,[13-17,19,28,35,38,40,47] 1.53 (95% CI, 1.15–1.91) during 2005 to 2007,[18-21,24,28,29,35-37,39,40,47,51] 4.10 (95% CI, 2.66–5.55) during 2008 to 2010,[19,22,25,28,29,35,37,39,40,42,50,51] 6.95 (95% CI, 5.60–8.30) during 2011 to 2013,[28,29,35-37,39,40,42-44,46,49-51] 8.42 (95% CI, 7.23–9.61) during 2014 to 2016,[36-39,42-44,46,48,49,51] and 6.81 (95% CI, 2.32–11.31) during 2017 to 2022.[39,42,46,47,50] The pooled incidence was highest in 2014 to 2016. Details of the characteristics of the time trends in pooled EoE incidence are provided in Supplementary Tables 8 and 9. The time trends in the incidence of EoE showed a significant increase in our systematic review (P_{trend} = .002) (Figure 2 and Supplementary Figures 2 and 3). In addition, temporal trends in the incidence rates of EoE within the longitudinal cohort studies included in our systematic review are presented in Figure 3. These global prevalence patterns of EoE in cohort studies followed similar patterns.

Global Pooled Prevalence of EoE

The global pooled prevalence of EoE in the 20 included studies was 40.04 cases per 100,000 inhabitant-years (95% CI, 31.10–48.98; I^2 = 99.6%), with a 95% PI of −1.86 to 81.94[13-19,21,22,24,28,31,35,37,39,40,42,43,47,50] (Table 3). The pooled prevalence of EoE was higher in HICs[13-19,21,22,24,28,37,39,40,43,47,50] than in LMICs[31,35,42] (45.05; 95% CI, 34.97–55.12 vs. 14.17;95% CI, 1.73–26.61 cases per 100,000 inhabitant-years, respectively). Prevalence studies have shown that LMICs include Serbia, China, and Brazil. The pooled prevalence of EoE was higher in males[17,22,37,39,50] than in females[17,22,37,39,50] (111.09; 95% CI, 84.70–137.47 vs 32.83; 95% CI, 14.16–51.50 cases per 100,000 inhabitant-years). The OR for EoE in males compared with females was 3.38 (95% CI, 1.69–6.74). The pooled prevalence of EoE was higher in adults[14,22,31,37,39] than in children[13,15,16,18,35,39,40,42,43,50] (52.95; 95% CI, 21.95–83.96 vs 32.90; 95% CI, 22.69–43.12 per 100,000 inhabitant-years) (Supplementary Tables 14 and 15). The OR for EoE in adults compared with children was 1.60 (95% CI, 0.77–3.39). However, when sorted by sex and age group, the pooled prevalence of EoE was highest in male children[39] (172.00; 95% CI, 96.30–283.50), followed by male adults[22,37,39] (131.40; 95% CI, 78.34–184.47 cases per 100,000 inhabitant-years), and lowest in female adults[22,37,39] (23.01; 95% CI, −1.08 to 47.09 cases per 100,000 inhabitant-years). The pooled prevalence of EoE was higher in North America[13,16,17,21,24,43] compared with Europe[14,18,19,22,28,37,39,40,42,47,50] (50.99; 95% CI, 18.95–83.03 vs 42.49; 95% CI, 29.04–55.93 cases per 100,000 inhabitant-years) (Supplementary Table 3).

The national pooled prevalence of EoE in individual countries is shown in Supplementary Tables 6 and 7 and Figure 1 (*B*). The prevalence of EoE has also increased over time. Before the year 2001:[19] 8.18; 95% CI, 3.67–12.69 cases per 100,000 inhabitant-years; 2002 to 2004:[13,14,16,17,19] 27.64; 95% CI, 11.04–44.23; 2005 to 2007:[18,19,21,24] 20.74; 95% CI, −3.85 to 45.32; 2008 to 2010:[19,22] 43.27; 95% CI, 35.92–50.61; 2011 to 2013:[28,40,50] 32.36; 95% CI, 20.24–44.49; 2014 to 2016:[31,37,43] 70.44; 95% CI, 0.74–140.14; and 2017 to 2022:[39,47,50] 74.42; 95% CI, 39.66–109.19. The pooled prevalence was the highest in 2017 to 2022. Details of the characteristics of the time trends in the pooled prevalence of EoE are provided in Supplementary Tables 10 and 11 and Figure 2. The time trends in the prevalence of EoE showed a significant increase in our systematic review (P_{trend} = .004) (Figure 2 and Supplementary Figures 2 and 3).

Publication Bias Assessment. Funnel plots were evaluated for asymmetry and were found to be at low risk of publication bias (Egger test: P = .181 for the overall incidence of EoE and P = .168 for the overall prevalence of EoE). However, funnel plots showed asymmetry in some subgroup analyses of the incidence and prevalence of EoE, indicating evidence of publication bias. Details of the funnel plots for the incidence and prevalence of EoE studies are provided in Supplementary Figures 4 through 70.

Forty-five studies were evaluated to determine the risk of bias. Five studies were evaluated as having a high risk of bias and excluded from the analysis.[52-56] Eight studies were evaluated as having a moderate risk of bias,[23,24,26-28,30,34,45] and 32 studies were evaluated as having a low risk of bias.[3,13-20,22,25,29,31-44,46-51] The questions used to evaluate the risk in most studies were "Was the study's target population a close representation of the national population in relation to relevant variables?" (which corresponds to 28 studies[13-22,24,27,28,30,31,36,37,39,40,42-44,46,48,49,52,53,56]); "Was some form of random selection used to select the sample or was a census undertaken?" (24 studies[3,20,21,23,24,26,32,33,38,41,42,44-56]); and "Was the study

Table 2. Global Pooled Incidence of EoE Included in Our Systematic Review (Researcher-validated Studies)

	Number of studies	Number of participants	Pooled estimates (95% CI)[a]	95% prediction interval	I^2, %	*P* value for I^2	Egger *P* value
Overall incidence	27	42,191,506	5.31 (3.98–6.63)	−1.72 to 12.34	99.7	< .0001	.181
Income							
HICs	26	41,527,705	5.63 (4.24–7.03)	−1.51 to 12.77	99.7	< .0001	.259
LMICs	2	663,801	1.64 (0.04–3.24)	NA	95.4	< .0001	NA
Gender							
Male	12	6,197,870	9.38 (7.49–11.28)	2.38–16.38	98.3	< .0001	.003
Female	12	6,265,280	2.83 (2.05–3.62)	0.04–5.62	96.0	< .0001	.012
Age group							
Children	18	7,482,819	4.95 (3.91–5.98)	0.77–9.14	97.7	< .0001	.001
Adults	9	4,433,903	7.20 (4.84–9.56)	−1.67 to 16.07	99.7	< .0001	.778
Gender and age group							
Male children	3	507,807	18.88 (15.31–22.44)	−4.20 to 41.96	<0.0001	.781	.032
Female children	3	482,621	8.71 (4.69–12.72)	−35.39 to 52.82	62.5	.07	.424
Male adults	3	127,632	13.36 (10.90–15.81)	−10.88 to 37.60	43.7	.169	.789
Female adults	3	131,680	2.22 (0.17–4.26)	−23.17 to 27.61	90.2	< .0001	.259
Geographical areas							
North America	8	2,564,963	10.02 (6.53–13.52)	−1.21 to 21.25	98.9	< .0001	.054
Europe	17	35,702,869	4.16 (2.47–5.86)	−3.54 to 11.86	99.8	< .0001	.139
Oceania	2	3,669,968	4.99 (1.22–8.76)	NA	97.6	< .0001	NA
Diagnostic criteria for EoE[a]							
Before 2007 consensus	4	3,598,411	3.67 (1.57–5.77)	−6.26 to 13.60	98.4	< .0001	.421
After 2007 consensus	3	726,164	2.36 (1.61–3.11)	−4.50 to 9.22	26.1	.258	.882
After updated consensus 2011	10	18,935,420	4.96 (2.19–7.73)	−4.62 to 14.54	99.9	< .0001	.484
After 2018 guidelines	12	34,822,591	6.32 (4.81–7.83)	0.31–12.33	98.9	< .0001	< .001

CI, Confidence interval; EoE, eosinophilic esophagitis; HICs, high-income countries; LMICs, low- or middle-income countries (Serbia and Brazil); NA, not available.
[a]Guideline definition: The 2007 consensus definition is based on its-related symptoms, biopsy findings (≥15 eosinophils/high-power field), and exclusion of other disorders associated with similar clinical, histological, or endoscopic features; updated 2011 consensus of EoE is inclusion of the word chronic, the term immune or antigen driven, and the term proton pump inhibitor-responsive esophageal eosinophilia; and 2018 guidelines definition of EoE includes symptoms of esophageal dysfunction, biopsy findings (≥15 eosinophils/ high-power field), and no significant other causes of symptoms or esophageal eosinophilia with removal of proton pump inhibitor trial requirement.

instrument that measured the parameter of interest shown to have reliability and validity?" (19 studies[21,23-28,30-34,38,41,45,53-56]). Details of the risk of bias for the prevalence studies are provided in Supplementary Table 16.

Discussion

Findings From Our Study

This systematic review and meta-analysis collected data from 1976 to 2022 and reports the incidence and prevalence of EoE in 40 studies with a total sample size of 287,974,384 participants and 147,668 patients. The global pooled incidence of EoE was 5.31 cases per 100,000 inhabitant-years, and the global pooled prevalence was 40.04 cases per 100,000 inhabitant-years. The pooled prevalence and incidence of EoE were higher in HICs, males, and North America. The pooled prevalence of EoE gradually increased from 1976 to 2022 (1976–2001: 8.18; 95% CI, 3.67–12.69 vs 2017–2022: 74.42; 95% CI, 39.66–109.19 cases per 100,000 inhabitant-years). The incidence and prevalence of EoE vary widely by region, which may be a consequence of underdiagnosis. In particular, in LMICs, the prevalence of EoE in the general population has not been studied, and the rate of endoscopy and doctors' disease awareness is probably low, leading to underdiagnosis.[45,57] To determine the incidence and prevalence of EoE in unanalyzed LMICs, it is necessary to raise awareness of EoE globally.

Comparison With Previous Studies

Several reviews have evaluated the incidence and prevalence of EoEs in the general population. The most recent systematic review was published in 2019, which analyzed 29 studies on EoE.[5] According to the study, the overall incidence of EoE was 4.4 cases per 100,000 inhabitant-years, and the overall prevalence of EoE was 34.2 cases per 100,000 inhabitant-years, which is similar to our study. By region, North America showed a higher incidence and prevalence than Europe, which is consistent with our results. However, some studies were excluded because the electronic medical database was

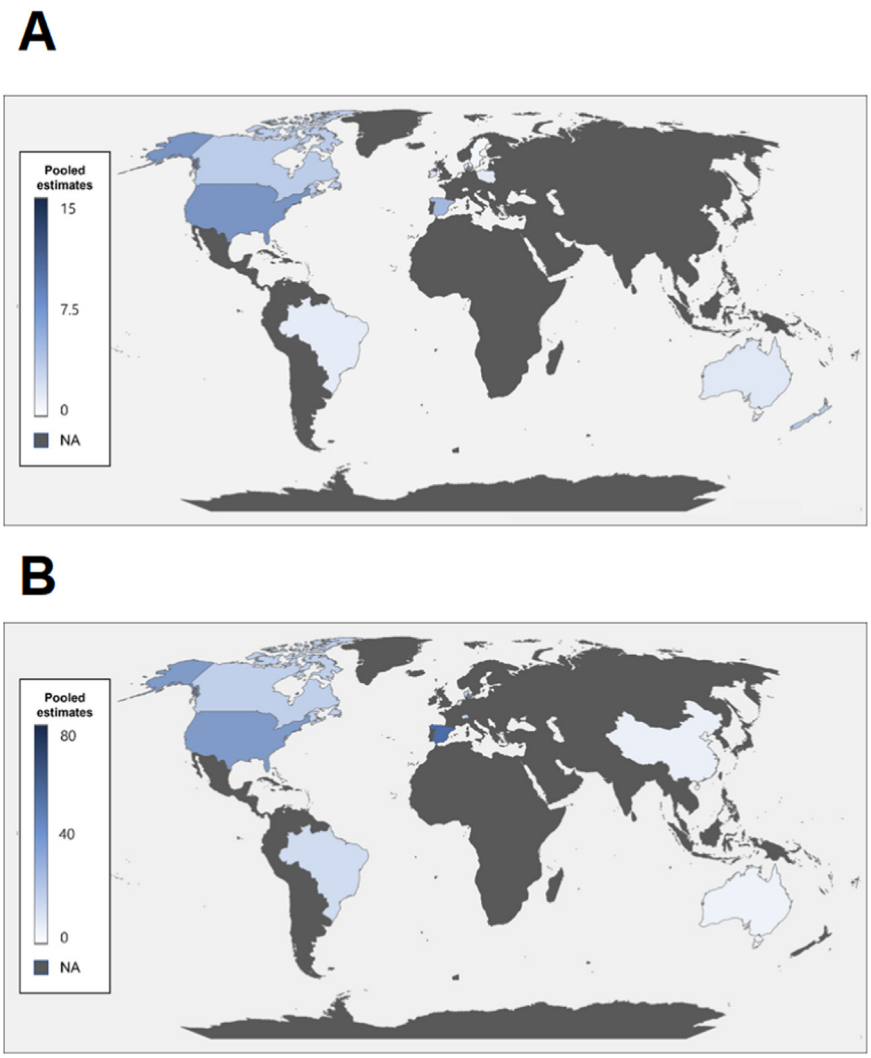

Figure 1. Global incidence (*A*) and prevalence (*B*) of EoE, 1976 to 2022. Pooled estimates, cases per 100,000 inhabitant-years.

not sufficiently included in their review; therefore, only 29 studies were included. In addition, since the new EoE diagnostic criteria were proposed in 2018 and the study was published in 2019, the ability to assess the incidence and prevalence of EoE after the 2018 diagnostic criteria was updated and expanded is limited. In addition, there were no data on sex, age, or racial comparisons, and only data from Western countries were included in the analysis. Other studies have analyzed the incidence and prevalence of EoE by country only,[5] not by looking at global or regional trends in EoE. This emphasizes the need for research that reflects the latest trends, such as those observed in our study.

Possible Explanation of Our Results

In our study, the incidence and prevalence of EoE increased by 27.2 and 9.1 times, respectively, compared with those before the 2000s. In the 2000s, it was reported that the incidence of EoE increased by 40% or 5 times, over 4 years,[13,21,] and by 27 times over 10 years.[17] Therefore, the incidence and prevalence of EoE have continued to increase, likely for several reasons. First, there were effects due to changes in EoE diagnostic criteria. The 2007 criteria required more than 15 eosinophils/HPF in the esophageal biopsy and the absence of pathologic GERD. However, the 2011 updated consensus included the term PPI-responsive esophageal eosinophilia, which indicates a potential disease phenotype. According to the 2018 guidelines, patients responding to PPI therapy were part of the EoE continuum, and EoE and GERD co-existed. Therefore, patients with EoE may have been underestimated by excluding those with response to PPIs, or GERD. Second, several studies have shown a relationship between early life exposure and EoE. The use of antibiotics during the first year of life,[58] admission to the neonatal intensive care unit,[59] maternal fever,[60] cesarean delivery,[58] and preterm labor[60] substantially increased the risk of developing EoE, whereas breastfeeding and having a pet at home decreased the risk of EoE.[59,60] In addition, studies have shown that Helicobacter pylori and EoE are strongly negatively correlated,[61] and PPI and EoE are positively correlated.[58,62] Advances in medicine have led to the increased use of antibiotics and PPI during the first year of life, an increased number of preterm infants

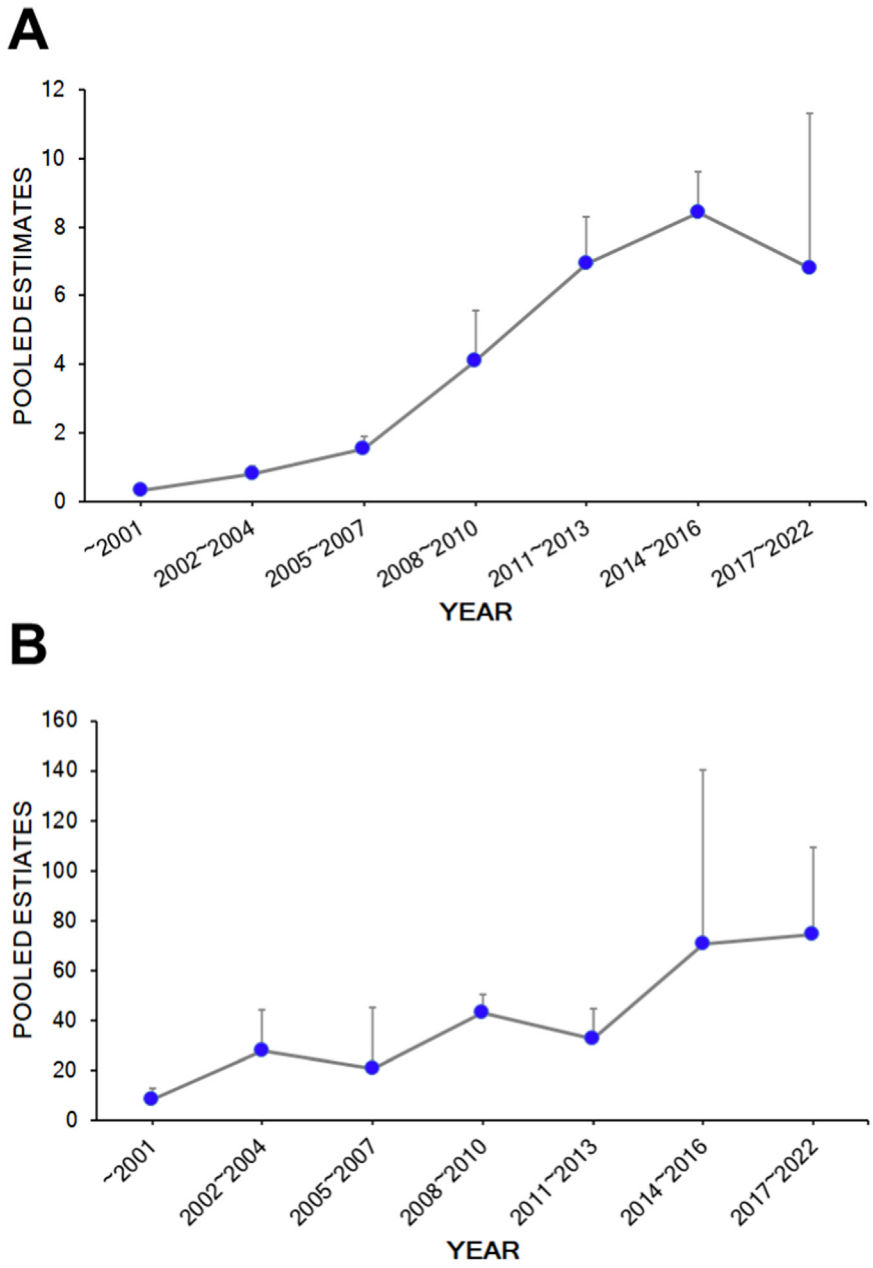

Figure 2. Time trends of incidence (*A*) and prevalence (*B*) of EoE, 1976 to 2022. Pooled estimates, cases per 100,000 inhabitant-years.

and neonatal intensive care unit admissions, and a reduced incidence of Helicobacter pylori infection. These factors may have contributed to the increased incidence of EoEs. Third, since endoscopy has become common in the diagnosis of gastrointestinal diseases, and because EoE diagnosis is based on patient symptoms and endoscopic biopsy, this has led to an increase in disease awareness and increased incidence and prevalence of EoE.[5] Fourth, it may be associated with an increased prevalence of immune-mediated diseases. The prevalence of atopic and allergic diseases is increasing.[4] Studies on the genetic etiology of EoE have been actively conducted, including the confirmation of significant genetic sharing between EoE and other immune-mediated diseases,[63] and the risk of EoE incidence increased with a history of atopy or food allergy.[64] Therefore, the increase in the prevalence of immune-mediated diseases such as EoE, atopy, and allergies may be interconnected and a global phenomenon.

There are several possible reasons for the differences in the incidence and prevalence of EoE between regions and countries. Each country or region has different sociocultural factors, degrees of perception of symptoms, dietary patterns, and environmental factors.[55,65] In particular, health care services differ from country to country, and, in the case of EoE,[66] because endoscopic biopsy is essential for diagnosis, the incidence may differ. In addition, the higher incidence and prevalence of EoE in HICs than in LMICs may be due to the differences in food allergies, allergic diseases, and atopic diseases.[67] LMICs have a lower incidence and prevalence of allergic diseases. With improved hygiene

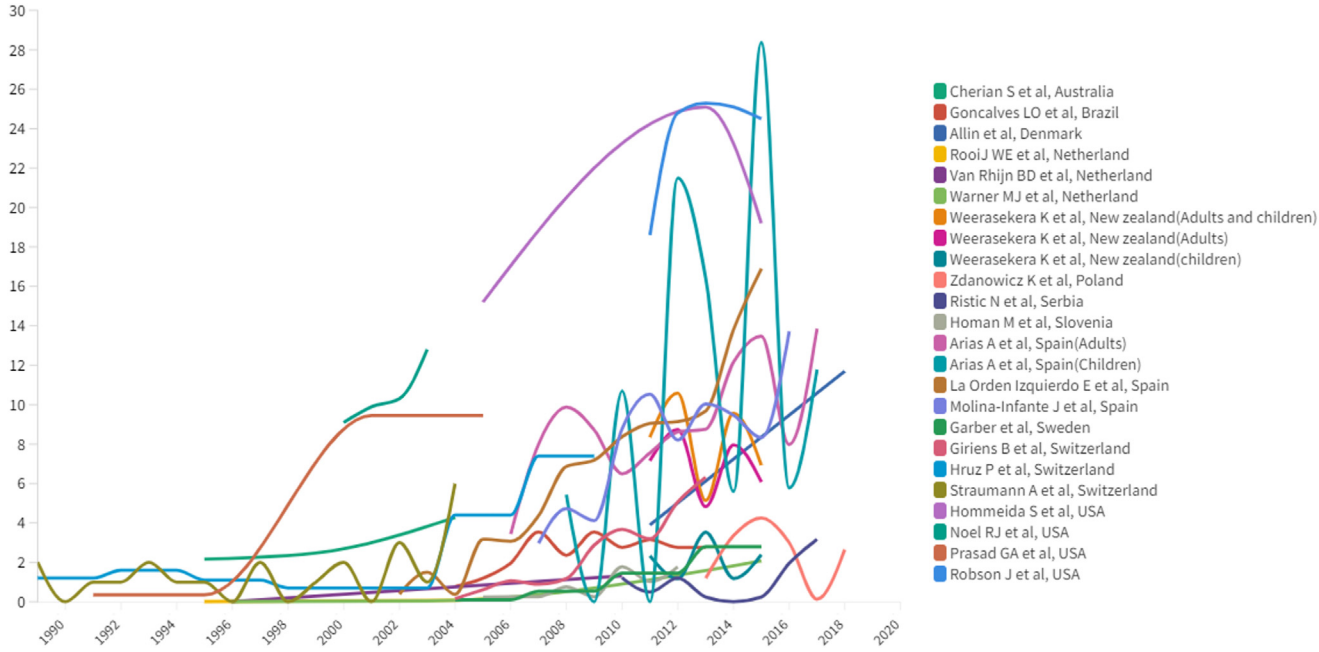

Figure 3. Temporal trends of incidence rates of EoE included in our systematic review.

and sanitation conditions, allergic diseases are more likely to appear.[68]

Strengths and Limitations

This study has several limitations. First, there is a lack of representation outside the United States and Europe in the incidence and prevalence of EoE. Here, we investigated the incidence and prevalence of EoE in the general population. North America and Europe were mainly included in the study; there was no literature available regarding South America, Asia, and Africa, except for Brazil and China. Therefore, it is difficult to clarify the regional differences in the incidence or prevalence of EoE. To address this, we attempted to express regional differences by presenting an analysis by country and race as much as possible. Second, for the diagnosis of EoE, endoscopic biopsy and patient symptoms are essential. As endoscopy has become more common, the incidence of EoE has inevitably increased. In addition, the symptoms of EoE may differ according to race,[69,70] and the difference in the rate of endoscopy based on the symptoms may appear as a racial difference. Moreover, in countries where endoscopy is difficult, the incidence of EoE can be misrepresented as being low. Further studies using a reliable noninvasive diagnostic method are needed to clearly identify regional and racial differences in EoE. However, the current study investigated the incidence and prevalence of EoE according to guidelines that require an invasive diagnostic method. Third, there was significant heterogeneity between the studies in our analysis; therefore, the results should be interpreted with caution. The possible reasons for this heterogeneity include the characteristics of prevalence studies, multiple changes in the diagnostic criteria for EoE, differences in biopsy protocols, differences in endoscopic operators, demographic or cultural differences between study populations, and the fact that EoE is diagnosed only with endoscopy.[71] In addition, the incidence and prevalence of EoE have increased significantly as the diagnostic criteria for EoE have been revised. Meta-analysis studies with increased incidence and prevalence of diseases have shown higher heterogeneity.[72,73] In addition, EoE is diagnosed only through endoscopy procedures, and therefore, the estimates of the incidence and prevalence of EoE are mainly dependent on the rate at which endoscopies are performed in a country and region. Therefore, regional differences appeared regardless of the actual prevalence of EoE, particularly in countries or regions with poor access to health care facilities. However, our summary data may be useful for understanding the incidence and prevalence of EoE from a global perspective despite the heterogeneity between studies. Fourth, only the studies published in English were included in the analysis. The diversity of our analysis may have been reduced by excluding foreign-language studies. Fifth, some pooled estimates or 95% prediction intervalss estimated as negative values in Tables 2 and 3 are considered to have sparse data bias.[74] Therefore, caution should be exercised when interpreting these results. Sixth, we did not perform a meta-regression analysis. Since there was a significant degree of heterogeneity between studies in our analysis, we should speculate the reason for the variance and perform meta-regression to explain it. However, the number of studies was insufficient to perform a meta-regression analysis. Therefore, we attempted to explain heterogeneity through various subgroup analyses.

Table 3. Global Pooled Prevalence of EoE Included in Our Systematic Review (Researcher-validated Studies)

	Number of studies	Number of participants	Pooled estimates (95% CI)[a]	95% prediction interval	I^2, %	*P* value for I^2	Egger *P* value
Overall prevalence	20	30,467,177	40.04 (31.10–48.98)	−1.86 to 81.94	99.6	< .0001	.168
Income							
HICs	16	29,799,776	45.05 (34.97–55.12)	0.61–89.49	99.6	< .0001	.133
LMICs	3	667,401	14.17 (1.73–26.61)	−141.26 to 169.60	93.0	< .0001	.506
Gender							
Male	6	2,917,196	111.09 (84.70–137.47)	23.82–198.36	88.8	< .0001	.620
Female	6	2,965,248	32.83 (14.16–51.50)	−32.33 to 97.99	96.4	< .0001	.619
Age group							
Children	10	6,992,753	32.90 (22.69–43.12)	−5.16 to 70.96	99.3	< .0001	.034
Adults	5	452,686	52.95 (21.95–83.96)	−68.12 to 174.02	96.6	< .0001	.047
Gender and age group							
Male children	1	8,721	172.00 (96.30–283.50)	NA	NA	NA	NA
Female children	1	8,263	48.41 (13.20–123.90)	NA	NA	NA	NA
Male adults	3	126,684	131.40 (78.34–184.47)	−525.91 to 788.71	89.2	< .0001	.513
Female adults	3	130,971	23.01 (-1.08–47.09)	−278.95 to 324.97	92.4	< .0001	.270
Geographical areas							
North America	5	2,564,963	50.99 (18.95–83.03)	−75.86 to 177.84	99.6	< .0001	.155
Europe	11	24,356,255	42.49 (29.04–55.93)	−10.17 to 95.15	99.6	< .0001	.436
Diagnostic criteria for EoE[a]							
Before 2007 consensus	4	3,598,411	18.41 (11.05–25.78)	−15.36 to 52.18	95.8	< .0001	.227
After 2007 consensus	2	376,164	27.79 (-22.87–78.45)	NA	98.6	< .0001	NA
After updated consensus 2011	6	18,467,705	27.64 (17.16–38.11)	−10.06 to 65.34	97.9	< .0001	.068
After 2018 guidelines	8	24,316,043	60.20 (39.94–80.45)	−14.74 to 135.14	99.7	< .0001	.190

CI, Confidence interval; EoE, eosinophilic esophagitis; HICs, high-income countries; LMICs, low- or middle-income countries (Serbia, China, and Brazil); NA, not available.

[a]Guideline definition: The 2007 consensus definition is based on its related symptoms, biopsy findings (≥15 eosinophils/high-power field), and exclusion of other disorders associated with similar clinical, histological, or endoscopic features; updated 2011 consensus of EoE is inclusion of the word chronic, the term immune or antigen driven, and the term proton pump inhibitor-responsive esophageal eosinophilia; and 2018 guidelines definition of EoE includes symptoms of esophageal dysfunction, biopsy findings (≥15 eosinophils/ high-power field), and no significant other causes of symptoms or esophageal eosinophilia with removal of proton pump inhibitor trial requirement.

Finally, EoE risk factors and the association between EoE and other atopic diseases were not examined. Studies have reported the risk factors for EoE,[75] and studies on its association with other atopic or allergic diseases have also been reported.[76] Further research is needed to determine the correlation between the incidence and prevalence of allergic diseases, including EoE, atopic disorders, and food allergies.

Despite these limitations, this study had several strengths. To identify all studies on EoE, we searched for studies using a number of literature databases. In addition, the incidence and prevalence after revision of the EoE diagnostic criteria were analyzed to determine trends according to the diagnostic criteria. Compared with a previous study conducted in 2019,[5] the incidence and prevalence of EoE were analyzed according to sex, age, race, and country. Based on this, the incidence and prevalence of EoE have been presented as world maps for the first time. We assessed for case validation of all studies included in the research, and overall incidence, overall prevalence, and subgroup analysis of EoE were conducted only with researcher validation cases studies. In addition, the subgroup analysis by researcher validation cases studies showed a lower incidence of EoE than code-based studies (5.31; 95% CI, 3.98–6.63 vs 9.53; 95% CI, 6.69–12.38 per 100,000 inhabitant-years), suggesting a code-based approach leads to an overestimation of incidence of EoE. By suggesting the prediction interval for EoE, sophisticated statistical techniques can be used to study the incidence and prevalence of EoE in the future. Finally, only studies involving the general EoE population were included in the analysis.

Conclusion

In conclusion, our study demonstrated the incidence and prevalence of EoE according to sex, age, race, geographical region, and diagnostic criteria. Our results showed that the incidence and prevalence of EoE are continuously increasing, indicating that EoE may become a global health burden in the future. This emphasizes the need to increase the sensitivity of the diagnostic method

and to develop well-established EoE treatment guidelines. Further research is needed in Asia, South America, and Africa to evaluate the incidence and prevalence of EoE in these regions. Finally, the significant variation in the incidence and prevalence of EoE worldwide underscores the importance of genetic, ethnic, and cultural differences in EoE.

Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Clinical Gastroenterology and Hepatology* at www.cghjournal.org, and at https://doi.org/10.1016/j.cgh.2023.06.005.

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Conflicts of interest
The authors disclose no conflicts.

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Supplementary Results

A total of 40 studies met the eligibility criteria.

Global Pooled Prevalence of Eosinophilic Esophagitis

In total, 4 studies used the diagnostic criteria of eosinophilic esophagitis (EoE) prior to the 2007 consensus, 2 studies used the 2007 consensus, 6 studies used the updated consensus 2011, and 8 studies used the 2018 guidelines. Overall, there was a trend of increasing the prevalence of EoE according to the diagnostic criteria for EoE: 18.41 (95% confidence interval [CI], 11.05–25.78) cases per 100,000 inhabitant-years before the 2007 consensus, 27.79 (95% CI, −22.87 to 78.45) after the 2007 consensus, 27.64 (95% CI, 17.16–38.11) after the updated consensus of 2011, and 60.20 (95% CI, 39.94–80.45) after the 2018 guidelines.

Global Pooled Incidence of EoE

In total, 4 studies used the diagnostic criteria of EoE prior to the 2007 consensus, 3 studies used the 2007 consensus, 10 studies used the updated consensus 2011, and 12 studies used the 2018 guidelines. Overall, there was a trend of increasing the incidence of EoE according to the diagnostic criteria for EoE: 3.67 (95% CI, 1.57–5.77) cases per 100,000 inhabitant-years before the 2007 consensus, 2.36 (95% CI, 1.61–3.11) after the 2007 consensus, 4.96 (95% CI, 2.19–7.73) after the updated consensus of 2011, and 6.32 (95% CI, 4.81–7.83) after the 2018 guidelines.

National Pooled Incidence of EoE

Most of the nationwide studies were conducted in North America and Europe. No studies have been conducted in Africa or Asia, and only 1 study was conducted in South America. The national pooled incidence of EoE in the individual countries is shown in Supplementary Table 4 and Figure 1 (*A*). The highest incidence of EoE occurred in the United States (10.76; 95% CI, 6.87–14.65) and the lowest in Slovenia (0.79; 95% CI, 0.51–1.16).

Time Trends in Pooled Incidence of EoE

A total of 139 subgroup studies reported the incidence of EoE over time, divided into 3-year intervals.

National Pooled Prevalence of EoE

Similar to incidence studies, most studies evaluating the national prevalence have been conducted in North America or Europe. No studies were conducted in Africa, and only 1 study was conducted in South America and Asia. The highest prevalence of EoE was observed in Spain (71.45 cases per 100,000 inhabitant-years; 95% CI, 47.18–95.72) and the lowest in Serbia (6.83 cases per 100,000 inhabitant-years; 95% CI, 4.96–9.52).

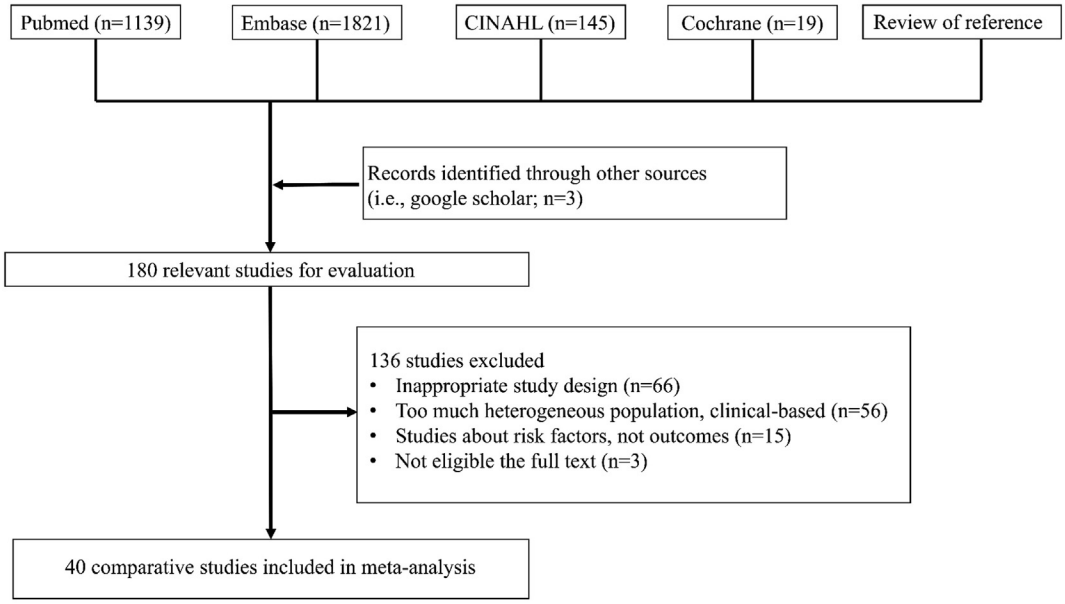
Time Trends in Pooled Prevalence of EoE

There were 24 subgroup studies which reported the prevalence of EoE over time, divided into 3-year intervals.

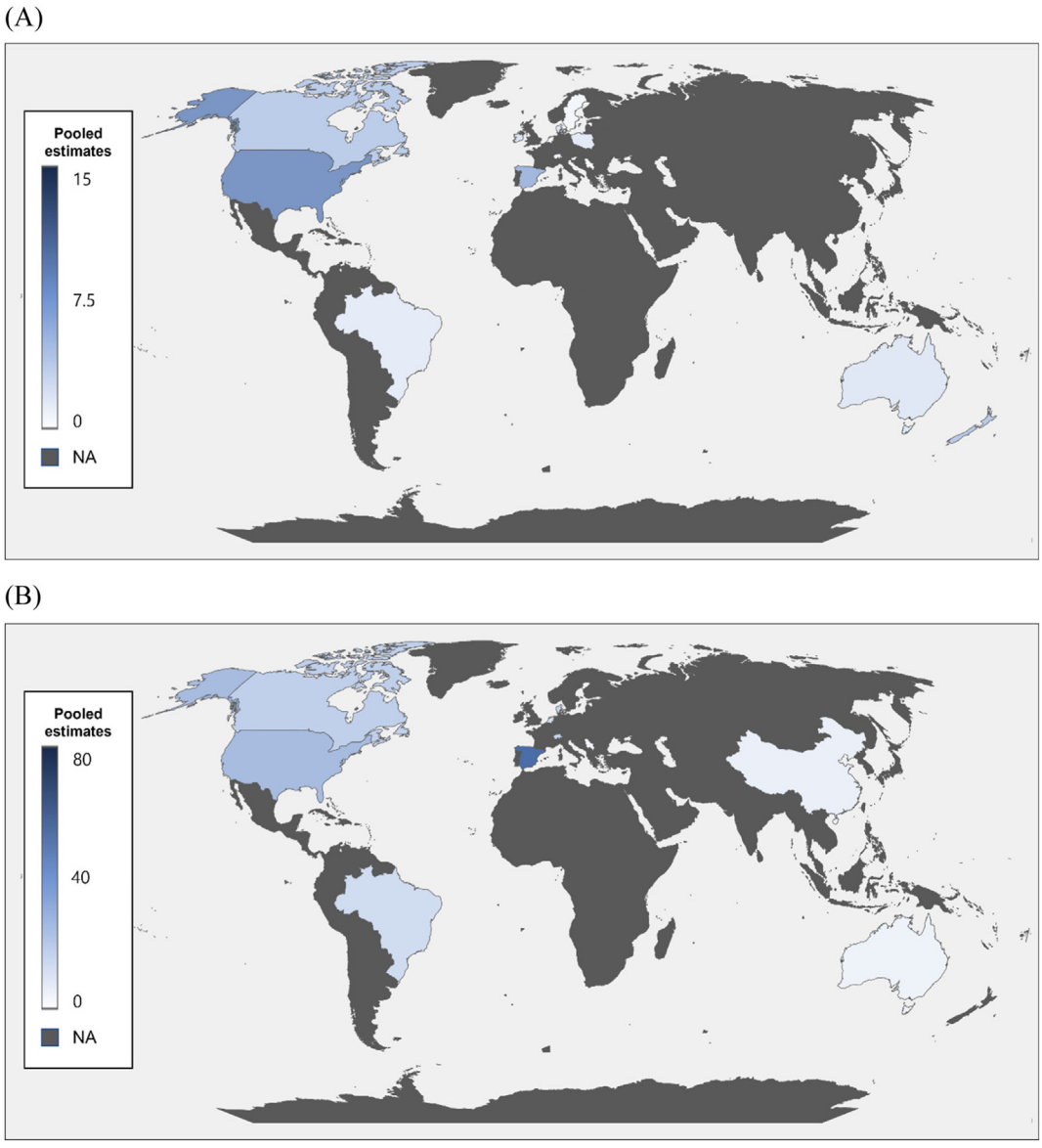
Supplementary discussion

Policy Implication

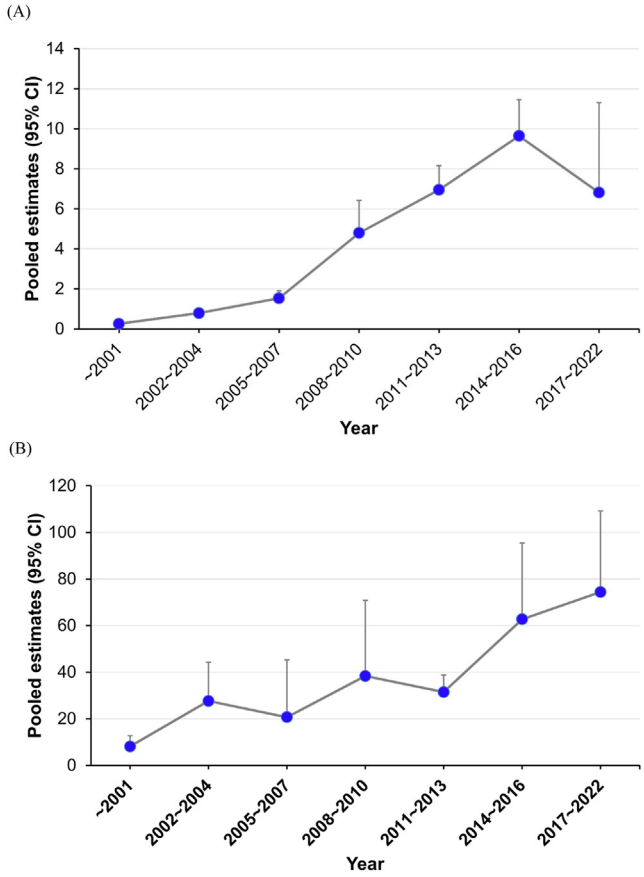
Our study showed that the incidence and prevalence of EoE has been increasing gradually, which deteriorates the quality of life of patients and serves as a health burden worldwide. Although diagnostic delays in EoE have decreased in recent years, EoE remains unrecognized, and complications are common in patients who receive their first medical evaluation. In addition, since disease spectrums have been widely reported, such as EoE being classified into several endotypes, raising disease awareness and sensitivity of the diagnostic method should be considered. To this end, it is necessary to conduct observational research on the incidence and prevalence of EoE in developing countries, where the prevalence of EoE has not been studied. In addition, there is a need to raise awareness of EoE among doctors. Moreover, since endoscopic diagnosis is essential for EoE, the endoscopic implementation rate of this region should also be increased. It is also necessary to develop noninvasive reliable diagnostic biomarkers. There may be limitations to increasing the implementation rate of endoscopes in developing countries, and complications can occur considerably due to the prolonged delay in diagnosing EoE with endoscopy alone. Currently, studies on eosinophil-associated proteins are being actively conducted, and studies on non-endoscopic minimally invasive tests are underway.



Supplementary Figure 1. Flow diagram of study selection.

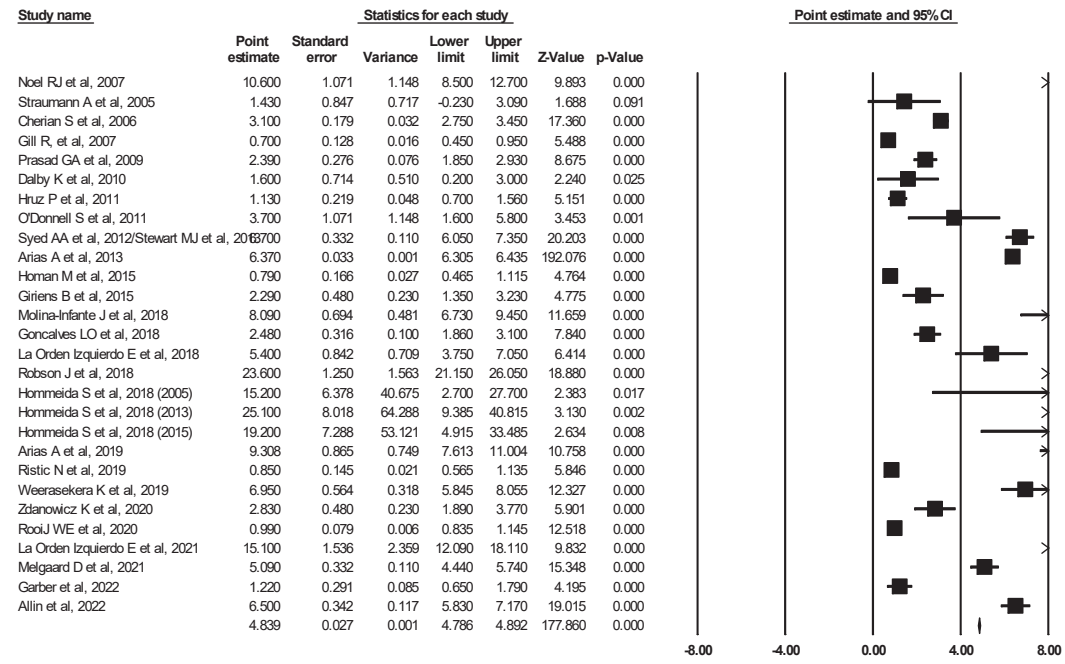


Supplementary Figure 2. Global incidence (*A*) and prevalence (*B*) of EoE, 1976 to 2022. Pooled estimates, cases per 100,000 inhabitant-years (total study).

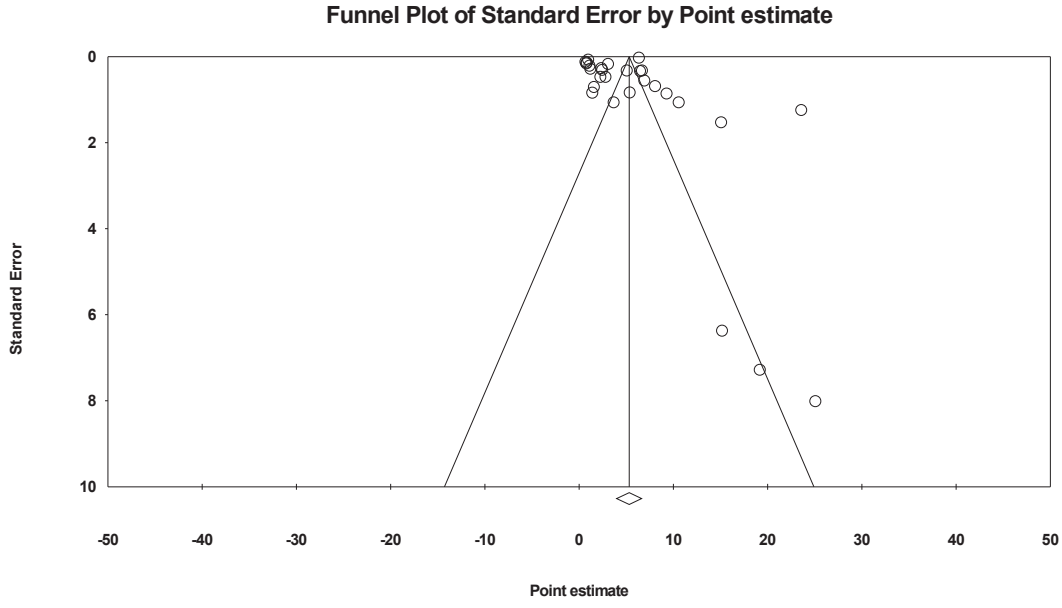


Supplementary Figure 3. Time trends of incidence (*A*) and prevalence (*B*) of EoE, 1976 to 2022. Pooled estimates, cases per 100,000 inhabitant-years (total study).

1) Forest plot

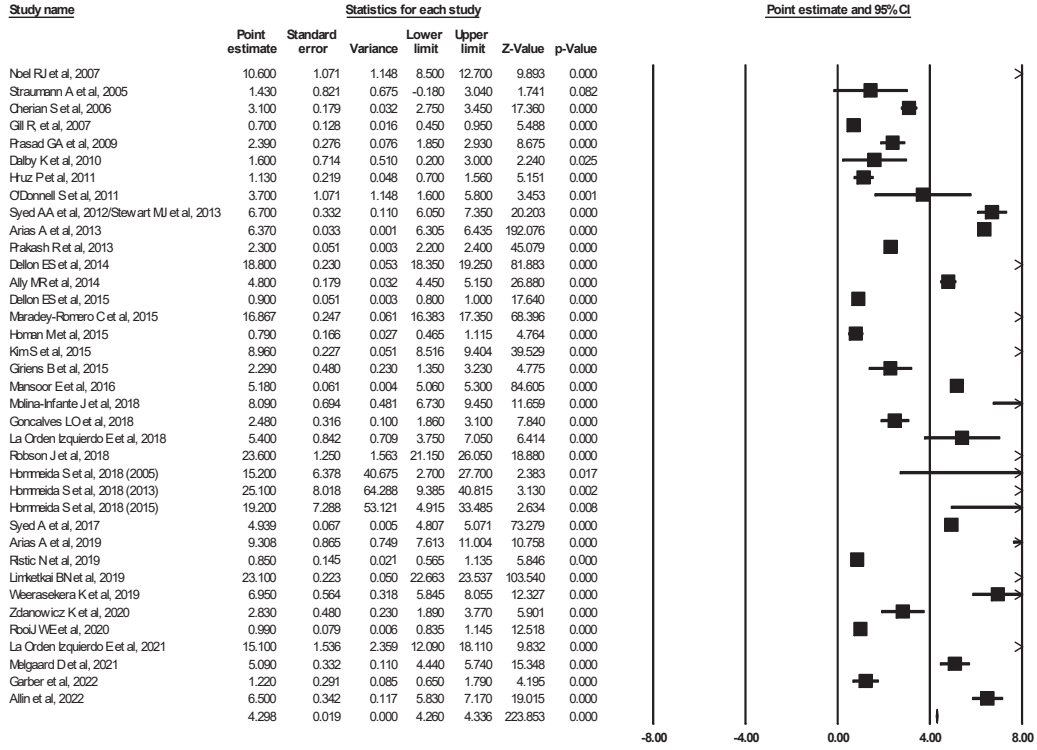


2) Funnel Plot



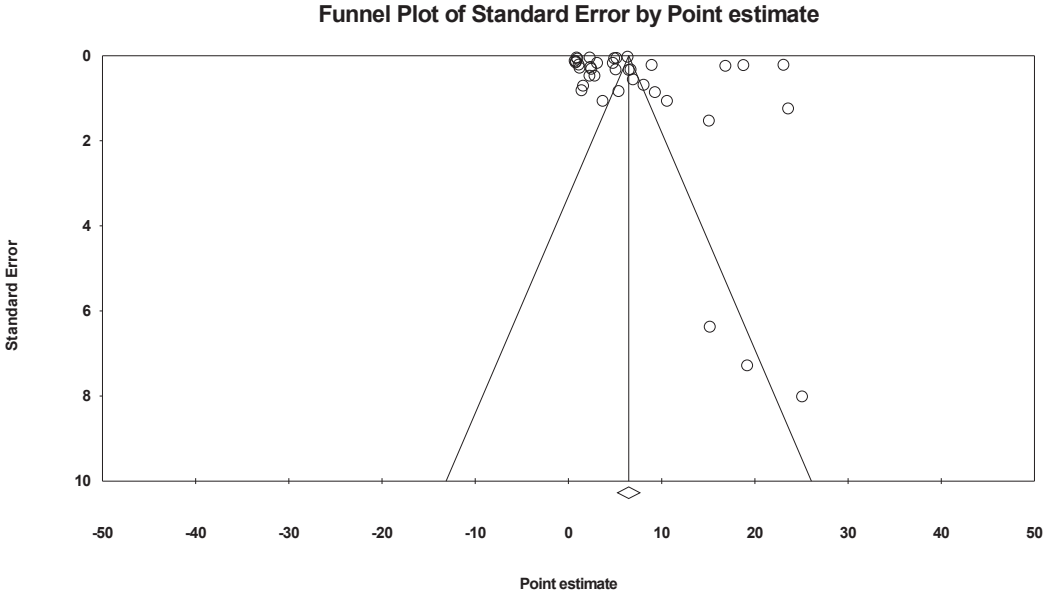
Supplementary Figure 4. Overall incidence of EoE included in our systematic review (researcher-validated studies). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot



Study name	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Noel RJ et al, 2007	10.600	1.071	1.148	8.500	12.700	9.893	0.000
Straumann A et al, 2005	1.430	0.821	0.675	-0.180	3.040	1.741	0.082
Cherian S et al, 2006	3.100	0.179	0.032	2.750	3.450	17.360	0.000
Gill R, et al, 2007	0.700	0.128	0.016	0.450	0.950	5.488	0.000
Prasad GA et al, 2009	2.390	0.276	0.076	1.850	2.930	8.675	0.000
Dalby K et al, 2010	1.600	0.714	0.510	0.200	3.000	2.240	0.025
Hruz P et al, 2011	1.130	0.219	0.048	0.700	1.560	5.151	0.000
O'Donnell S et al, 2011	3.700	1.071	1.148	1.600	5.800	3.453	0.001
Syed AA et al, 2012/Stewart MJ et al, 2013	6.700	0.332	0.110	6.050	7.350	20.203	0.000
Arias A et al, 2013	6.370	0.033	0.001	6.305	6.435	192.076	0.000
Prakash R et al, 2013	2.300	0.051	0.003	2.200	2.400	45.079	0.000
Dellon ES et al, 2014	18.800	0.230	0.053	18.350	19.250	81.883	0.000
Ally MR et al, 2014	4.800	0.179	0.032	4.450	5.150	26.880	0.000
Dellon ES et al, 2015	0.900	0.051	0.003	0.800	1.000	17.640	0.000
Maradey-Romero C et al, 2015	16.867	0.247	0.061	16.383	17.350	68.396	0.000
Homan M et al, 2015	0.790	0.166	0.027	0.465	1.115	4.764	0.000
Kim S et al, 2015	8.960	0.227	0.051	8.516	9.404	39.529	0.000
Giriens B et al, 2015	2.290	0.480	0.230	1.350	3.230	4.775	0.000
Mansoor E et al, 2016	5.180	0.061	0.004	5.060	5.300	84.605	0.000
Molina-Infante J et al, 2018	8.090	0.694	0.481	6.730	9.450	11.659	0.000
Goncalves LO et al, 2018	2.480	0.316	0.100	1.860	3.100	7.840	0.000
La Orden Izquierdo E et al, 2018	5.400	0.842	0.709	3.750	7.050	6.414	0.000
Robson J et al, 2018	23.600	1.250	1.563	21.150	26.050	18.880	0.000
Hommeida S et al, 2018 (2005)	15.200	6.378	40.675	2.700	27.700	2.383	0.017
Hommeida S et al, 2018 (2013)	25.100	8.018	64.288	9.385	40.815	3.130	0.002
Hommeida S et al, 2018 (2015)	19.200	7.288	53.121	4.915	33.485	2.634	0.008
Syed A et al, 2017	4.939	0.067	0.005	4.807	5.071	73.279	0.000
Arias A et al, 2019	9.308	0.865	0.749	7.613	11.004	10.758	0.000
Ristic N et al, 2019	0.850	0.145	0.021	0.565	1.135	5.846	0.000
Limketkai BN et al, 2019	23.100	0.223	0.050	22.663	23.537	103.540	0.000
Weerasekera K et al, 2019	6.950	0.564	0.318	5.845	8.055	12.327	0.000
Zdanowicz K et al, 2020	2.830	0.480	0.230	1.890	3.770	5.901	0.000
Rocu JM E et al, 2020	0.990	0.079	0.006	0.835	1.145	12.518	0.000
La Orden Izquierdo E et al, 2021	15.100	1.536	2.359	12.090	18.110	9.832	0.000
Melgaard D et al, 2021	5.090	0.332	0.110	4.440	5.740	15.348	0.000
Garber et al, 2022	1.220	0.291	0.085	0.650	1.790	4.195	0.000
Allin et al, 2022	6.500	0.342	0.117	5.830	7.170	19.015	0.000
	4.298	0.019	0.000	4.260	4.336	223.853	0.000

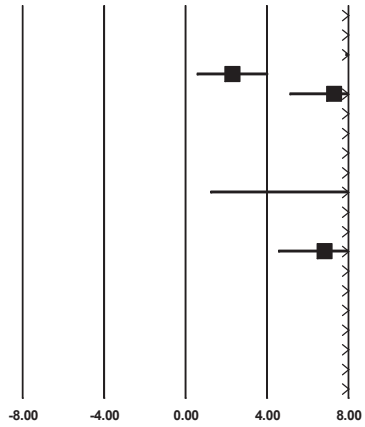
2) Funnel plot



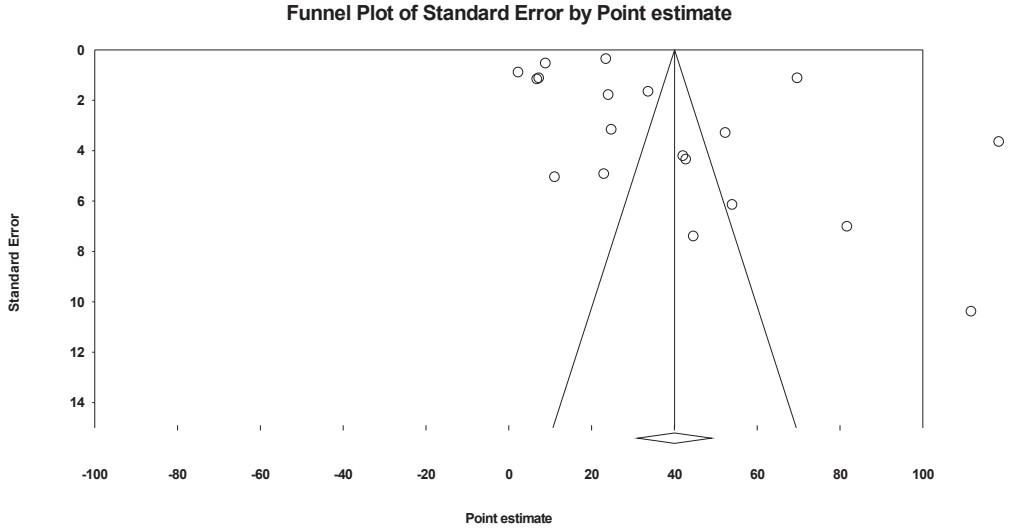
Supplementary Figure 5. Overall incidence of EoE included in our systematic review (total study). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot

Study name	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Arias A et al, 2013	44.620	7.398	54.732	30.120	59.120	6.031	0.000
Arias A et al, 2019	111.700	10.383	107.803	91.350	132.050	10.758	0.000
Cherian S et al, 2006	8.900	0.536	0.287	7.850	9.950	16.613	0.000
Dalby K et al, 2010	2.300	0.893	0.797	0.550	4.050	2.576	0.010
Gill R, et al, 2007	7.300	1.122	1.260	5.100	9.500	6.504	0.000
Giriens B et al, 2015	24.080	1.786	3.189	20.580	27.580	13.485	0.000
Goncalves LO et al, 2018	24.800	3.163	10.007	18.600	31.000	7.840	0.000
Hruz P et al, 2011	42.800	4.347	18.897	34.280	51.320	9.846	0.000
La Orden Izquierdo E et al, 2018	52.330	3.291	10.830	45.880	58.780	15.902	0.000
Ma X et al, 2015	11.110	5.046	25.462	1.220	21.000	2.202	0.028
Noel RJ et al, 2007	42.100	4.209	17.718	33.850	50.350	10.002	0.000
Prasad GA et al, 2009	54.000	6.148	37.799	41.950	66.050	8.783	0.000
Ristic N et al, 2019	6.830	1.163	1.353	4.550	9.110	5.871	0.000
Robson J et al, 2018	118.400	3.648	13.308	111.250	125.550	32.456	0.000
RooiJ WE et al, 2020	23.500	0.357	0.128	22.800	24.200	65.799	0.000
Straumann A et al, 2005	23.000	4.924	24.241	13.350	32.650	4.671	0.000
Syed AA et al, 2012/Stewart MJ et al, 2013	33.700	1.658	2.750	30.450	36.950	20.323	0.000
Allin et al, 2022	69.700	1.122	1.260	67.500	71.900	62.095	0.000
Molina-Infante J et al, 2018	81.730	7.013	49.181	67.985	95.475	11.654	0.000
	20.559	0.249	0.062	20.070	21.047	82.526	0.000



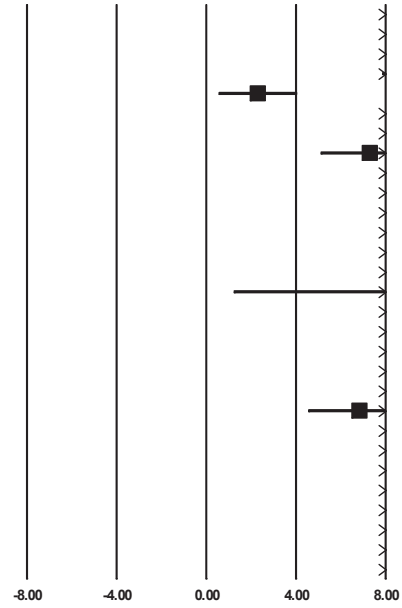
2) Funnel plot



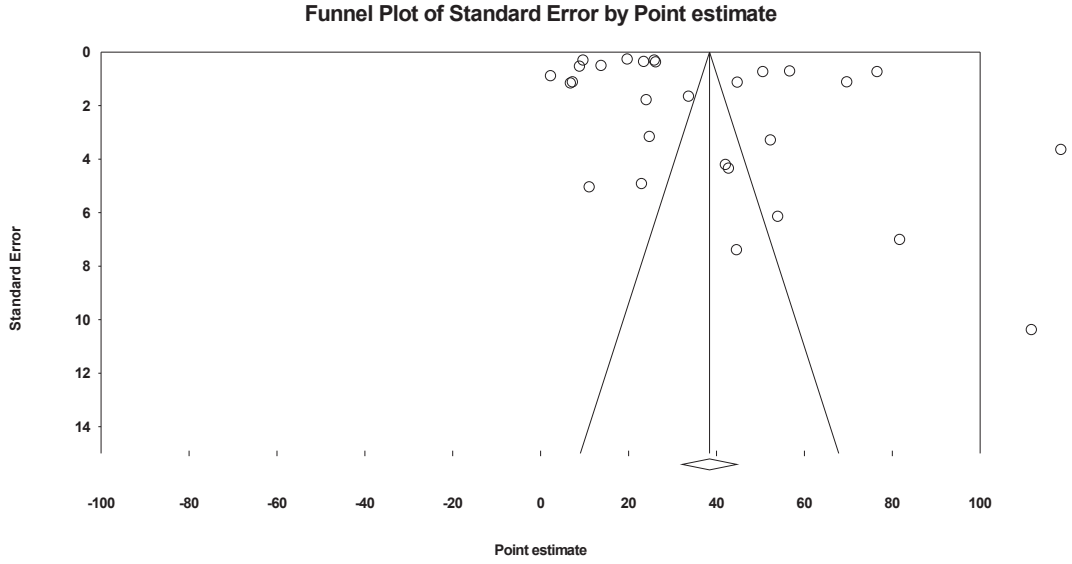
Supplementary Figure 6. Overall prevalence of EoE included in our systematic review (researcher-validated studies). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot

Study name	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Ally MR et al, 2014	9.700	0.306	0.094	9.100	10.300	31.686	0.000
Arias A et al, 2013	44.620	7.398	54.732	30.120	59.120	6.031	0.000
Arias A et al, 2019	111.700	10.383	107.803	91.350	132.050	10.758	0.000
Cherian S et al, 2006	8.900	0.536	0.287	7.850	9.950	16.613	0.000
Dalby K et al, 2010	2.300	0.893	0.797	0.550	4.050	2.576	0.010
Dellon ES et al, 2014	56.700	0.714	0.510	55.300	58.100	79.379	0.000
Dellon ES et al, 2015	13.800	0.510	0.260	12.800	14.800	27.048	0.000
Gill R, et al, 2007	7.300	1.122	1.260	5.100	9.500	6.504	0.000
Giriens B et al, 2015	24.080	1.786	3.189	20.580	27.580	13.485	0.000
Goncalves LO et al, 2018	24.800	3.163	10.007	18.600	31.000	7.840	0.000
Hruz P et al, 2011	42.800	4.347	18.897	34.280	51.320	9.846	0.000
Kim S et al, 2015	44.800	1.133	1.284	42.579	47.021	39.529	0.000
La Orden Izquierdo E et al, 2018	52.330	3.291	10.830	45.880	58.780	15.902	0.000
Limketkai BN et al, 2019	76.600	0.740	0.547	75.150	78.050	103.540	0.000
Ma X et al, 2015	11.110	5.046	25.462	1.220	21.000	2.202	0.028
Mansoor E et al, 2016	25.900	0.306	0.094	25.300	26.500	84.605	0.000
Maradey-Romero C et al, 2015	50.600	0.740	0.547	49.150	52.050	68.396	0.000
McGowan EC et al, 2020	26.210	0.377	0.142	25.471	26.949	69.548	0.000
Noel RJ et al, 2007	42.100	4.209	17.718	33.850	50.350	10.002	0.000
Prasad GA et al, 2009	54.000	6.148	37.799	41.950	66.050	8.783	0.000
Ristic N et al, 2019	6.830	1.163	1.353	4.550	9.110	5.871	0.000
Robson J et al, 2018	118.400	3.648	13.308	111.250	125.550	32.456	0.000
RooiJ WE et al, 2020	23.500	0.357	0.128	22.800	24.200	65.799	0.000
Straumann A et al, 2005	23.000	4.924	24.241	13.350	32.650	4.671	0.000
Syed A et al, 2017	19.750	0.270	0.073	19.220	20.280	73.036	0.000
Syed AA et al, 2012/Stewart MJ et al, 2013	33.700	1.658	2.750	30.450	36.950	20.323	0.000
Allin et al, 2022	69.700	1.122	1.260	67.500	71.900	62.095	0.000
Molina-Infante J et al, 2018	81.730	7.013	49.181	67.985	95.475	11.654	0.000
	23.349	0.121	0.015	23.112	23.586	193.115	0.000

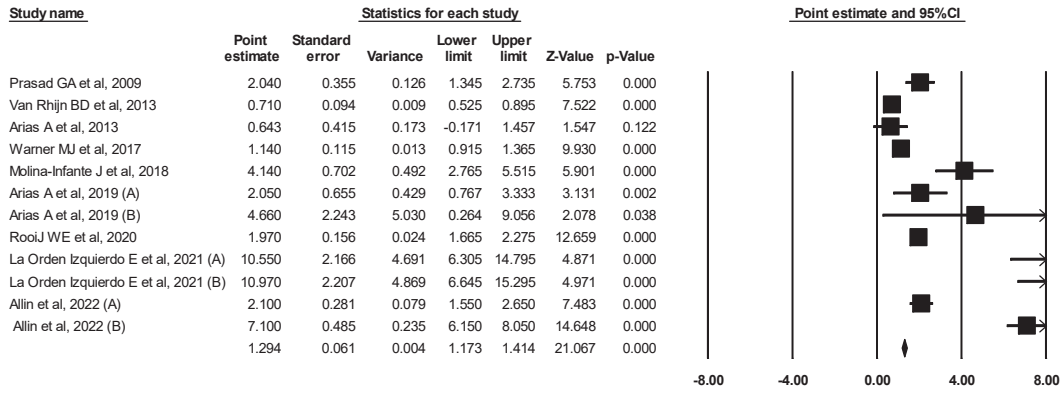


2) Funnel plot

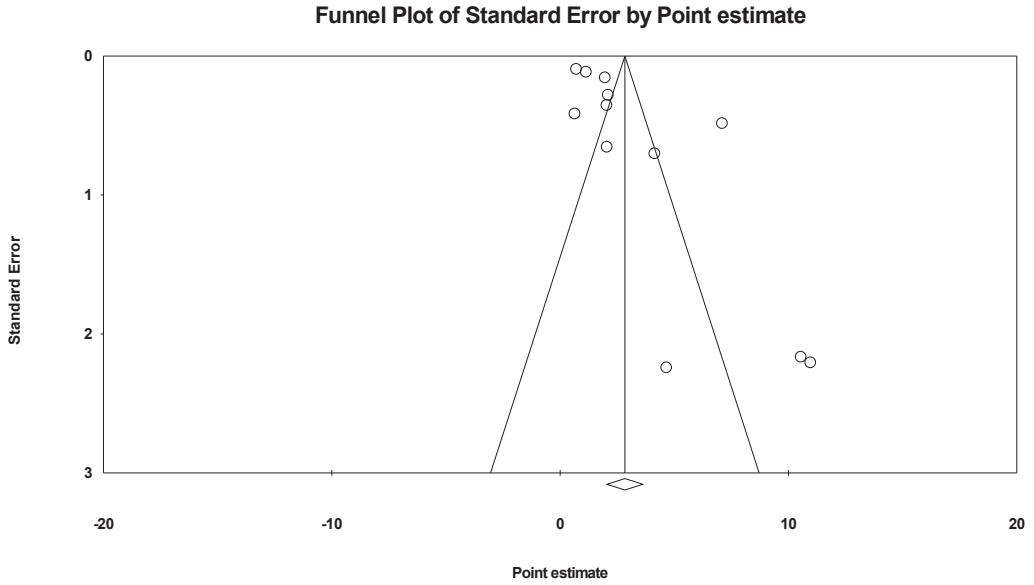


Supplementary Figure 7. Overall prevalence of EoE included in our systematic review (total study). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot



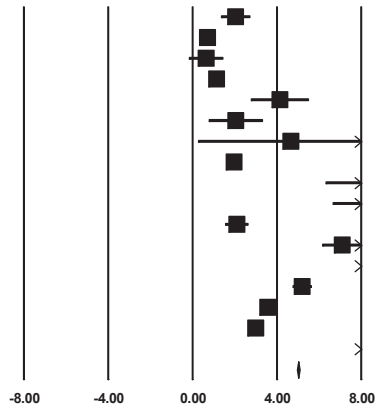
2) Funnel plot



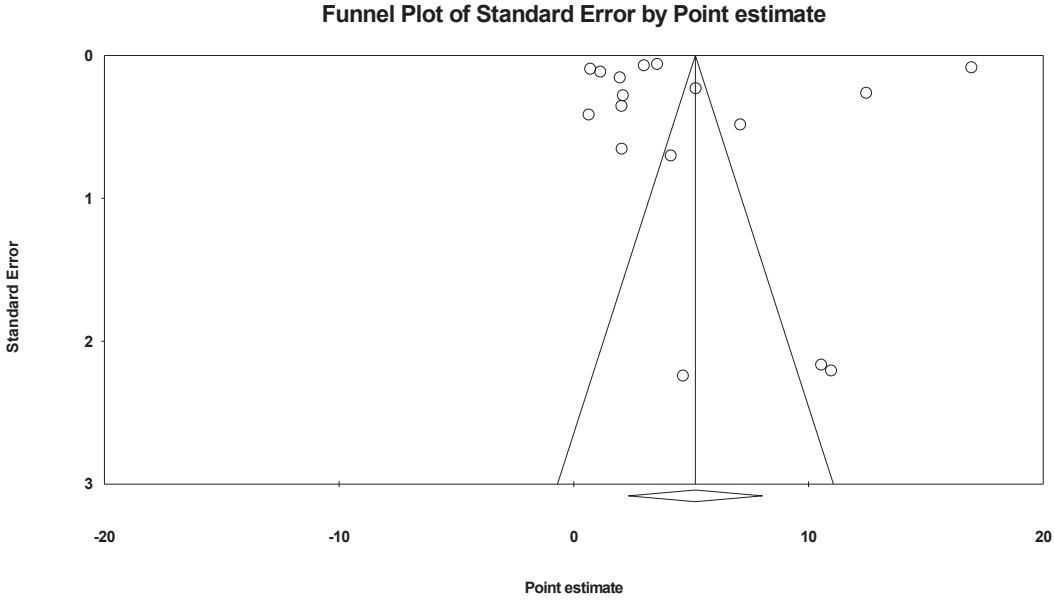
Supplementary Figure 8. Female incidence of EoE included in our systematic review (researcher-validated studies). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot

Study name	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Prasad GA et al, 2009	2.040	0.355	0.126	1.345	2.735	5.753	0.000
Van Rhijn BD et al, 2013	0.710	0.094	0.009	0.525	0.895	7.522	0.000
Arias A et al, 2013	0.643	0.415	0.173	-0.171	1.457	1.547	0.122
Warner MJ et al, 2017	1.140	0.115	0.013	0.915	1.365	9.930	0.000
Molina-Infante J et al, 2018	4.140	0.702	0.492	2.765	5.515	5.901	0.000
Arias A et al, 2019 (A)	2.050	0.655	0.429	0.767	3.333	3.131	0.002
Arias A et al, 2019 (B)	4.660	2.243	5.030	0.264	9.056	2.078	0.038
RooiJ WE et al, 2020	1.970	0.156	0.024	1.665	2.275	12.659	0.000
La Orden Izquierdo E et al, 2021 (A)	10.550	2.166	4.691	6.305	14.795	4.871	0.000
La Orden Izquierdo E et al, 2021 (B)	10.970	2.207	4.869	6.645	15.295	4.971	0.000
Allin et al, 2022 (A)	2.100	0.281	0.079	1.550	2.650	7.483	0.000
Allin et al, 2022 (B)	7.100	0.485	0.235	6.150	8.050	14.648	0.000
Dellon ES et al, 2014	12.467	0.264	0.069	11.950	12.983	47.292	0.000
Kim S et al, 2015	5.200	0.231	0.053	4.747	5.653	22.500	0.000
Mansoor E et al, 2016	3.560	0.061	0.004	3.440	3.680	58.146	0.000
Syed A et al, 2017	2.996	0.071	0.005	2.857	3.135	42.296	0.000
Limketkai BN et al, 2019	16.948	0.085	0.007	16.782	17.114	200.273	0.000
	5.015	0.033	0.001	4.950	5.080	150.776	0.000



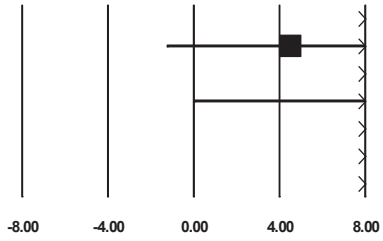
2) Funnel plot



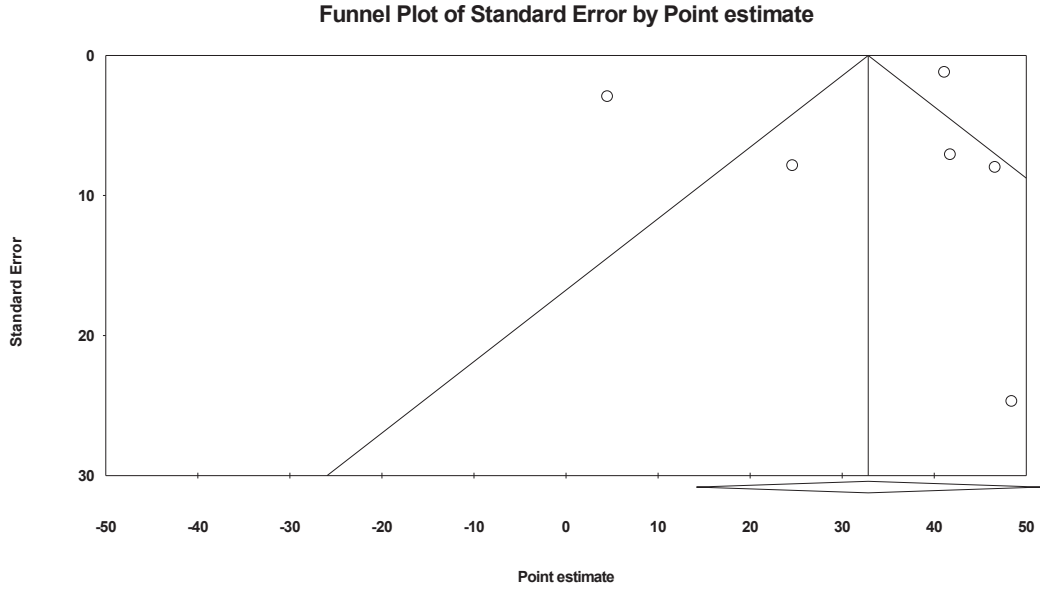
Supplementary Figure 9. Female incidence of EoE included in our systematic review (total study). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot

Study name	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Prasad GA et al, 2009	46.600	7.985	63.758	30.950	62.250	5.836	0.000
Arias A et al, 2013	4.500	2.934	8.607	-1.250	10.250	1.534	0.125
Arias A et al, 2019 (A)	24.600	7.857	61.737	9.200	40.000	3.131	0.002
Arias A et al, 2019 (B)	48.410	24.694	609.810	0.010	96.810	1.960	0.050
Molina-Infante J et al, 2018	41.740	7.079	50.115	27.865	55.615	5.896	0.000
Allin et al, 2022 (B)	41.100	1.199	1.438	38.750	43.450	34.279	0.000
	36.005	1.075	1.156	33.898	38.112	33.492	0.000



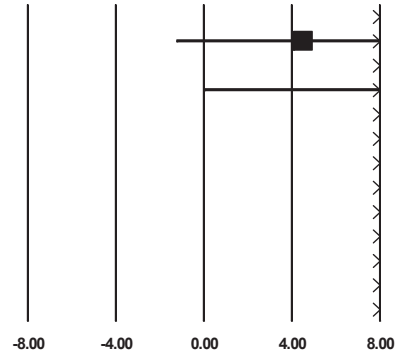
2) Funnel plot



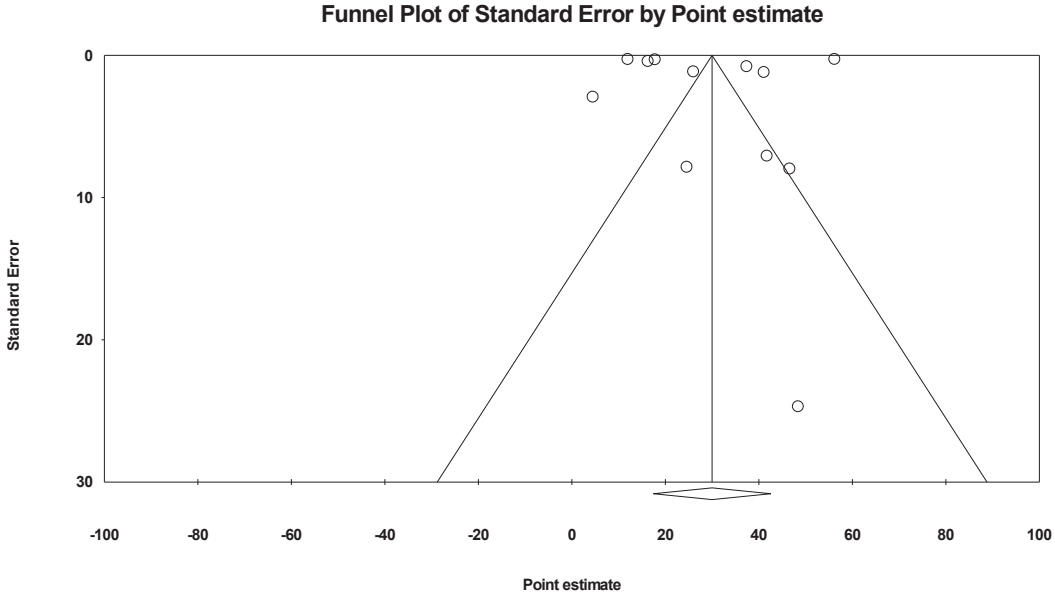
Supplementary Figure 10. Female prevalence of EoE included in our systematic review (researcher-validated studies). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot

Study name	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Prasad GA et al, 2009	46.600	7.985	63.758	30.950	62.250	5.836	0.000
Arias A et al, 2013	4.500	2.934	8.607	-1.250	10.250	1.534	0.125
Arias A et al, 2019 (A)	24.600	7.857	61.737	9.200	40.000	3.131	0.002
Arias A et al, 2019 (B)	48.410	24.694	609.810	0.010	96.810	1.960	0.050
Molina-Infante J et al, 2018	41.740	7.079	50.115	27.865	55.615	5.896	0.000
Allin et al, 2022 (B)	41.100	1.199	1.438	38.750	43.450	34.279	0.000
Dellon ES et al, 2014	37.400	0.791	0.625	35.850	38.950	47.292	0.000
Kim S et al, 2015	26.000	1.156	1.335	23.735	28.265	22.500	0.000
Mansoor E et al, 2016	17.800	0.306	0.094	17.200	18.400	58.146	0.000
Syed A et al, 2017	11.983	0.283	0.080	11.428	12.539	42.296	0.000
Limketkai BN et al, 2019	56.200	0.281	0.079	55.650	56.750	200.273	0.000
McGowan EC et al, 2020	16.290	0.425	0.181	15.457	17.123	38.309	0.000
	28.122	0.150	0.022	27.828	28.416	187.747	0.000



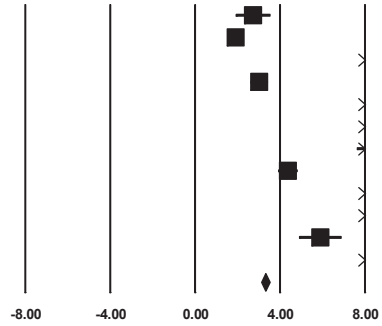
2) Funnel plot



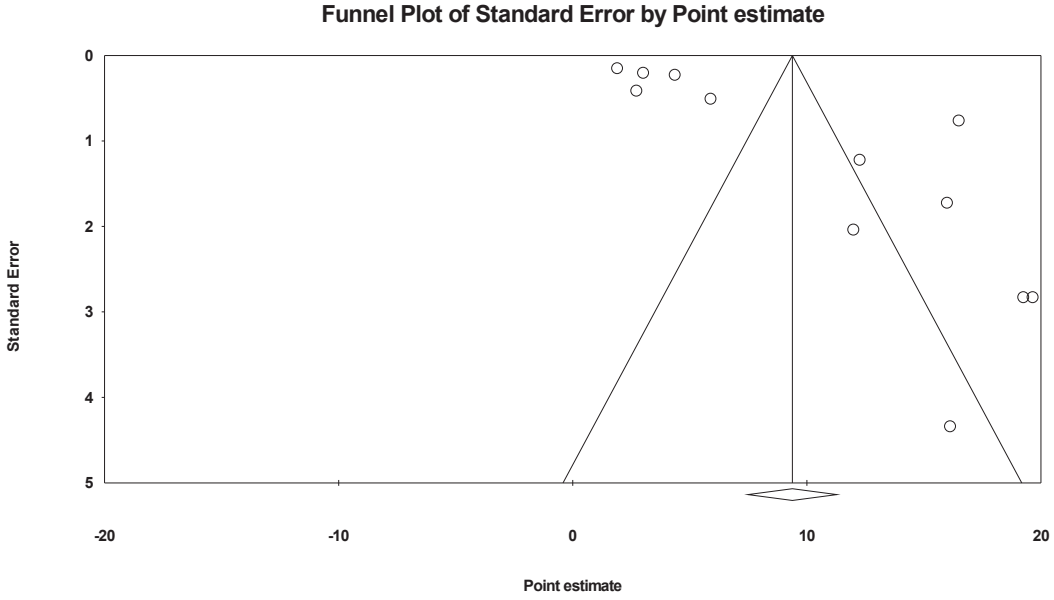
Supplementary Figure 11. Female prevalence of eosinophilic esophagitis included in our systematic review (total study). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot

Study name	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Prasad GA et al, 2009	2.730	0.416	0.173	1.915	3.545	6.565	0.000
Van Rhijn BD et al, 2013	1.910	0.153	0.023	1.610	2.210	12.478	0.000
Arias A et al, 2013	12.000	2.041	4.165	8.000	16.000	5.880	0.000
Warner MJ et al, 2017	3.020	0.207	0.043	2.615	3.425	14.615	0.000
Molina-Infante J et al, 2018	12.270	1.225	1.499	9.870	14.670	10.020	0.000
Arias A et al, 2019 (A)	16.000	1.726	2.980	12.617	19.383	9.269	0.000
Arias A et al, 2019 (B)	16.130	4.341	18.844	7.622	24.638	3.716	0.000
RooiJ WE et al, 2020	4.370	0.230	0.053	3.920	4.820	19.033	0.000
La Orden Izquierdo E et al, 2021 (A)	19.660	2.832	8.018	14.110	25.210	6.943	0.000
La Orden Izquierdo E et al, 2021 (B)	19.260	2.832	8.018	13.710	24.810	6.802	0.000
Allin et al, 2022 (A)	5.900	0.510	0.260	4.900	6.900	11.564	0.000
Allin et al, 2022 (B)	16.500	0.765	0.586	15.000	18.000	21.560	0.000
	3.307	0.101	0.010	3.109	3.505	32.729	0.000



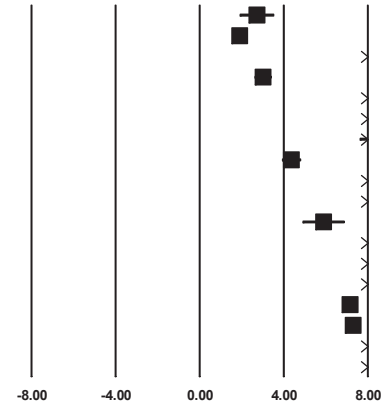
2) Funnel plot



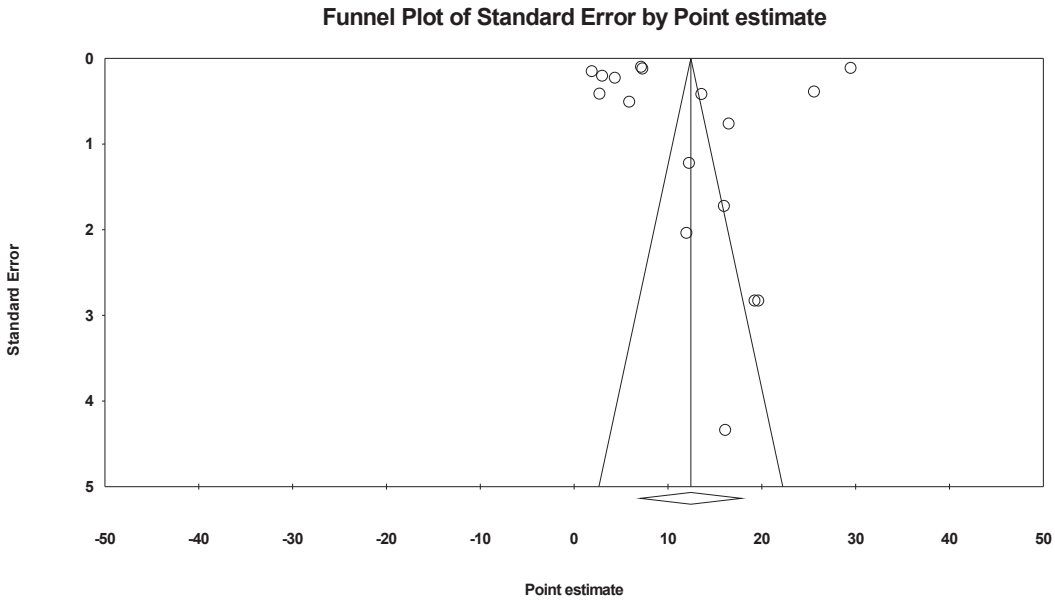
Supplementary Figure 12. Male incidence of EoE included in our systematic review (researcher-validated studies). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot

Study name	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Prasad GA et al, 2009	2.730	0.416	0.173	1.915	3.545	6.565	0.000
Van Rhijn BD et al, 2013	1.910	0.153	0.023	1.610	2.210	12.478	0.000
Arias A et al, 2013	12.000	2.041	4.165	8.000	16.000	5.880	0.000
Warner MJ et al, 2017	3.020	0.207	0.043	2.615	3.425	14.615	0.000
Molina-Infante J et al, 2018	12.270	1.225	1.499	9.870	14.670	10.020	0.000
Arias A et al, 2019 (A)	16.000	1.726	2.980	12.617	19.383	9.269	0.000
Arias A et al, 2019 (B)	16.130	4.341	18.844	7.622	24.638	3.716	0.000
RooiJ WE et al, 2020	4.370	0.230	0.053	3.920	4.820	19.033	0.000
La Orden Izquierdo E et al, 2021 (A)	19.660	2.832	8.018	14.110	25.210	6.943	0.000
La Orden Izquierdo E et al, 2021 (B)	19.260	2.832	8.018	13.710	24.810	6.802	0.000
Allin et al, 2022 (A)	5.900	0.510	0.260	4.900	6.900	11.564	0.000
Allin et al, 2022 (B)	16.500	0.765	0.586	15.000	18.000	21.560	0.000
Dellon ES et al, 2014	25.600	0.391	0.153	24.833	26.367	65.446	0.000
Kim S et al, 2015	13.600	0.420	0.176	12.777	14.423	32.405	0.000
Mansoor E et al, 2016	7.160	0.102	0.010	6.960	7.360	70.167	0.000
Syed A et al, 2017	7.309	0.122	0.015	7.069	7.548	59.831	0.000
Limketkai BN et al, 2019	29.493	0.115	0.013	29.267	29.720	255.579	0.000
	11.371	0.054	0.003	11.266	11.476	212.217	0.000



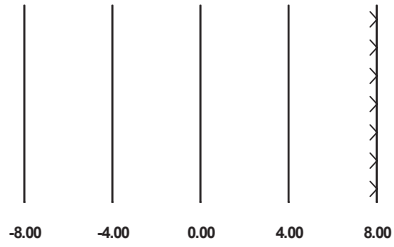
2) Funnel plot



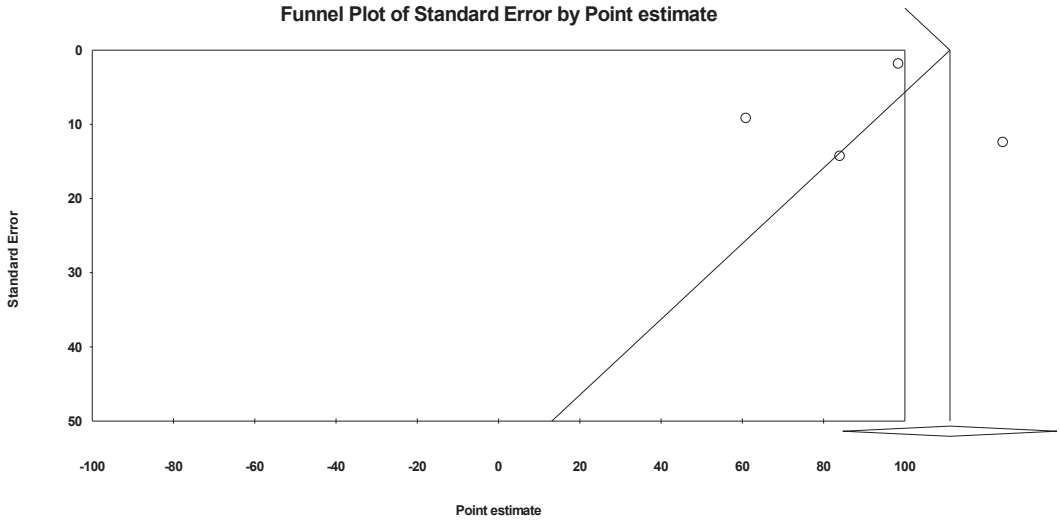
Supplementary Figure 13. Male incidence of EoE included in our systematic review (total study). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot

Study name	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Prasad GA et al, 2009	60.900	9.184	84.343	42.900	78.900	6.631	0.000
Arias A et al, 2013	84.000	14.286	204.089	56.000	112.000	5.880	0.000
Arias A et al, 2019 (A)	192.000	20.715	429.097	151.400	232.600	9.269	0.000
Arias A et al, 2019 (B)	172.000	47.756	2280.634	78.400	265.600	3.602	0.000
Molina-Infante J et al, 2018	124.130	12.421	154.285	99.785	148.475	9.993	0.000
Allin et al, 2022 (B)	98.400	1.837	3.374	94.800	102.000	53.572	0.000
	98.096	1.761	3.102	94.644	101.548	55.701	0.000



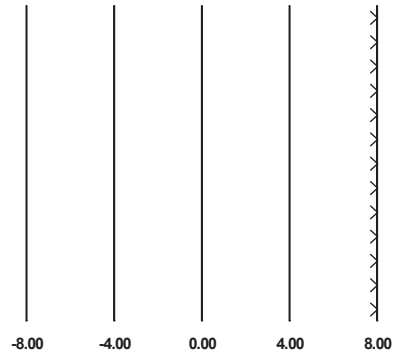
2) Funnel plot



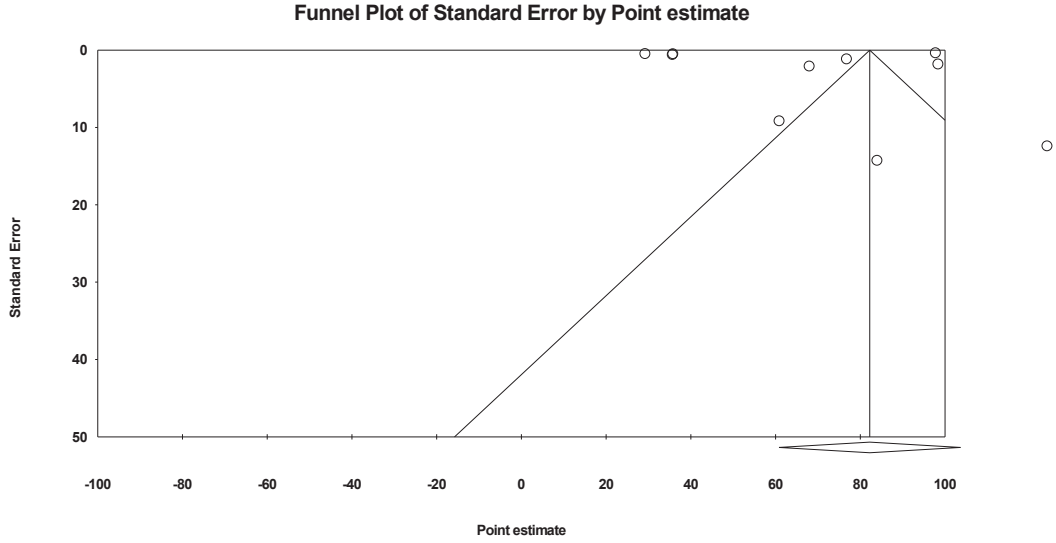
Supplementary Figure 14. Male prevalence of EoE included in our systematic review (researcher-validated studies). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot

Study name	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Prasad GA et al, 2009	60.900	9.184	84.343	42.900	78.900	6.631	0.000
Arias A et al, 2013	84.000	14.286	204.089	56.000	112.000	5.880	0.000
Arias A et al, 2019 (A)	192.000	20.715	429.097	151.400	232.600	9.269	0.000
Arias A et al, 2019 (B)	172.000	47.756	2280.634	78.400	265.600	3.602	0.000
Molina-Infante J et al, 2018	124.130	12.421	154.285	99.785	148.475	9.993	0.000
Allin et al, 2022 (B)	98.400	1.837	3.374	94.800	102.000	53.572	0.000
Dellon ES et al, 2014	76.800	1.173	1.377	74.500	79.100	65.446	0.000
Kim S et al, 2015	68.000	2.098	4.404	63.887	72.113	32.405	0.000
Mansoor E et al, 2016	35.800	0.510	0.260	34.800	36.800	70.167	0.000
Syed A et al, 2017	29.234	0.489	0.239	28.276	30.192	59.831	0.000
Limketkai BN et al, 2019	97.800	0.383	0.146	97.050	98.550	255.579	0.000
McGowan EC et al, 2020	35.680	0.615	0.378	34.475	36.885	58.033	0.000
	59.908	0.231	0.053	59.456	60.361	259.621	0.000



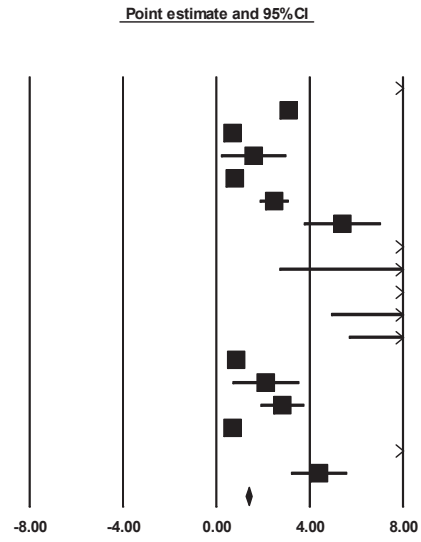
2) Funnel plot



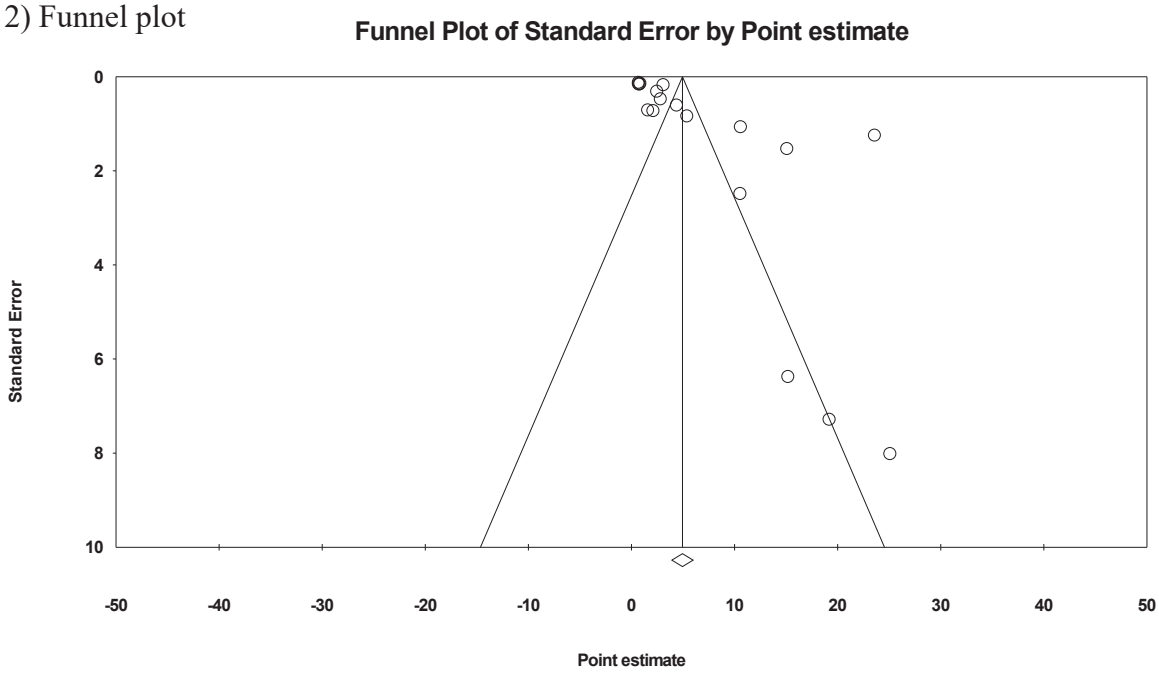
Supplementary Figure 15. Male prevalence of EoE included in our systematic review (total study). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot

Study name	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Noel RJ et al, 2007 (B)	10.600	1.071	1.148	8.500	12.700	9.893	0.000
Cherian S et al, 2006	3.100	0.179	0.032	2.750	3.450	17.360	0.000
Gill R, et al, 2007	0.700	0.128	0.016	0.450	0.950	5.488	0.000
Dalby K et al, 2010	1.600	0.714	0.510	0.200	3.000	2.240	0.025
Homan M et al, 2015	0.790	0.166	0.027	0.465	1.115	4.764	0.000
Goncalves LO et al, 2018	2.480	0.316	0.100	1.860	3.100	7.840	0.000
La Orden Izquierdo E et al, 2018	5.400	0.842	0.709	3.750	7.050	6.414	0.000
Robson J et al, 2018	23.600	1.250	1.563	21.150	26.050	18.880	0.000
Hommeida S et al, 2018 (2005)	15.200	6.378	40.675	2.700	27.700	2.383	0.017
Hommeida S et al, 2018 (2013)	25.100	8.018	64.288	9.385	40.815	3.130	0.002
Hommeida S et al, 2018 (2015)	19.200	7.288	53.121	4.915	33.485	2.634	0.008
Arias A et al, 2019	10.560	2.491	6.203	5.678	15.442	4.240	0.000
Ristic N et al, 2019	0.850	0.145	0.021	0.565	1.135	5.846	0.000
Weerasekera K et al, 2019	2.120	0.730	0.532	0.690	3.550	2.906	0.004
Zdanowicz K et al, 2020	2.830	0.480	0.230	1.890	3.770	5.901	0.000
RooiJ WE et al, 2020	0.700	0.158	0.025	0.390	1.010	4.426	0.000
La Orden Izquierdo E et al, 2021	15.100	1.536	2.359	12.090	18.110	9.832	0.000
Allin et al, 2022	4.400	0.612	0.375	3.200	5.600	7.187	0.000
	1.388	0.064	0.004	1.262	1.514	21.539	0.000



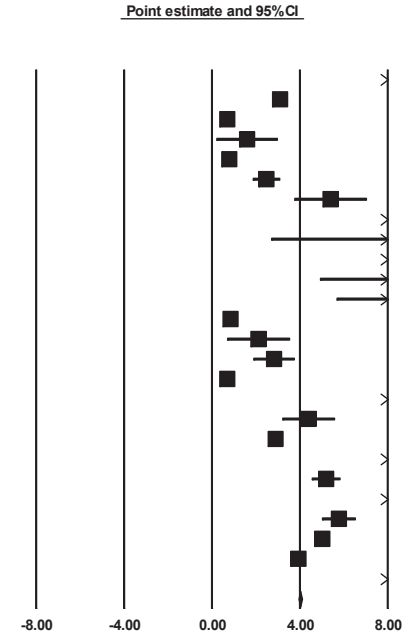
2) Funnel plot



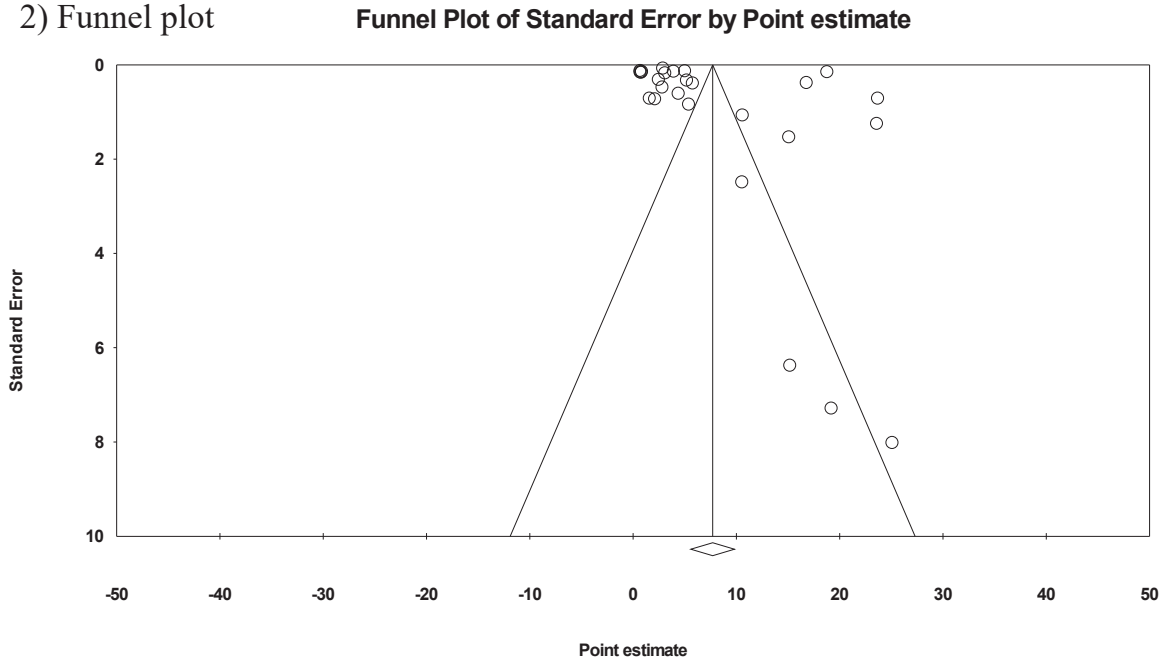
Supplementary Figure 16. Children incidence of EoE included in our systematic review (researcher-validated studies). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot

Study name	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Noel RJ et al, 2007 (B)	10.600	1.071	1.148	8.500	12.700	9.893	0.000
Cherian S et al, 2006	3.100	0.179	0.032	2.750	3.450	17.360	0.000
Gill R, et al, 2007	0.700	0.128	0.016	0.450	0.950	5.488	0.000
Dalby K et al, 2010	1.600	0.714	0.510	0.200	3.000	2.240	0.025
Homan M et al, 2015	0.790	0.166	0.027	0.465	1.115	4.764	0.000
Goncalves LO et al, 2018	2.480	0.316	0.100	1.860	3.100	7.840	0.000
La Orden Izquierdo E et al, 2018	5.400	0.842	0.709	3.750	7.050	6.414	0.000
Robson J et al, 2018	23.600	1.250	1.563	21.150	26.050	18.880	0.000
Hommeida S et al, 2018 (2005)	15.200	6.378	40.675	2.700	27.700	2.383	0.017
Hommeida S et al, 2018 (2013)	25.100	8.018	64.288	9.385	40.815	3.130	0.002
Hommeida S et al, 2018 (2015)	19.200	7.288	53.121	4.915	33.485	2.634	0.008
Arias A et al, 2019	10.560	2.491	6.203	5.678	15.442	4.240	0.000
Ristic N et al, 2019	0.850	0.145	0.021	0.565	1.135	5.846	0.000
Weerasekera K et al, 2019	2.120	0.730	0.532	0.690	3.550	2.906	0.004
Zdanowicz K et al, 2020	2.830	0.480	0.230	1.890	3.770	5.901	0.000
RooiJ WE et al, 2020	0.700	0.158	0.025	0.390	1.010	4.426	0.000
La Orden Izquierdo E et al, 2021	15.100	1.536	2.359	12.090	18.110	9.832	0.000
Allin et al, 2022	4.400	0.612	0.375	3.200	5.600	7.187	0.000
Prakash R et al, 2013	2.900	0.077	0.006	2.750	3.050	37.893	0.000
Dellon ES et al, 2014	16.800	0.383	0.146	16.050	17.550	43.903	0.000
Ally MR et al, 2014	5.200	0.332	0.110	4.550	5.850	15.680	0.000
Maradey-Romero C et al, 2015	23.700	0.714	0.510	22.300	25.100	33.179	0.000
Kim S et al, 2015	5.780	0.392	0.154	5.011	6.549	14.732	0.000
Mansoor E et al, 2016	5.020	0.133	0.018	4.760	5.280	37.842	0.000
Syed A et al, 2017	3.938	0.143	0.020	3.658	4.218	27.547	0.000
Limketkai BN et al, 2019	18.788	0.154	0.024	18.486	19.089	122.106	0.000
	4.019	0.041	0.002	3.938	4.100	97.120	0.000



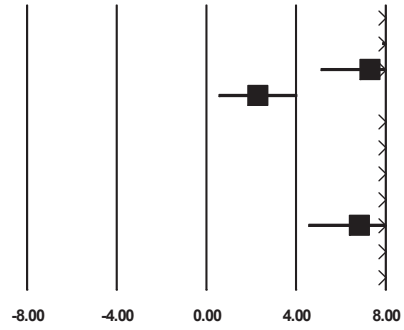
2) Funnel plot



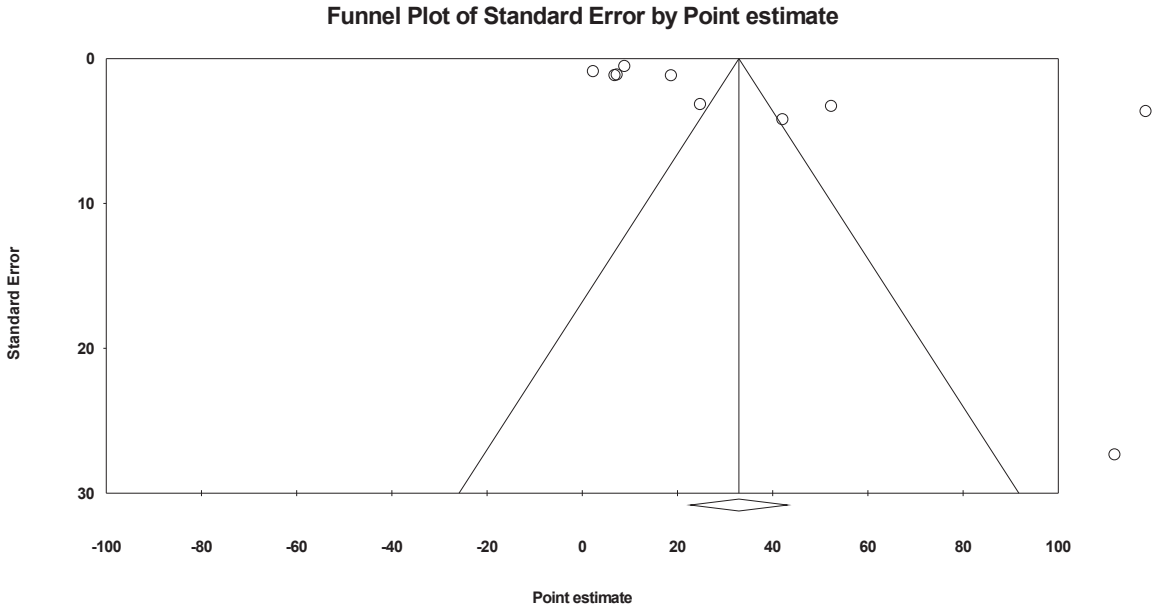
Supplementary Figure 17. Children incidence of EoE included in our systematic review (total study). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot

Study name	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Noel RJ et al, 2007 (B)	42.100	4.209	17.718	33.850	50.350	10.002	0.000
Gill R, et al, 2007	8.900	0.536	0.287	7.850	9.950	16.613	0.000
Dalby K et al, 2010	7.300	1.122	1.260	5.100	9.500	6.504	0.000
Homan M et al, 2015	2.300	0.893	0.797	0.550	4.050	2.576	0.010
La Orden Izquierdo E et al, 2018	24.800	3.163	10.007	18.600	31.000	7.840	0.000
Robson J et al, 2018	52.330	3.291	10.830	45.880	58.780	15.902	0.000
Hommeida S et al, 2018 (2005)	18.400	3.648	13.308	11.250	125.550	32.456	0.000
Ristic N et al, 2019	111.870	27.347	747.883	58.270	165.470	4.091	0.000
Weerasekera K et al, 2019	6.830	1.163	1.353	4.550	9.110	5.871	0.000
Prakash R et al, 2013	18.700	1.173	1.377	16.400	21.000	15.935	0.000
	10.522	0.370	0.137	9.798	11.246	28.473	0.000



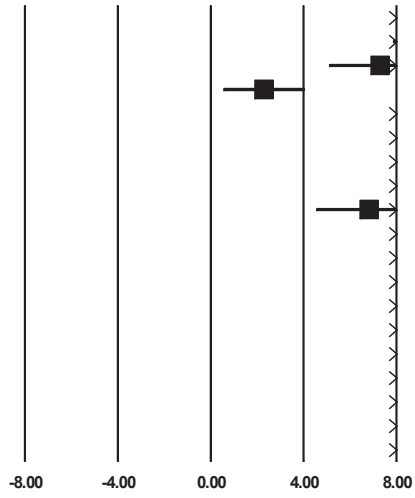
2) Funnel plot



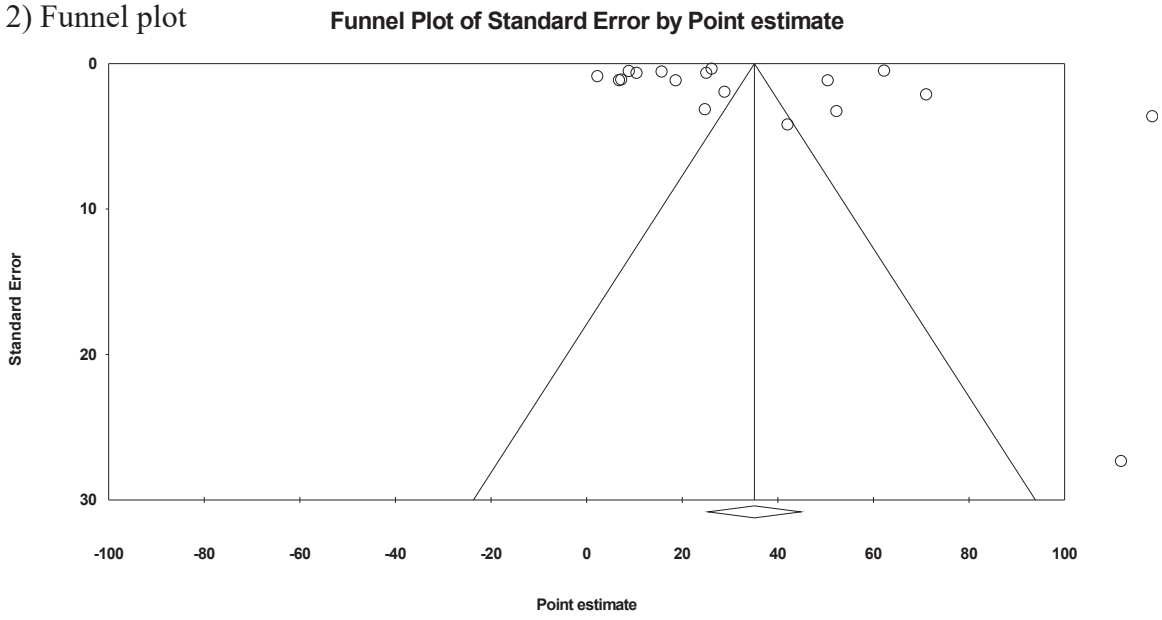
Supplementary Figure 18. Children prevalence of EoE included in our systematic review (researcher-validated studies). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot

Study name	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Noel RJ et al, 2007 (A)	42.100	4.209	17.718	33.850	50.350	10.002	0.000
Cherian S et al, 2006	8.900	0.536	0.287	7.850	9.950	16.613	0.000
Gill R, et al, 2007	7.300	1.122	1.260	5.100	9.500	6.504	0.000
Dalby K et al, 2010	2.300	0.893	0.797	0.550	4.050	2.576	0.010
Goncalves LO et al, 2018	24.800	3.163	10.007	18.600	31.000	7.840	0.000
La Orden Izquierdo E et al, 2018	52.330	3.291	10.830	45.880	58.780	15.902	0.000
Robson J et al, 2018	118.400	3.648	13.308	111.250	125.550	32.456	0.000
Arias A et al, 2019	111.870	27.347	747.883	58.270	165.470	4.091	0.000
Ristic N et al, 2019	6.830	1.163	1.353	4.550	9.110	5.871	0.000
Allin et al, 2022	18.700	1.173	1.377	16.400	21.000	15.935	0.000
Dellon ES et al, 2014	50.500	1.173	1.377	48.200	52.800	43.034	0.000
Ally MR et al, 2014	10.500	0.663	0.440	9.200	11.800	15.830	0.000
Maradey-Romero C et al, 2015	71.100	2.143	4.592	66.900	75.300	33.179	0.000
Kim S et al, 2015	28.900	1.962	3.848	25.055	32.745	14.732	0.000
Mansoor E et al, 2016	25.100	0.663	0.440	23.800	26.400	37.842	0.000
Syed A et al, 2017	15.752	0.572	0.327	14.632	16.873	27.547	0.000
Limketkai BN et al, 2019	62.300	0.510	0.260	61.300	63.300	122.106	0.000
McGowan EC et al, 2020	26.210	0.377	0.142	25.471	26.949	69.548	0.000
	25.531	0.192	0.037	25.154	25.908	132.696	0.000



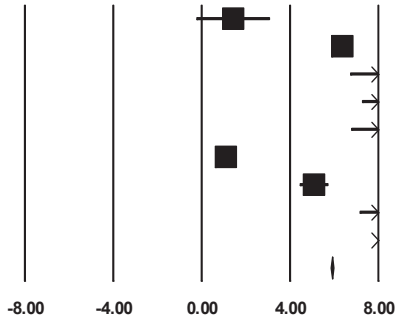
2) Funnel plot



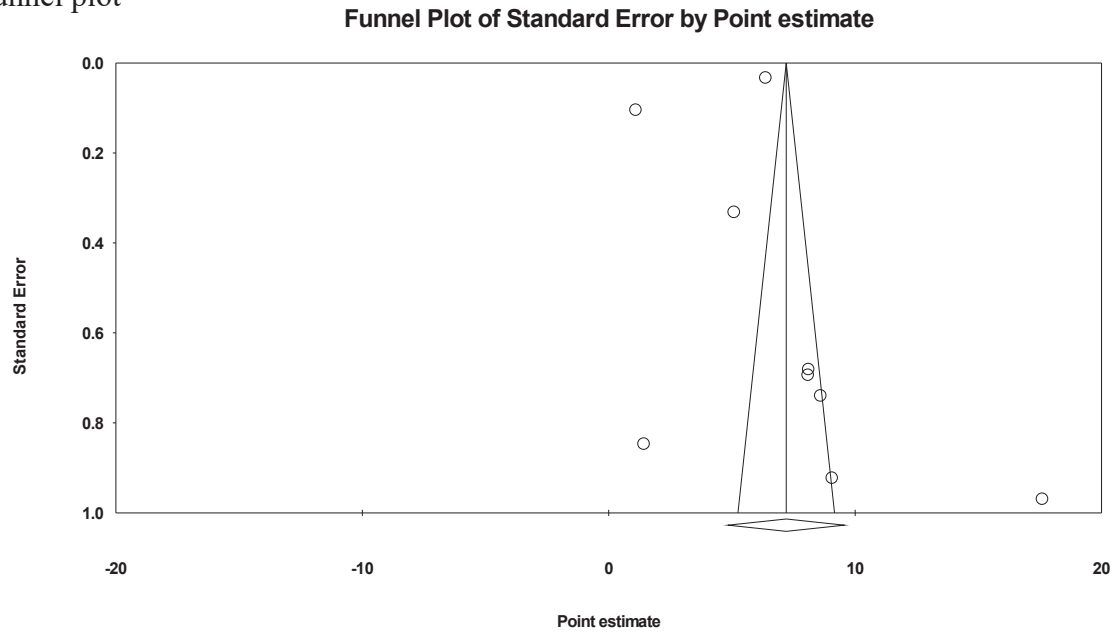
Supplementary Figure 19. Children prevalence of EoE included in our systematic review (total study). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot

Study name	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Straumann A et al, 2005	1.430	0.847	0.717	-0.230	3.090	1.688	0.091
Arias A et al, 2013	6.370	0.033	0.001	6.305	6.435	192.076	0.000
Molina-Infante J et al, 2018	8.090	0.694	0.481	6.730	9.450	11.659	0.000
Arias A et al, 2019	9.067	0.923	0.851	7.258	10.875	9.827	0.000
Weerasekera K et al, 2019	8.110	0.681	0.464	6.775	9.445	11.907	0.000
RooiJ WE et al, 2020	1.100	0.105	0.011	0.895	1.305	10.517	0.000
Melgaard D et al, 2021	5.090	0.332	0.110	4.440	5.740	15.348	0.000
Allin et al, 2022 (A)	8.600	0.740	0.547	7.150	10.050	11.625	0.000
Allin et al, 2022 (B)	17.600	0.969	0.940	15.700	19.500	18.155	0.000
	5.905	0.031	0.001	5.844	5.967	188.546	0.000



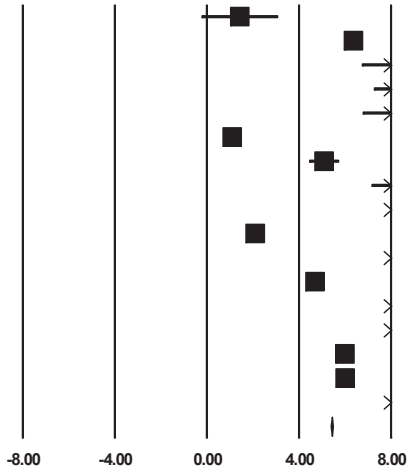
2) Funnel plot



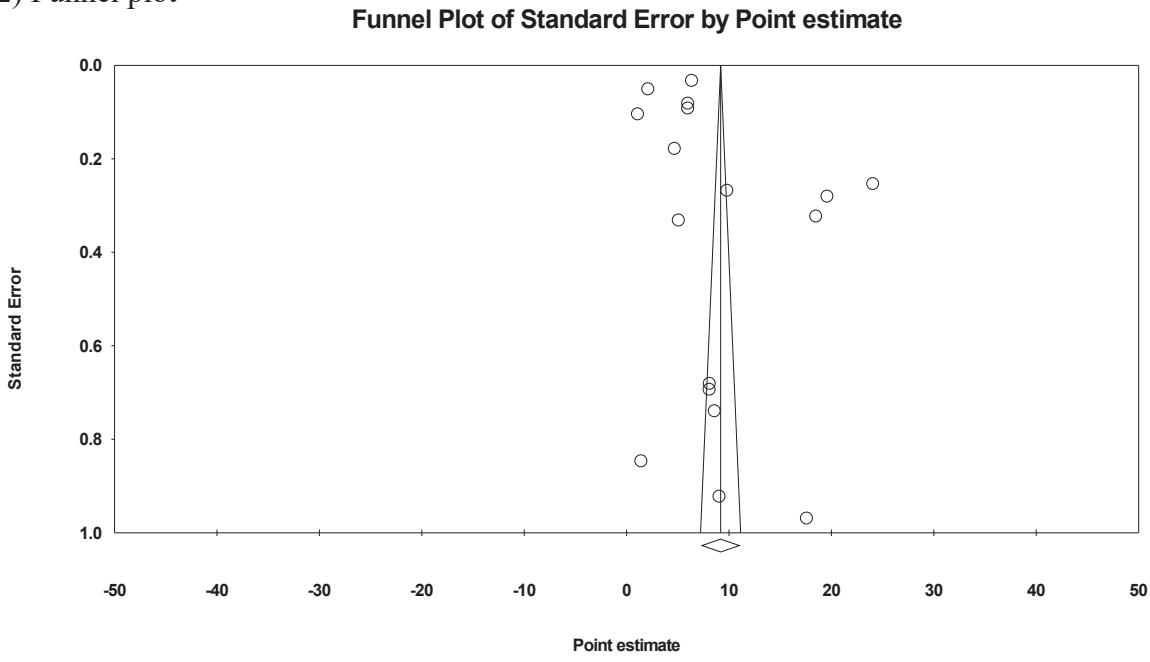
Supplementary Figure 20. Adults incidence of EoE included in our systematic review (researcher-validated studies). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot

Study name	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Straumann A et al, 2005	1.430	0.847	0.717	-0.230	3.090	1.688	0.091
Arias A et al, 2013	6.370	0.033	0.001	6.305	6.435	192.076	0.000
Molina-Infante J et al, 2018	8.090	0.694	0.481	6.730	9.450	11.659	0.000
Arias A et al, 2019	9.067	0.923	0.851	7.258	10.875	9.827	0.000
Weerasekera K et al, 2019	8.110	0.681	0.464	6.775	9.445	11.907	0.000
RooiJ WE et al, 2020	1.100	0.105	0.011	0.895	1.305	10.517	0.000
Melgaard D et al, 2021	5.090	0.332	0.110	4.440	5.740	15.348	0.000
Allin et al, 2022 (A)	8.600	0.740	0.547	7.150	10.050	11.625	0.000
Allin et al, 2022 (B)	17.600	0.969	0.940	15.700	19.500	18.155	0.000
Prakash R et al, 2013	2.100	0.051	0.003	2.000	2.200	41.159	0.000
Dellon ES et al, 2014	19.600	0.281	0.079	19.050	20.150	69.846	0.000
Ally MR et al, 2014	4.700	0.179	0.032	4.350	5.050	26.320	0.000
Maradey-Romero C et al, 2015	18.500	0.323	0.104	17.867	19.133	57.252	0.000
Kim S et al, 2015	9.820	0.268	0.072	9.295	10.345	36.632	0.000
Mansoor E et al, 2016	6.000	0.082	0.007	5.840	6.160	73.499	0.000
Syed A et al, 2017	6.002	0.092	0.008	5.821	6.183	65.113	0.000
Limketkai BN et al, 2019	24.065	0.254	0.064	23.568	24.563	94.791	0.000
	5.425	0.024	0.001	5.378	5.471	227.213	0.000



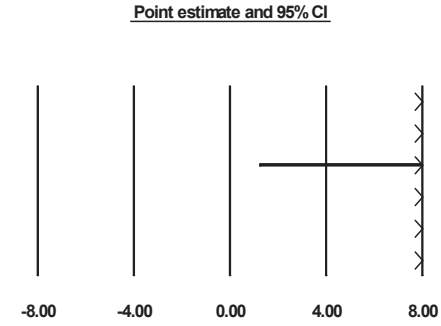
2) Funnel plot



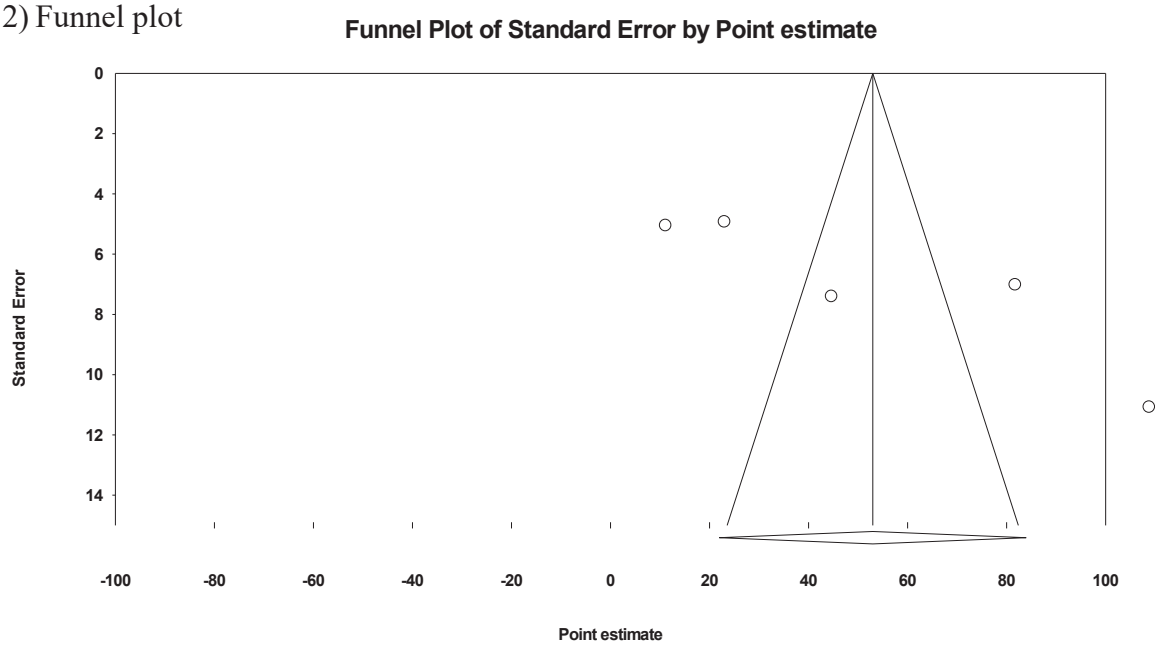
Supplementary Figure 21. Adults incidence of EoE included in our systematic review (total study). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot

Study name	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Straumann A et al, 2005	23.000	4.924	24.241	13.350	32.650	4.671	0.000
Arias A et al, 2013	44.620	7.398	54.732	30.120	59.120	6.031	0.000
Ma X et al, 2015	11.110	5.046	25.462	1.220	21.000	2.202	0.028
Molina-Infante J et al, 2018	81.730	7.013	49.181	67.985	95.475	11.654	0.000
Arias A et al, 2019	108.800	11.072	122.581	87.100	130.500	9.827	0.000
	37.315	2.803	7.856	31.822	42.809	13.313	0.000



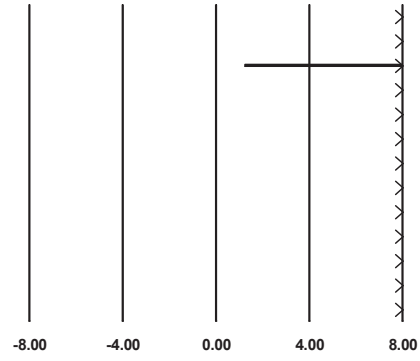
2) Funnel plot



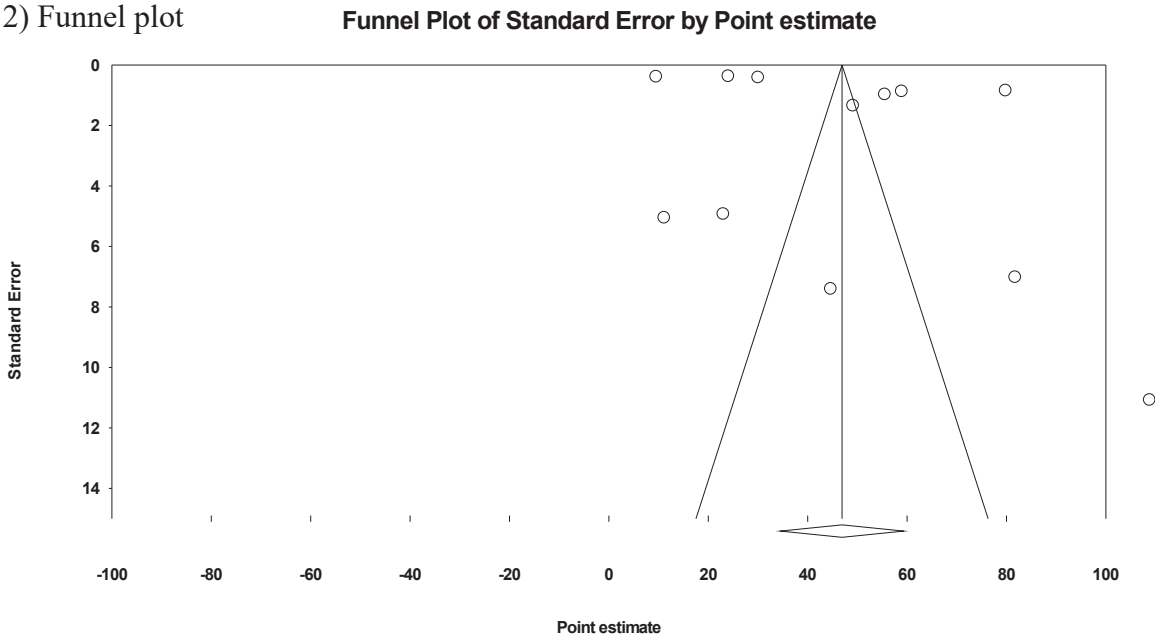
Supplementary Figure 22. Adults prevalence of EoE included in our systematic review (researcher-validated studies). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot

Study name	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Straumann A et al, 2005	23.000	4.924	24.241	13.350	32.650	4.671	0.000
Arias A et al, 2013	44.620	7.398	54.732	30.120	59.120	6.031	0.000
Ma X et al, 2015	11.110	5.046	25.462	1.220	21.000	2.202	0.028
Molina-Infante J et al, 2018	81.730	7.013	49.181	67.985	95.475	11.654	0.000
Arias A et al, 2019	108.800	11.072	122.581	87.100	130.500	9.827	0.000
Dellon ES et al, 2014	58.900	0.867	0.752	57.200	60.600	67.907	0.000
Ally MR et al, 2014	9.500	0.383	0.146	8.750	10.250	24.826	0.000
Maradey-Romero C et al, 2015	55.500	0.969	0.940	53.600	57.400	57.252	0.000
Kim S et al, 2015	49.100	1.340	1.797	46.473	51.727	36.632	0.000
Mansoor E et al, 2016	30.000	0.408	0.167	29.200	30.800	73.499	0.000
Syed A et al, 2017	24.008	0.369	0.136	23.285	24.731	65.113	0.000
Limketkai BN et al, 2019	79.800	0.842	0.709	78.150	81.450	94.791	0.000
	28.513	0.201	0.041	28.118	28.908	141.636	0.000



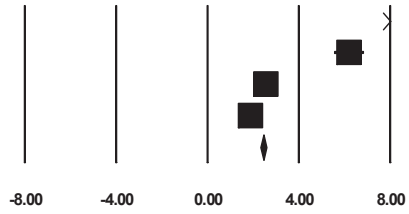
2) Funnel plot



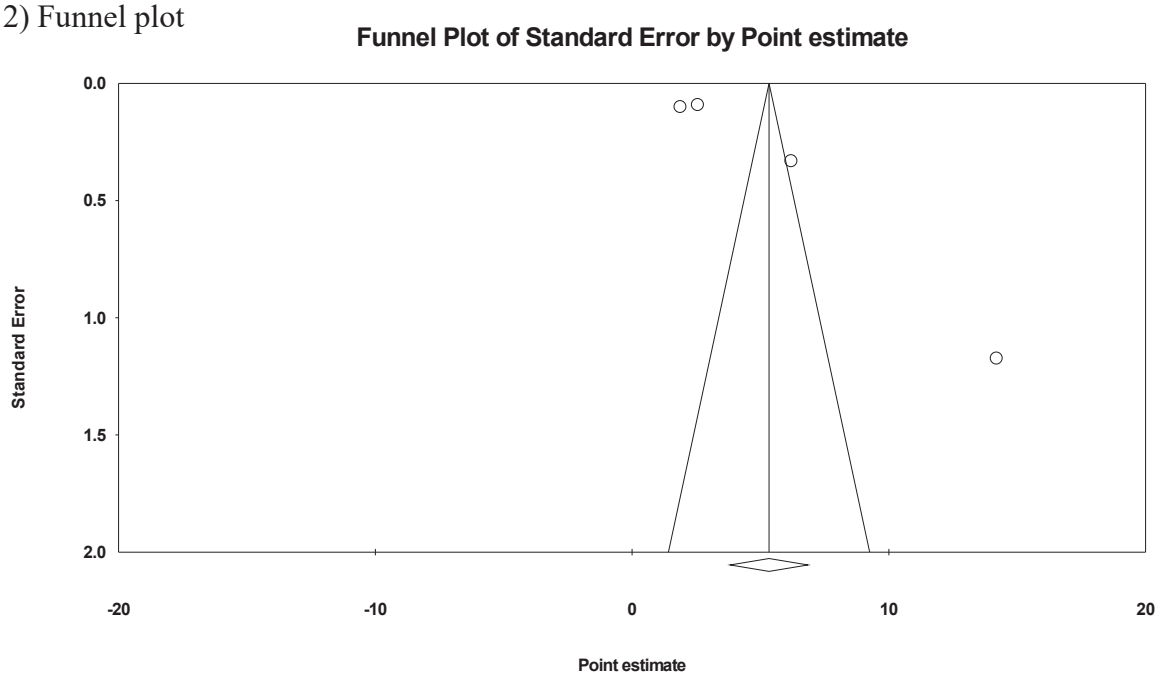
Supplementary Figure 23. Adults prevalence of EoE included in our systematic review (total study). (*A*) Forest plot; (*B*) Funnel plot.

1) Forset plot

Study name	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Allin et al, 2022	14.200	1.173	1.377	11.900	16.500	12.101	0.000
Maradey-Romero C et al, 2015	6.200	0.332	0.110	5.550	6.850	18.695	0.000
Mansoor E et al, 2016	2.560	0.092	0.008	2.380	2.740	27.875	0.000
Syed A et al, 2017	1.882	0.101	0.010	1.684	2.079	18.675	0.000
	2.449	0.066	0.004	2.319	2.579	36.883	0.000

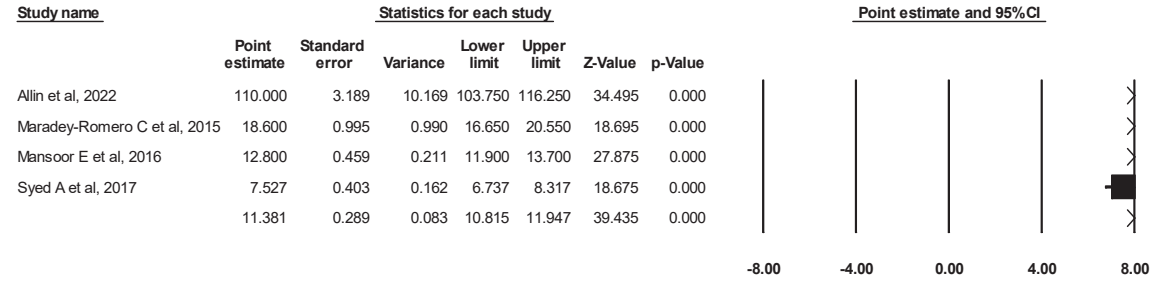


2) Funnel plot

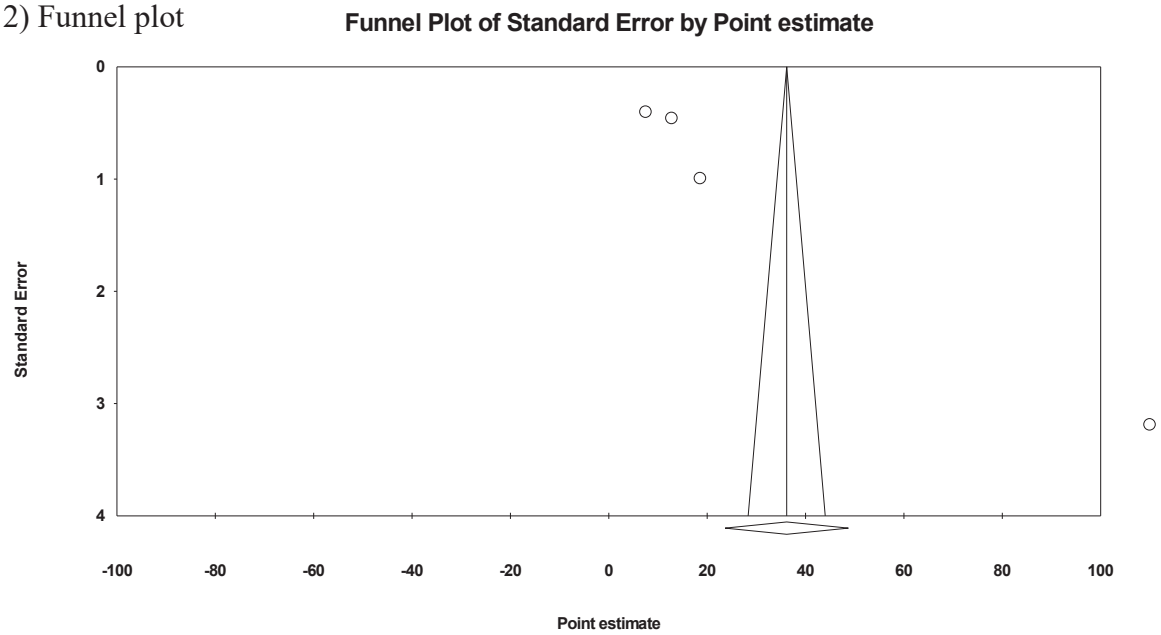


Supplementary Figure 24. Elderly incidence of EoE included in our systematic review (total study). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot

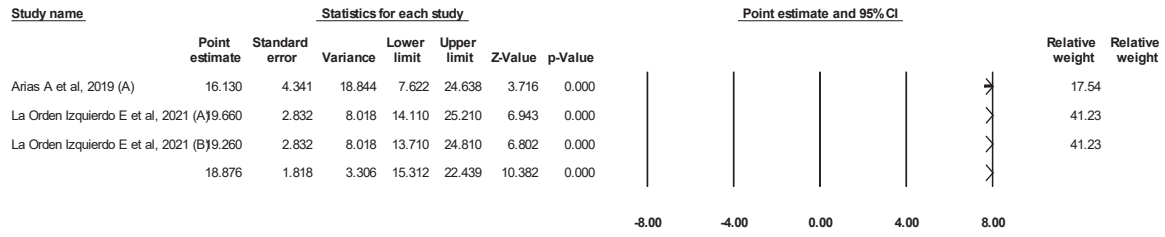


2) Funnel plot

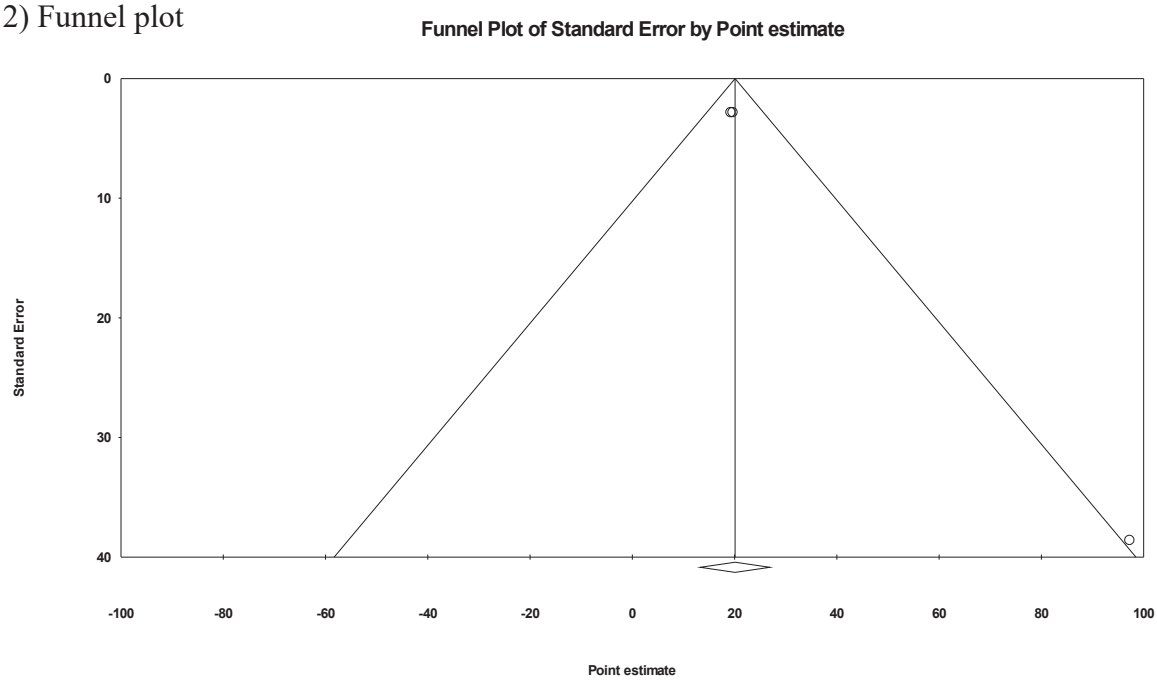


Supplementary Figure 25. Elderly prevalence of EoE included in our systematic review (total study). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot

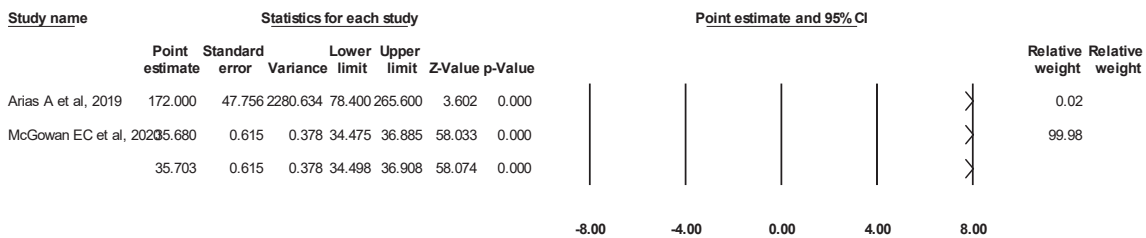


2) Funnel plot



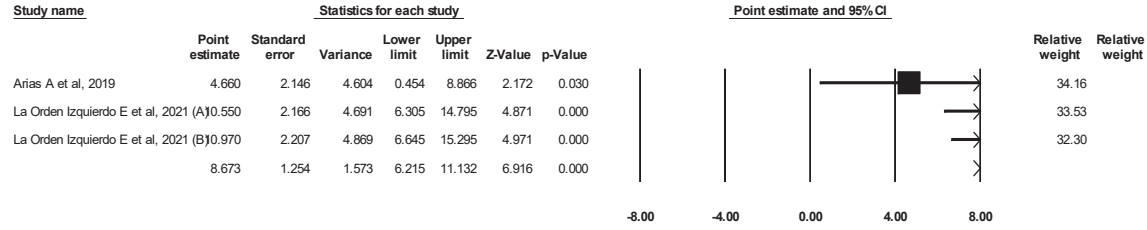
Supplementary Figure 26. Male children incidence of EoE included in our systematic review (total study). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot

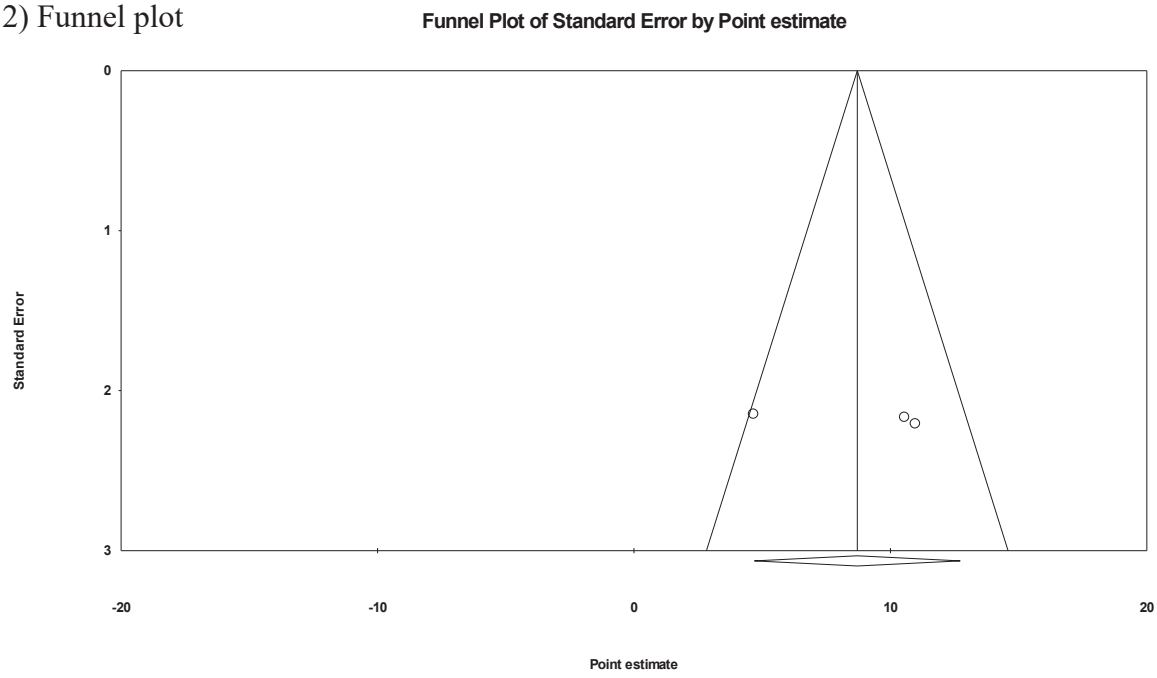


Supplementary Figure 27. Male children prevalence of EoE included in our systematic review (total study). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot

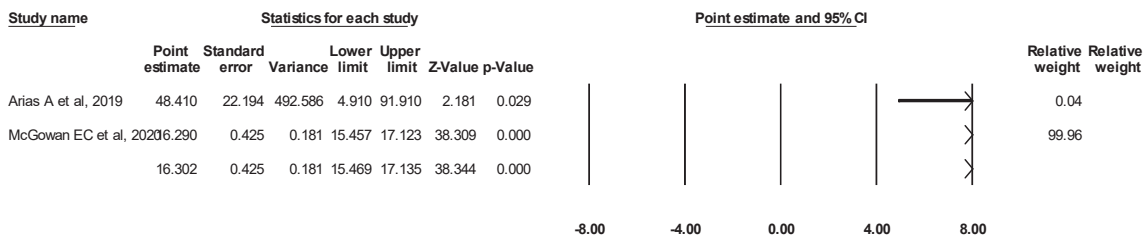


2) Funnel plot



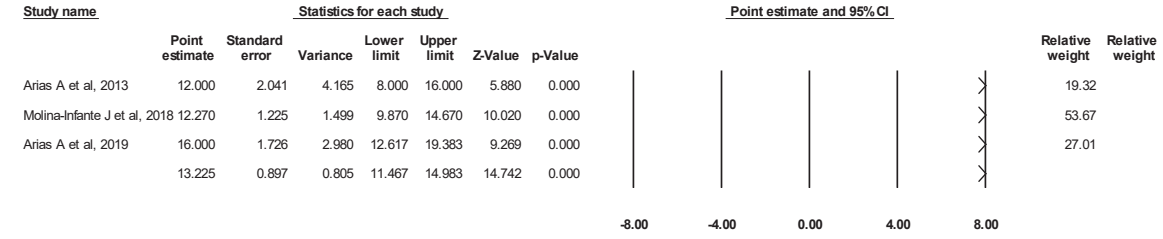
Supplementary Figure.28. Female children incidence of EoE included in our systematic review (total study). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot

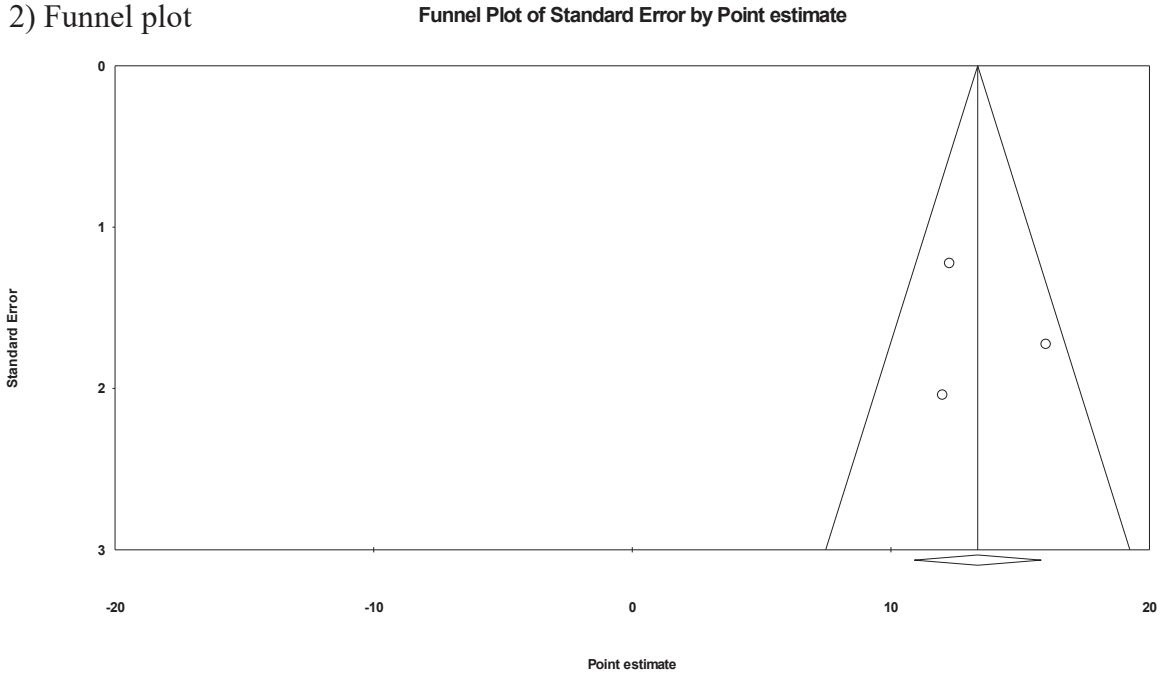


Supplementary Figure 29. Female children prevalence of EoE included in our systematic review (total study). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot

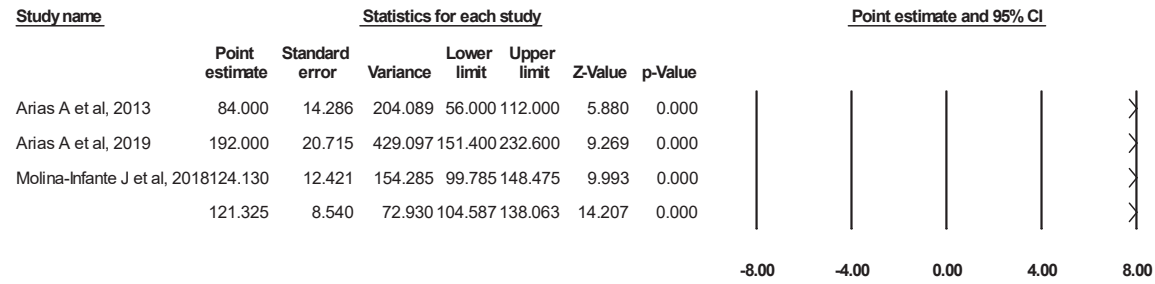


2) Funnel plot



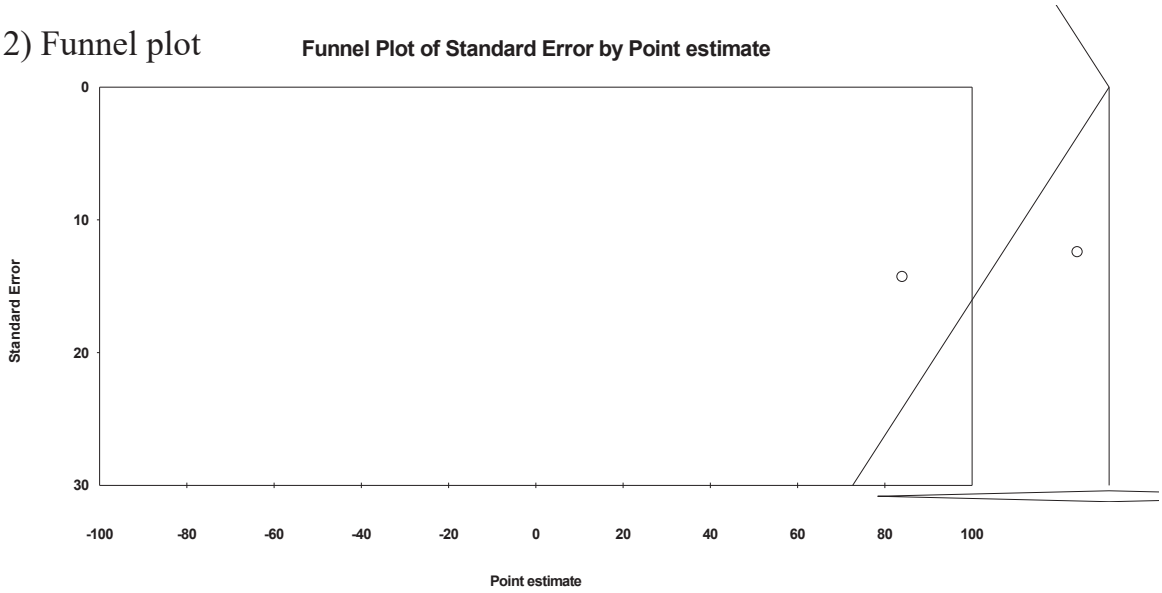
Supplementary Figure 30. Male adults incidence of EoE included in our systematic review (total study). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot



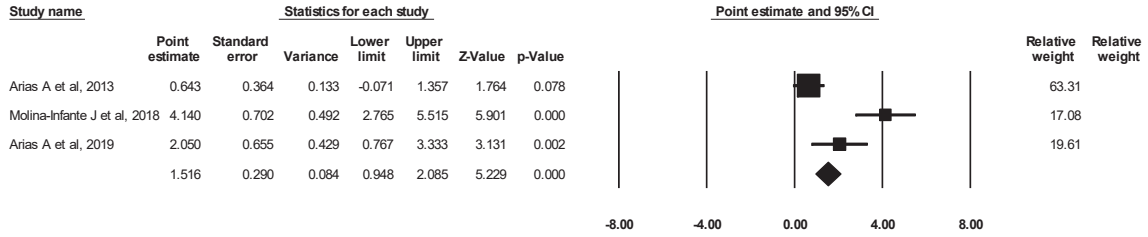
Study name	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Arias A et al, 2013	84.000	14.286	204.089	56.000	112.000	5.880	0.000
Arias A et al, 2019	192.000	20.715	429.097	151.400	232.600	9.269	0.000
Molina-Infante J et al, 2018	124.130	12.421	154.285	99.785	148.475	9.993	0.000
	121.325	8.540	72.930	104.587	138.063	14.207	0.000

2) Funnel plot

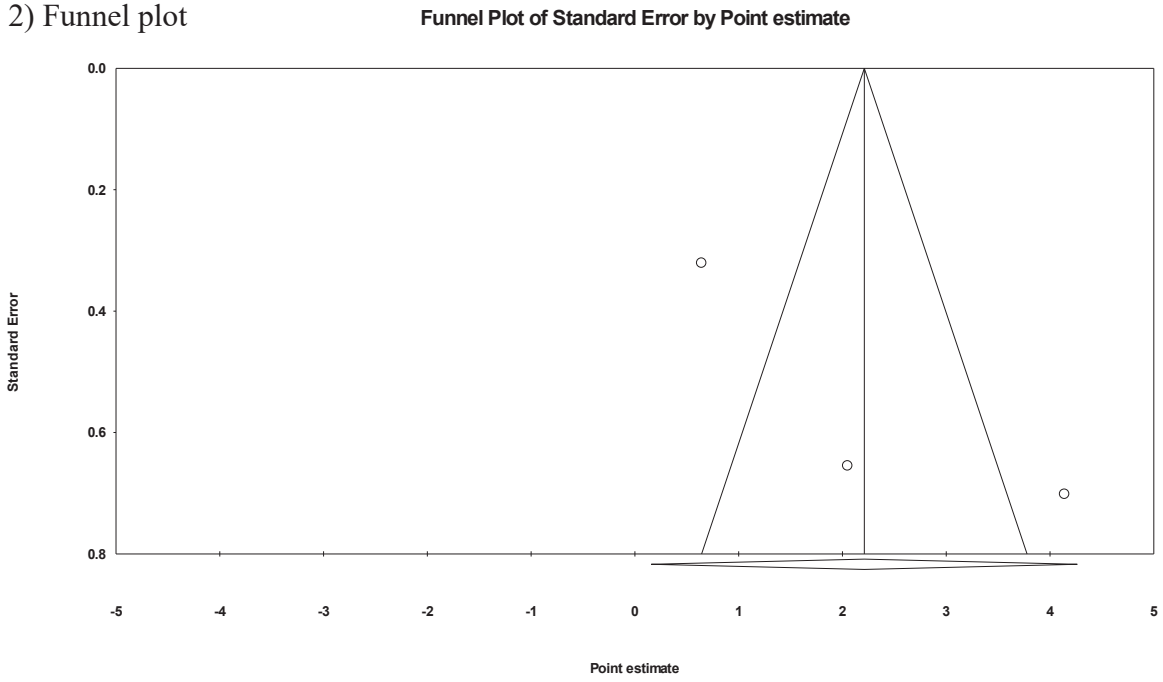


Supplementary Figure 31. Male adults prevalence of EoE included in our systematic review (total study). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot



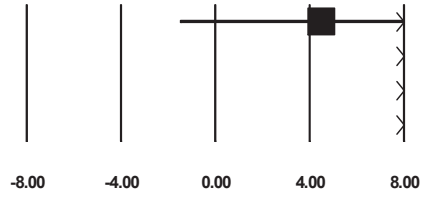
2) Funnel plot



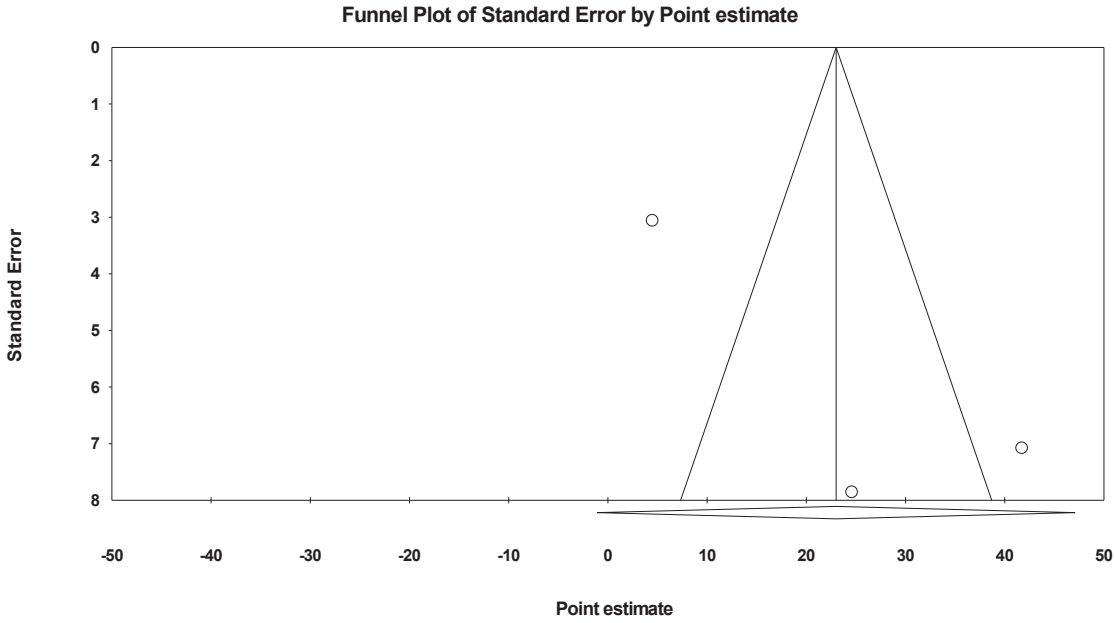
Supplementary Figure 32. Female adults incidence of EoE included in our systematic review (total study). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot

Study name	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Arias A et al, 2013	4.500	3.061	9.371	-1.500	10.500	1.470	0.142
Arias A et al, 2019	24.600	7.857	61.737	9.200	40.000	3.131	0.002
Molina-Infante J et al, 2018	41.740	7.079	50.115	27.865	55.615	5.896	0.000
	11.981	2.646	7.000	6.795	17.166	4.528	0.000

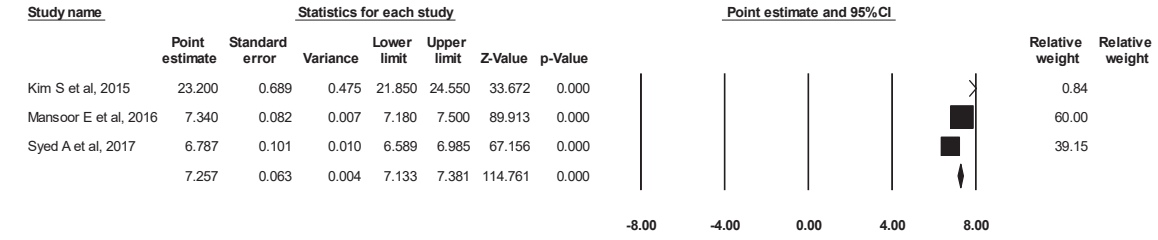


2) Funnel plot

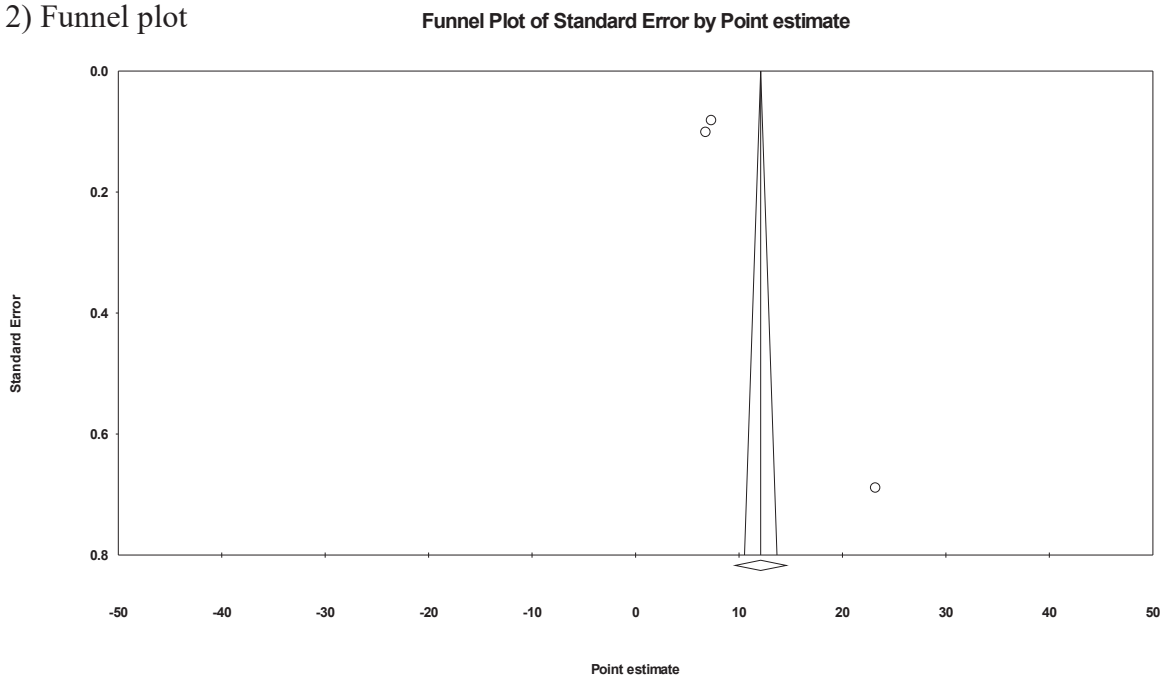


Supplementary Figure 33. Female adults prevalence of EoE included in our systematic review (total study). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot

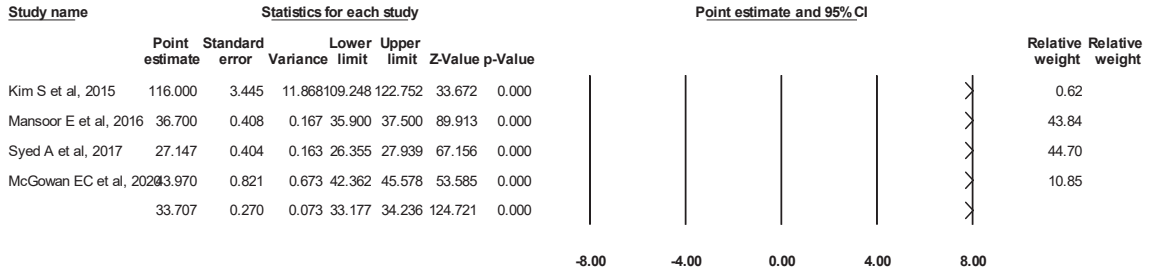


2) Funnel plot

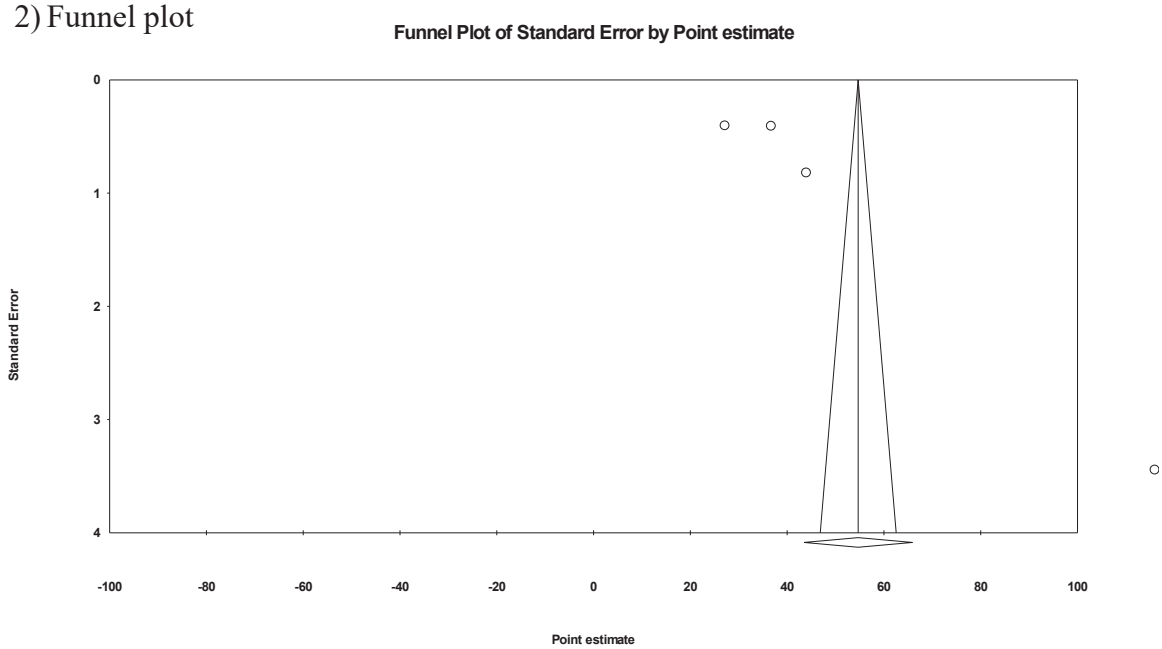


Supplementary Figure 34. White incidence of EoE included in our systematic review (total study). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot

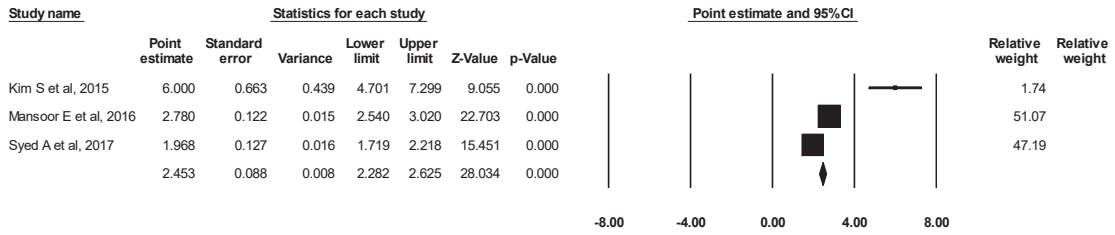


2) Funnel plot

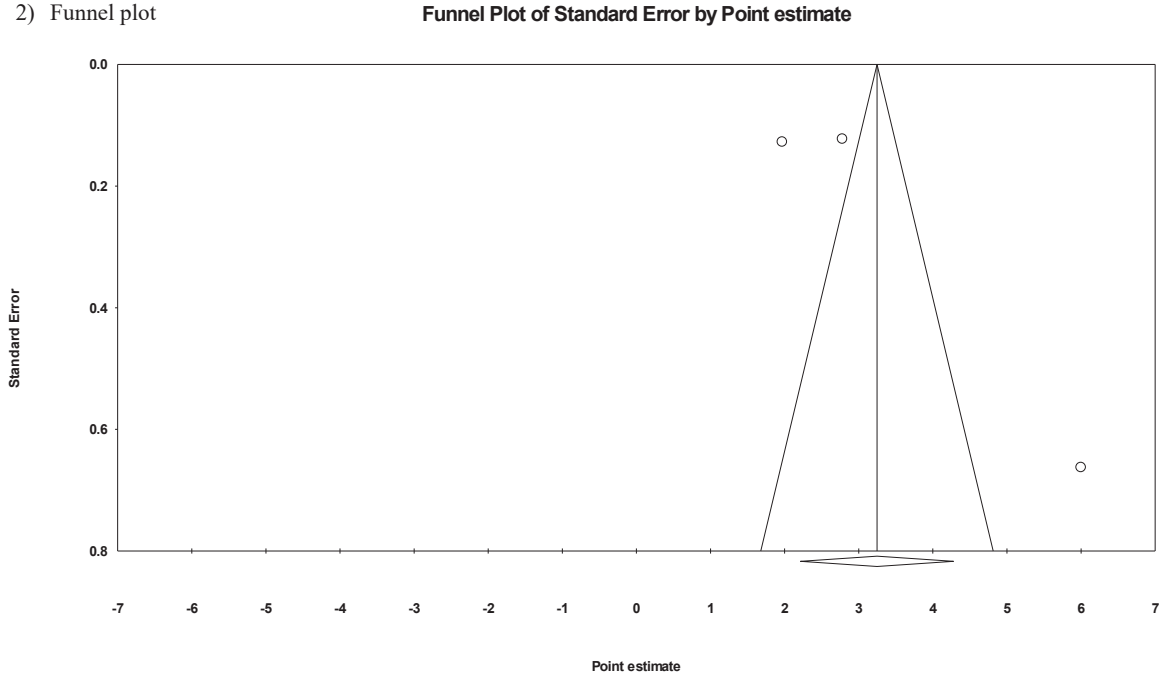


Supplementary Figure 35. White prevalence of EoE included in our systematic review (total study). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot

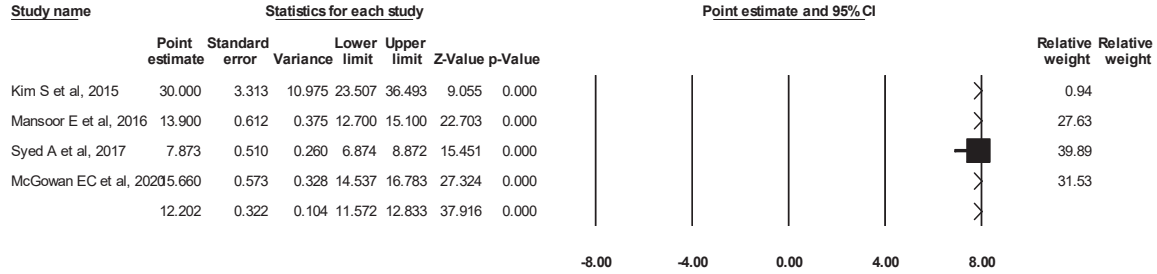


2) Funnel plot

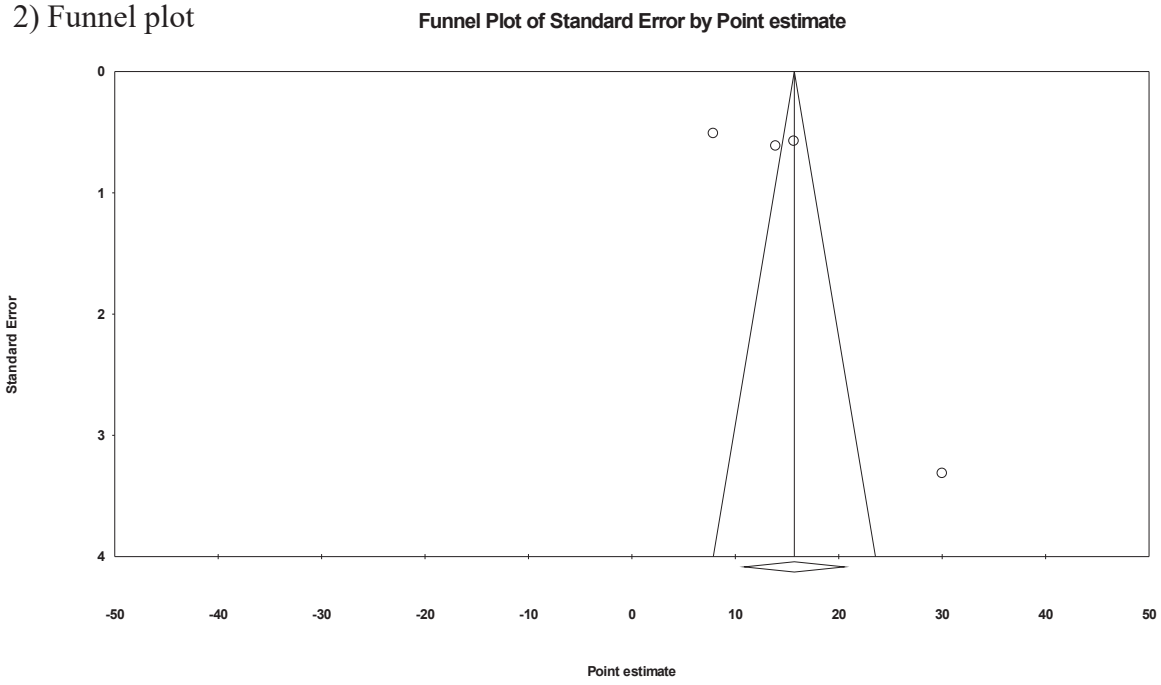


Supplementary Figure 36. Black incidence of EoE included in our systematic review (total study). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot

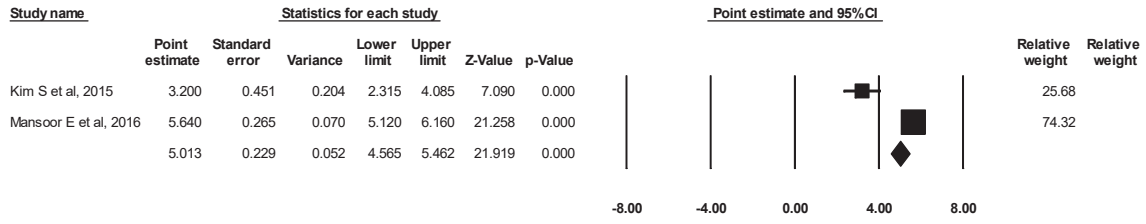


2) Funnel plot



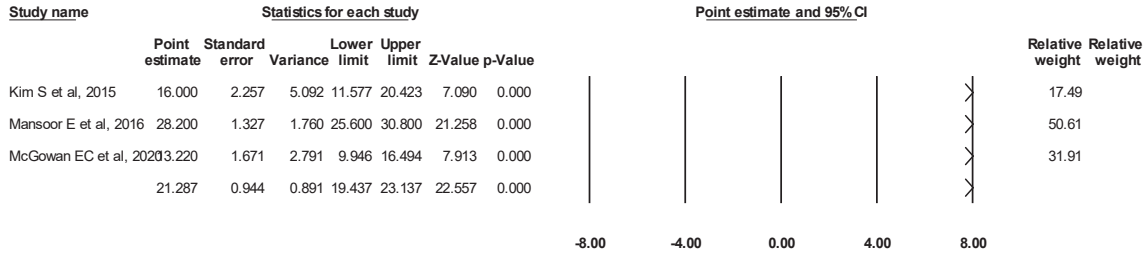
Supplementary Figure 37. Black prevalence of EoE included in our systematic review (total study). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot

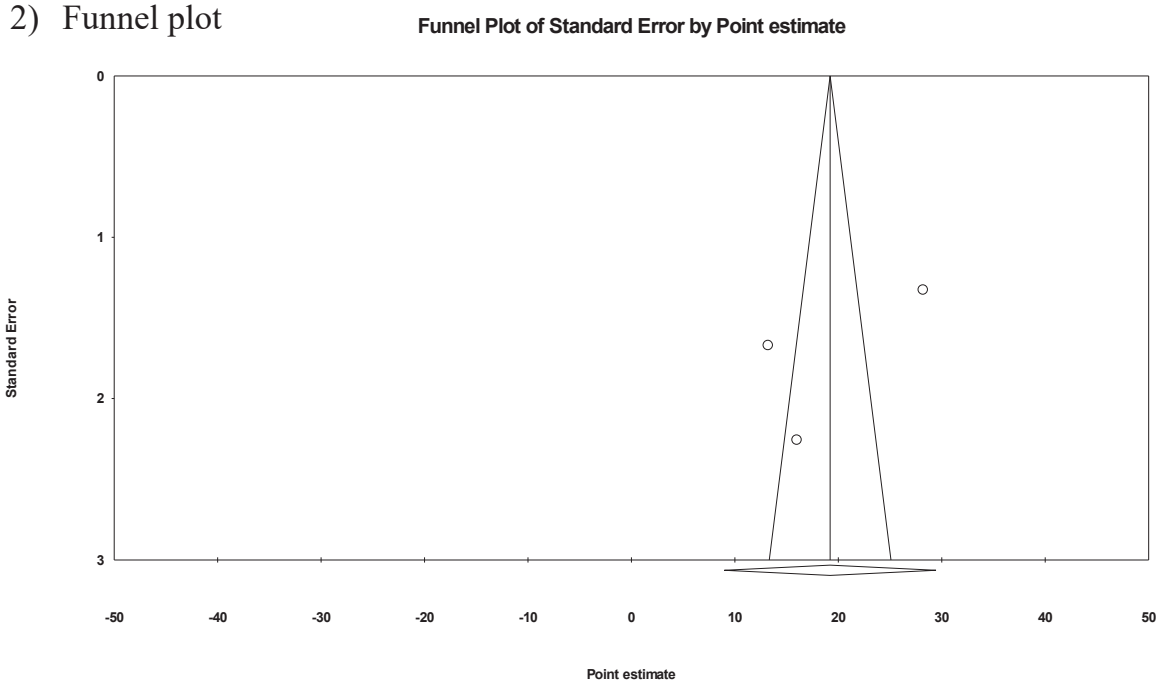


Supplementary Figure 38. Asian incidence of EoE included in our systematic review (total study). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot

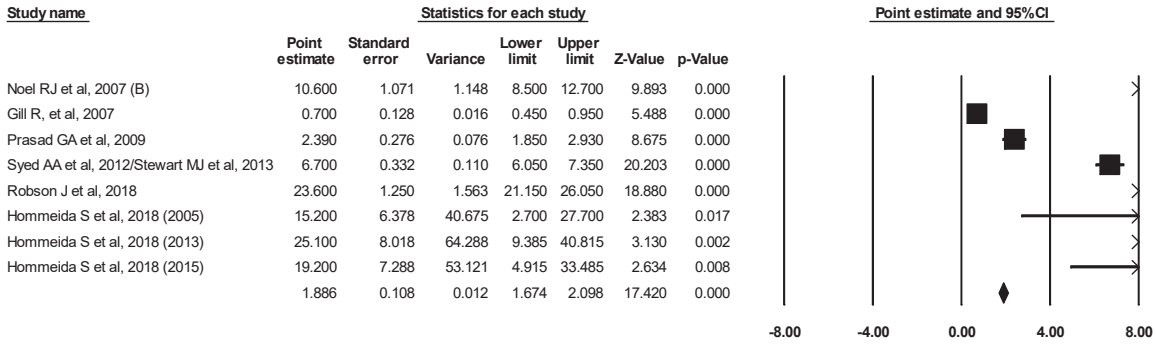


2) Funnel plot

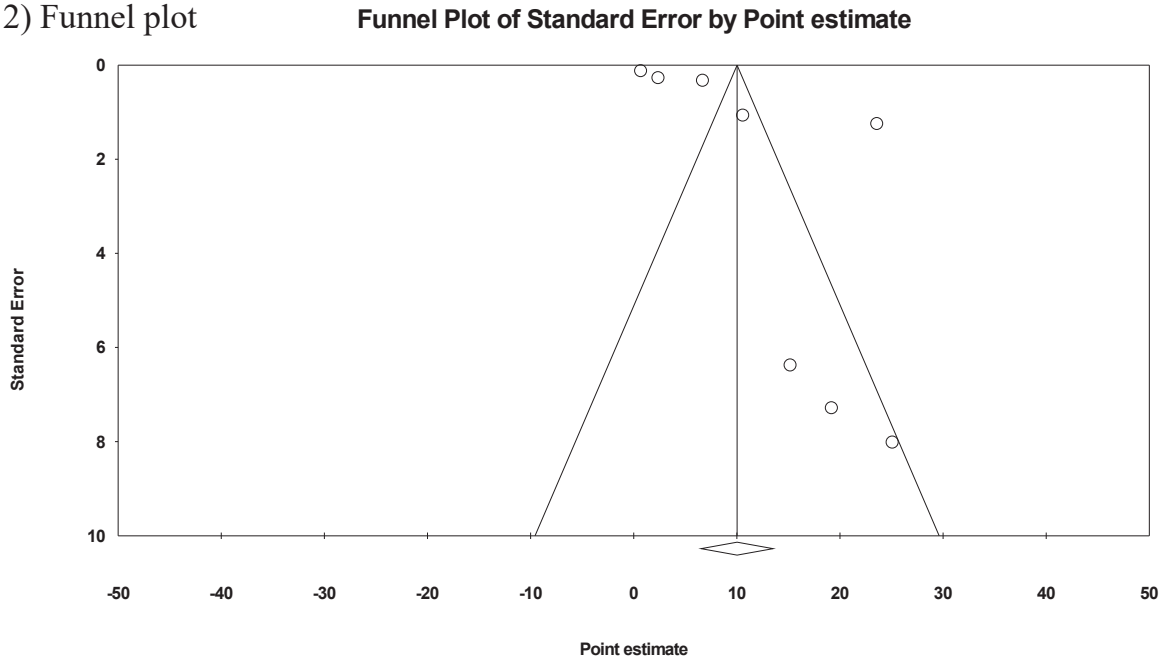


Supplementary Figure 39. Asian prevalence of EoE included in our systematic review (total study). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot



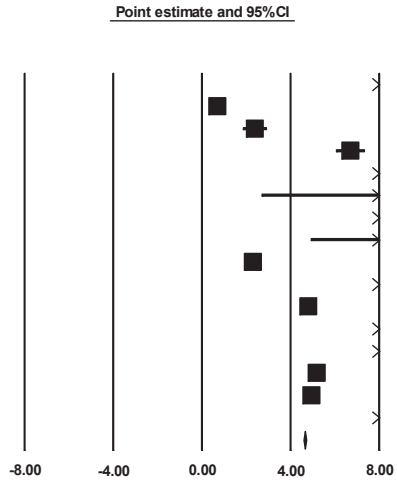
2) Funnel plot



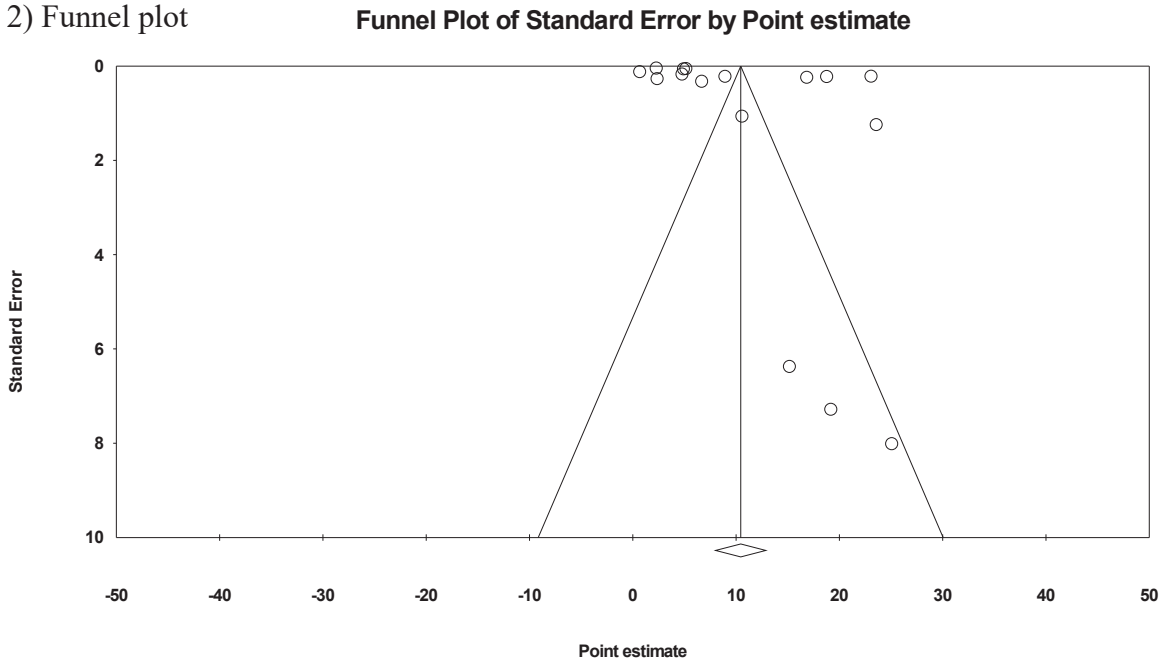
Supplementary Figure 40. North America incidence of EoE included in our systematic review (researcher-validated studies). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot

Study name	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Noel RJ et al, 2007 (B)	10.600	1.071	1.148	8.500	12.700	9.893	0.000
Gill R, et al, 2007	0.700	0.128	0.016	0.450	0.950	5.488	0.000
Prasad GA et al, 2009	2.390	0.276	0.076	1.850	2.930	8.675	0.000
Syed AA et al, 2012/Stewart MJ et al, 2013	6.700	0.332	0.110	6.050	7.350	20.203	0.000
Robson J et al, 2018	23.600	1.250	1.563	21.150	26.050	18.880	0.000
Hommeida S et al, 2018 (2005)	15.200	6.378	40.675	2.700	27.700	2.383	0.017
Hommeida S et al, 2018 (2013)	25.100	8.018	64.288	9.385	40.815	3.130	0.002
Hommeida S et al, 2018 (2015)	19.200	7.288	53.121	4.915	33.485	2.634	0.008
Prakash R et al, 2013	2.300	0.051	0.003	2.200	2.400	45.079	0.000
Dellon ES et al, 2014	18.800	0.230	0.053	18.350	19.250	81.883	0.000
Ally MR et al, 2014	4.800	0.179	0.032	4.450	5.150	26.880	0.000
Maradey-Romero C et al, 2015	16.867	0.247	0.061	16.383	17.350	68.396	0.000
Kim S et al, 2015	8.960	0.227	0.051	8.516	9.404	39.529	0.000
Mansoor E et al, 2016	5.180	0.061	0.004	5.060	5.300	84.605	0.000
Syed A et al, 2017	4.939	0.067	0.005	4.807	5.071	73.279	0.000
Limketkai BN et al, 2019	23.100	0.223	0.050	22.663	23.537	103.540	0.000
	4.645	0.031	0.001	4.585	4.705	151.433	0.000

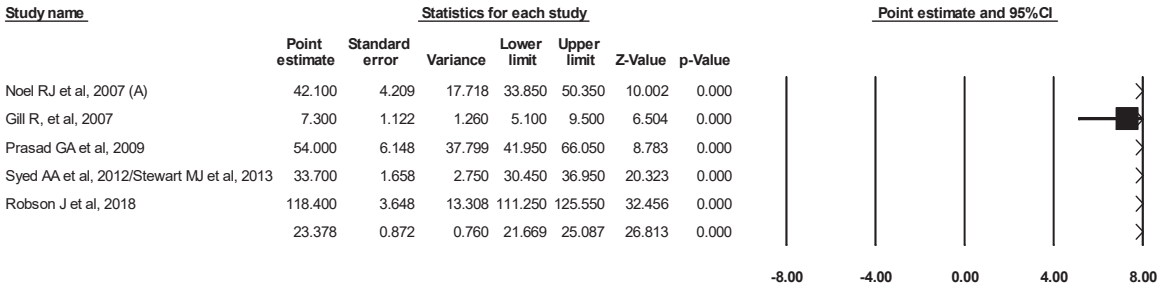


2) Funnel plot

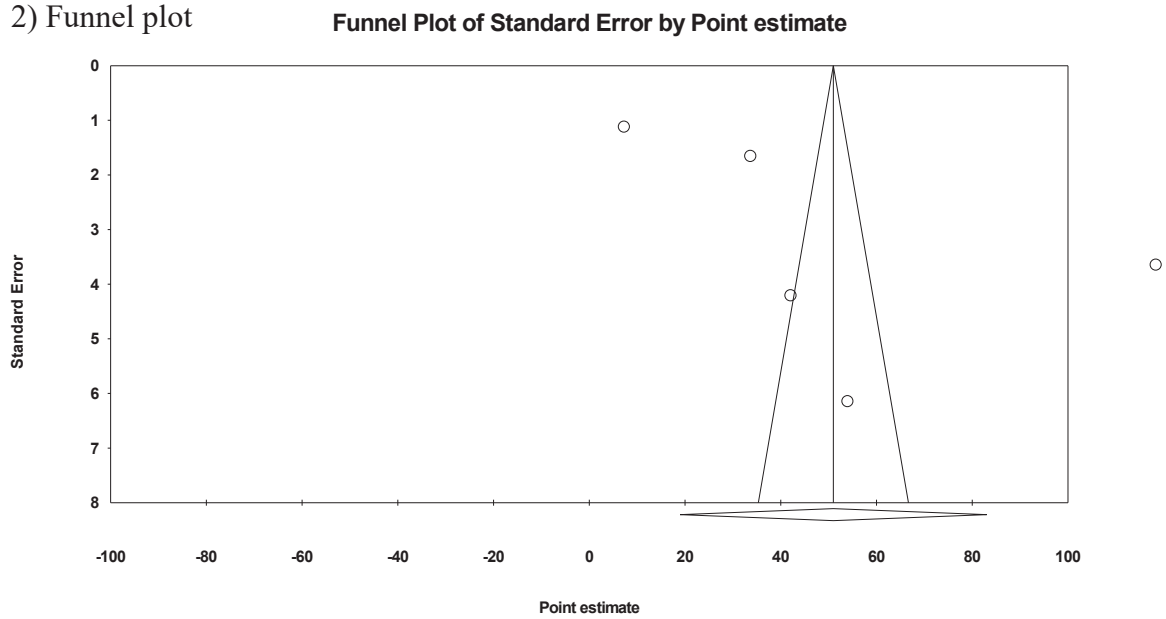


Supplementary Figure 41. North America incidence of EoE included in our systematic review (total study). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot



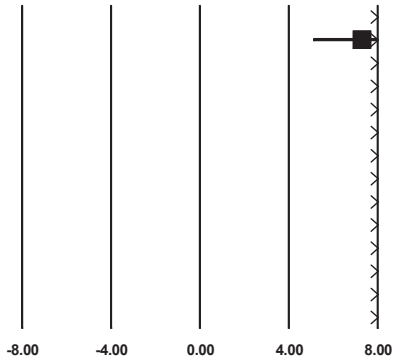
2) Funnel plot



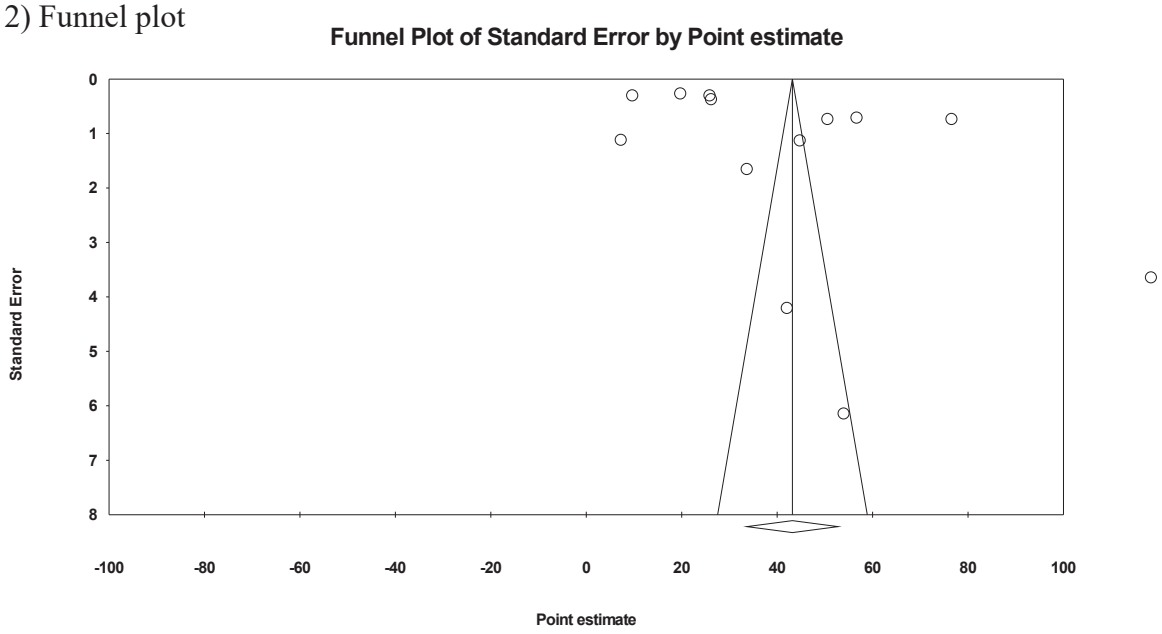
Supplementary Figure 42. North America prevalence of EoE included in our systematic review (researcher-validated studies). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot

Study name	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Noel RJ et al, 2007 (A)	42.100	4.209	17.718	33.850	50.350	10.002	0.000
Gill R, et al, 2007	7.300	1.122	1.260	5.100	9.500	6.504	0.000
Prasad GA et al, 2009	54.000	6.148	37.799	41.950	66.050	8.783	0.000
Syed AA et al, 2012/Stewart MJ et al, 2013	33.700	1.658	2.750	30.450	36.950	20.323	0.000
Robson J et al, 2018	118.400	3.648	13.308	111.250	125.550	32.456	0.000
Dellon ES et al, 2014	56.700	0.714	0.510	55.300	58.100	79.379	0.000
Ally MR et al, 2014	9.700	0.306	0.094	9.100	10.300	31.686	0.000
Maradey-Romero C et al, 2015	50.600	0.740	0.547	49.150	52.050	68.396	0.000
Kim S et al, 2015	44.800	1.133	1.284	42.579	47.021	39.529	0.000
Mansoor E et al, 2016	25.900	0.306	0.094	25.300	26.500	84.605	0.000
Syed A et al, 2017	19.750	0.270	0.073	19.220	20.280	73.036	0.000
Limketkai BN et al, 2019	76.600	0.740	0.547	75.150	78.050	103.540	0.000
McGowan EC et al, 2020	26.210	0.377	0.142	25.471	26.949	69.548	0.000
	24.990	0.142	0.020	24.713	25.268	176.296	0.000



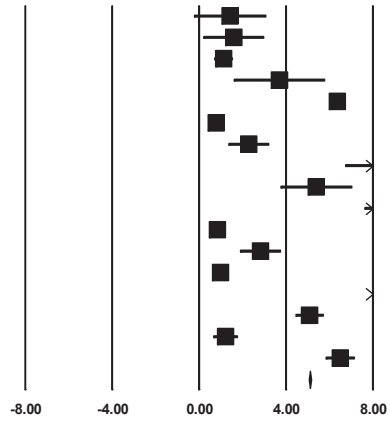
2) Funnel plot



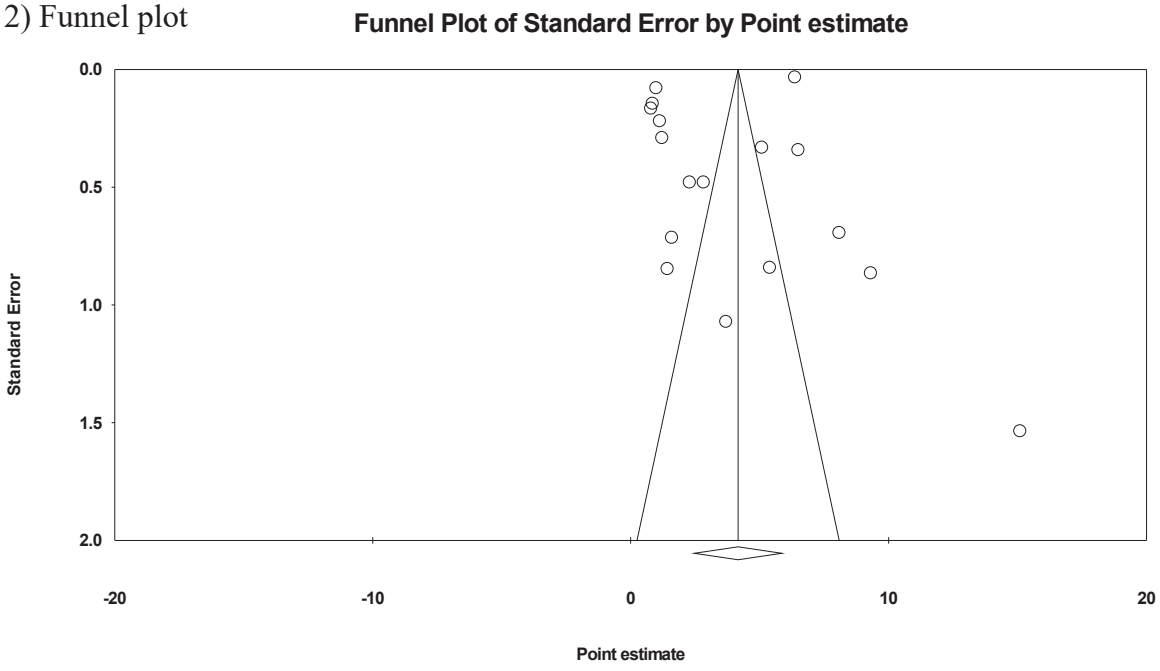
Supplementary Figure 43. North America prevalence of EoE included in our systematic review (total study). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot

Study name	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Straumann A et al, 2005 (B)	1.430	0.847	0.717	-0.230	3.090	1.688	0.091
Dalby K et al, 2010	1.600	0.714	0.510	0.200	3.000	2.240	0.025
Hruz P et al, 2011	1.130	0.219	0.048	0.700	1.560	5.151	0.000
O'Donnell S et al, 2011	3.700	1.071	1.148	1.600	5.800	3.453	0.001
Arias A et al, 2013	6.370	0.033	0.001	6.305	6.435	192.076	0.000
Homan M et al, 2015	0.790	0.166	0.027	0.465	1.115	4.764	0.000
Giriens B et al, 2015	2.290	0.480	0.230	1.350	3.230	4.775	0.000
Molina-Infante J et al, 2018	8.090	0.694	0.481	6.730	9.450	11.659	0.000
La Orden Izquierdo E et al, 2018	5.400	0.842	0.709	3.750	7.050	6.414	0.000
Arias A et al, 2019	9.308	0.865	0.749	7.613	11.004	10.758	0.000
Ristic N et al, 2019	0.850	0.145	0.021	0.565	1.135	5.846	0.000
Zdanowicz K et al, 2020	2.830	0.480	0.230	1.890	3.770	5.901	0.000
RooiJ WE et al, 2020	0.990	0.079	0.006	0.835	1.145	12.518	0.000
La Orden Izquierdo E et al, 2021	15.100	1.536	2.359	12.090	18.110	9.832	0.000
Melgaard D et al, 2021	5.090	0.332	0.110	4.440	5.740	15.348	0.000
Garber et al, 2022	1.220	0.291	0.085	0.650	1.790	4.195	0.000
Allin et al, 2022	6.500	0.342	0.117	5.830	7.170	19.015	0.000
	5.104	0.029	0.001	5.048	5.160	178.353	0.000



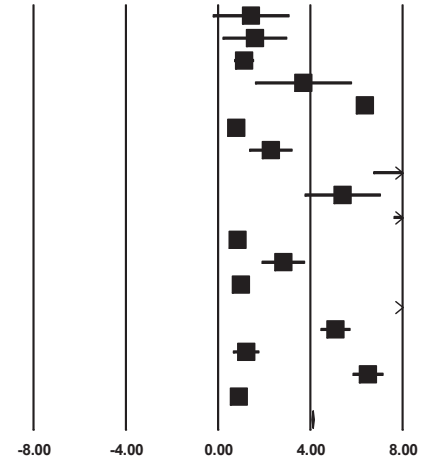
2) Funnel plot



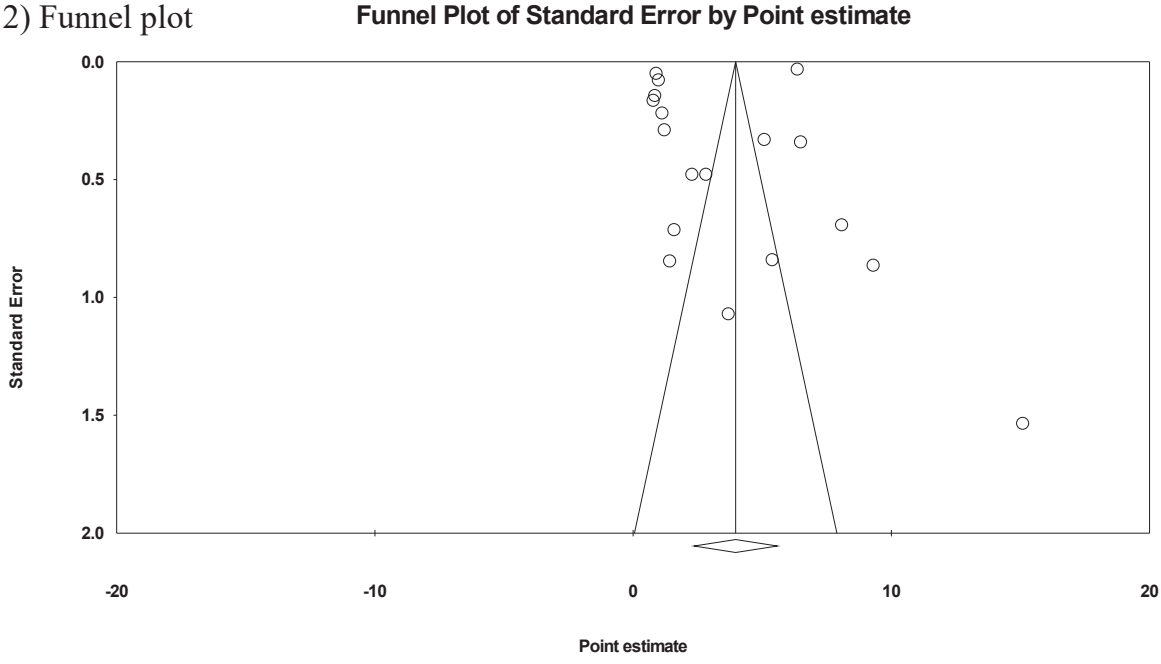
Supplementary Figure 44. Europe incidence of EoE included in our systematic review (researcher-validated studies). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot

Study name	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Straumann A et al, 2005 (B)	1.430	0.847	0.717	-0.230	3.090	1.688	0.091
Dalby K et al, 2010	1.600	0.714	0.510	0.200	3.000	2.240	0.025
Hruz P et al, 2011	1.130	0.219	0.048	0.700	1.560	5.151	0.000
O'Donnell S et al, 2011	3.700	1.071	1.148	1.600	5.800	3.453	0.001
Arias A et al, 2013	6.370	0.033	0.001	6.305	6.435	192.076	0.000
Homan M et al, 2015	0.790	0.166	0.027	0.465	1.115	4.764	0.000
Giriens B et al, 2015	2.290	0.480	0.230	1.350	3.230	4.775	0.000
Molina-Infante J et al, 2018	8.090	0.694	0.481	6.730	9.450	11.659	0.000
La Orden Izquierdo E et al, 2018	5.400	0.842	0.709	3.750	7.050	6.414	0.000
Arias A et al, 2019	9.308	0.865	0.749	7.613	11.004	10.758	0.000
Ristic N et al, 2019	0.850	0.145	0.021	0.565	1.135	5.846	0.000
Zdanowicz K et al, 2020	2.830	0.480	0.230	1.890	3.770	5.901	0.000
RooiJ WE et al, 2020	0.990	0.079	0.006	0.835	1.145	12.518	0.000
La Orden Izquierdo E et al, 2021	15.100	1.536	2.359	12.090	18.110	9.832	0.000
Melgaard D et al, 2021	5.090	0.332	0.110	4.440	5.740	15.348	0.000
Garber et al, 2022	1.220	0.291	0.085	0.650	1.790	4.195	0.000
Allin et al, 2022	6.500	0.342	0.117	5.830	7.170	19.015	0.000
Dellon ES et al, 2015	0.900	0.051	0.003	0.800	1.000	17.640	0.000
	4.098	0.025	0.001	4.049	4.147	164.185	0.000

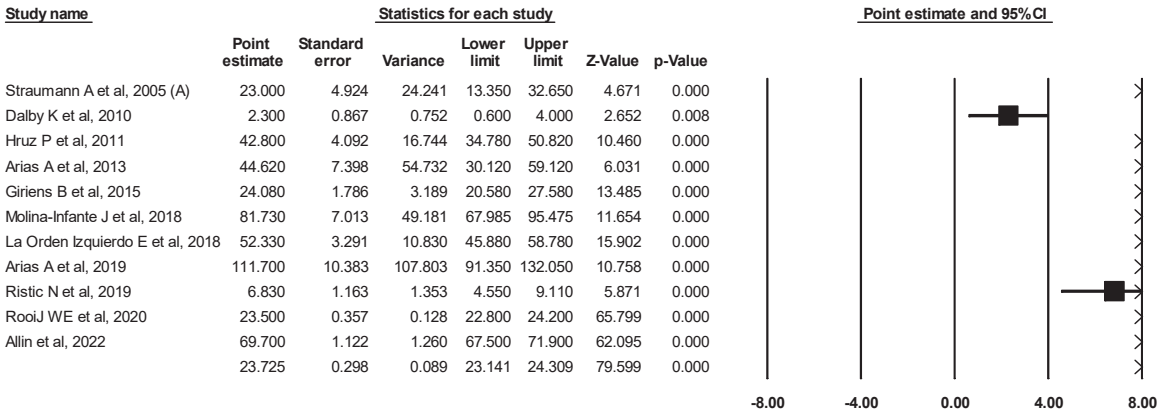


2) Funnel plot



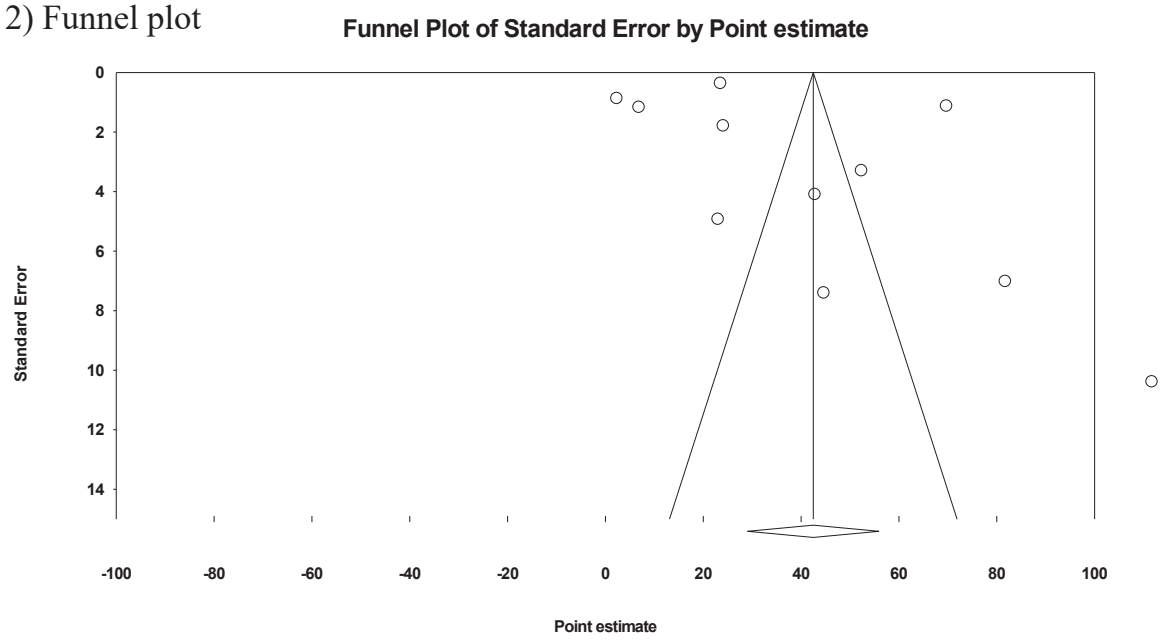
Supplementary Figure 45. Europe incidence of EoE included in our systematic review (total study). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot



Study name	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Straumann A et al, 2005 (A)	23.000	4.924	24.241	13.350	32.650	4.671	0.000
Dalby K et al, 2010	2.300	0.867	0.752	0.600	4.000	2.652	0.008
Hruz P et al, 2011	42.800	4.092	16.744	34.780	50.820	10.460	0.000
Arias A et al, 2013	44.620	7.398	54.732	30.120	59.120	6.031	0.000
Giriens B et al, 2015	24.080	1.786	3.189	20.580	27.580	13.485	0.000
Molina-Infante J et al, 2018	81.730	7.013	49.181	67.985	95.475	11.654	0.000
La Orden Izquierdo E et al, 2018	52.330	3.291	10.830	45.880	58.780	15.902	0.000
Arias A et al, 2019	111.700	10.383	107.803	91.350	132.050	10.758	0.000
Ristic N et al, 2019	6.830	1.163	1.353	4.550	9.110	5.871	0.000
RooiJ WE et al, 2020	23.500	0.357	0.128	22.800	24.200	65.799	0.000
Allin et al, 2022	69.700	1.122	1.260	67.500	71.900	62.095	0.000
	23.725	0.298	0.089	23.141	24.309	79.599	0.000

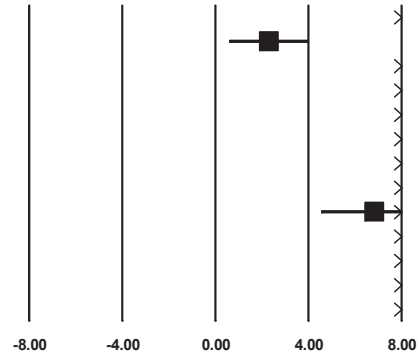
2) Funnel plot



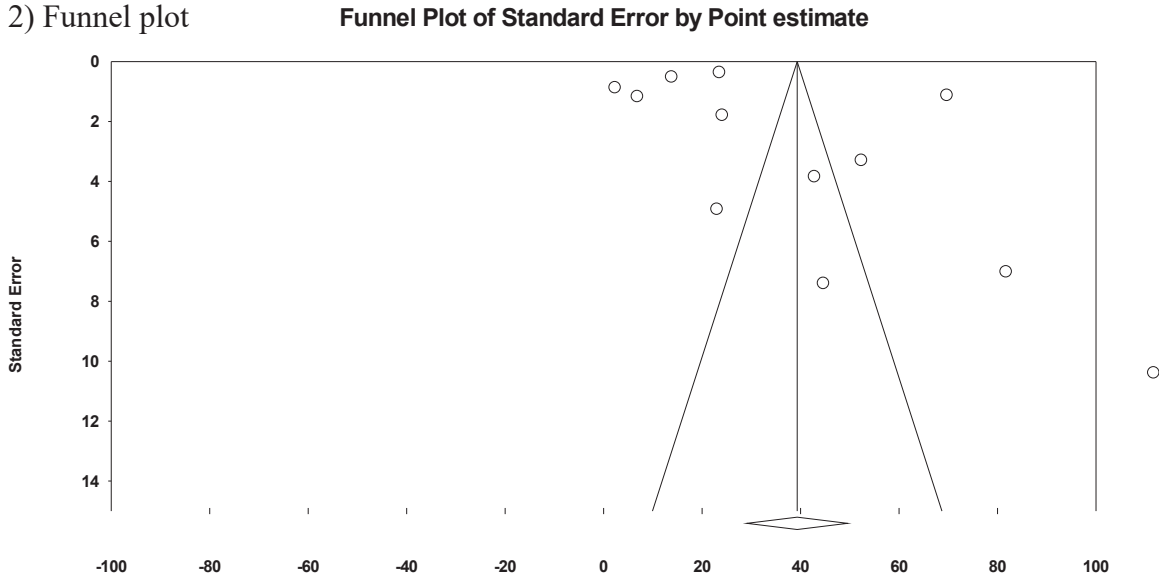
Supplementary Figure 46. Europe prevalence of EoE included in our systematic review (researcher-validated studies). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot

Study name	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Straumann A et al, 2005 (A)	23.000	4.924	24.241	13.350	32.650	4.671	0.000
Dalby K et al, 2010	2.300	0.867	0.752	0.600	4.000	2.652	0.008
Hruz P et al, 2011	42.800	3.837	14.721	35.280	50.320	11.155	0.000
Arias A et al, 2013	44.620	7.398	54.732	30.120	59.120	6.031	0.000
Giriens B et al, 2015	24.080	1.786	3.189	20.580	27.580	13.485	0.000
Molina-Infante J et al, 2018	81.730	7.013	49.181	67.985	95.475	11.654	0.000
La Orden Izquierdo E et al, 2018	52.330	3.291	10.830	45.880	58.780	15.902	0.000
Arias A et al, 2019	111.700	10.383	107.803	91.350	132.050	10.758	0.000
Ristic N et al, 2019	6.830	1.163	1.353	4.550	9.110	5.871	0.000
RooiJ WE et al, 2020	23.500	0.357	0.128	22.800	24.200	65.799	0.000
Allin et al, 2022	69.700	1.122	1.260	67.500	71.900	62.095	0.000
Dellon ES et al, 2015	13.800	0.510	0.260	12.800	14.800	27.048	0.000
	21.212	0.257	0.066	20.707	21.716	82.442	0.000



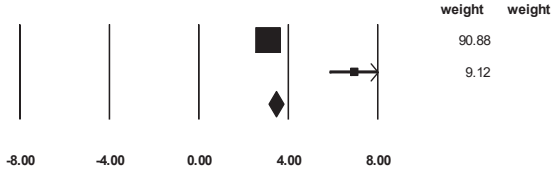
2) Funnel plot



Supplementary Figure 47. Europe prevalence of EoE included in our systematic review (total study). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot

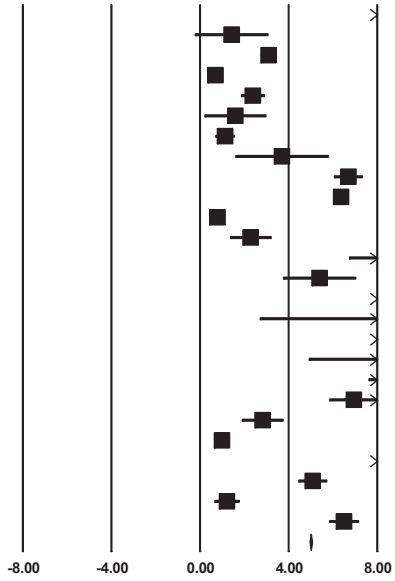
Study name	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value	Relative weight
Cherian S et al, 2006	3.100	0.179	0.032	2.750	3.450	17.360	0.000	90.88
Weerasekera K et al, 2019	6.950	0.564	0.318	5.845	8.055	12.327	0.000	9.12
	3.451	0.170	0.029	3.117	3.785	20.272	0.000	



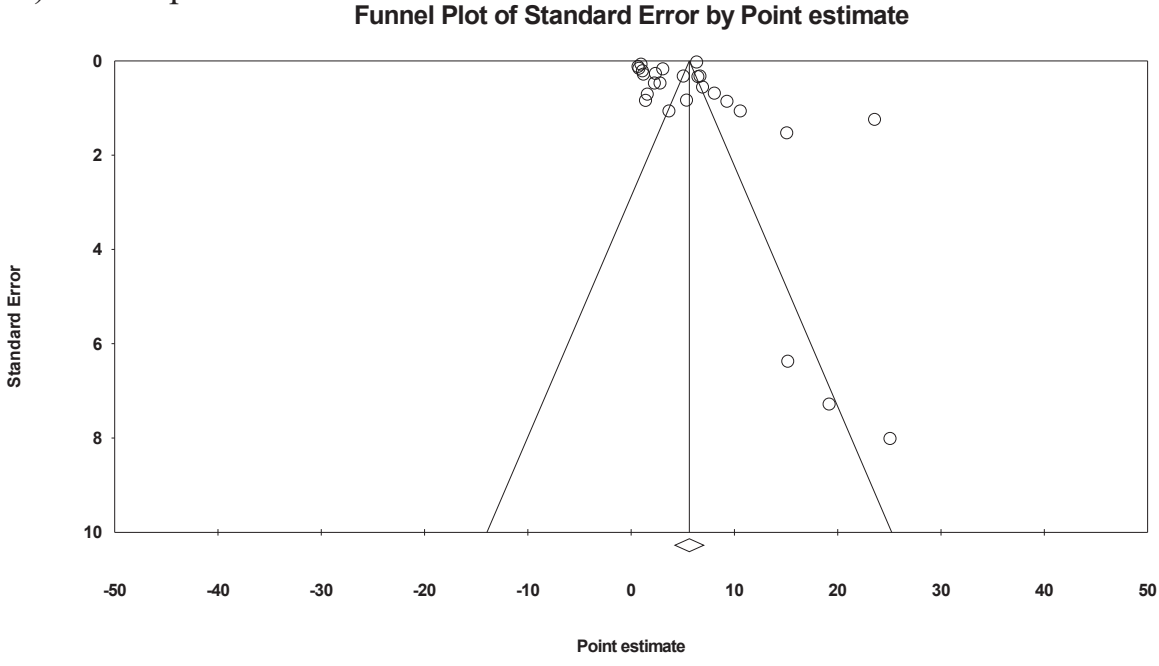
Supplementary Figure 48. Oceania incidence of EoE included in our systematic review (total study). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot

Study name	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Noel RJ et al, 2007	10.600	1.071	1.148	8.500	12.700	9.893	0.000
Straumann A et al, 2005	1.430	0.847	0.717	-0.230	3.090	1.688	0.091
Cherian S et al, 2006	3.100	0.179	0.032	2.750	3.450	17.360	0.000
Gill R, et al, 2007	0.700	0.128	0.016	0.450	0.950	5.488	0.000
Prasad GA et al, 2009	2.390	0.276	0.076	1.850	2.930	8.675	0.000
Dalby K et al, 2010	1.600	0.714	0.510	0.200	3.000	2.240	0.025
Hruz P et al, 2011	1.130	0.219	0.048	0.700	1.560	5.151	0.000
O'Donnell S et al, 2011	3.700	1.071	1.148	1.600	5.800	3.453	0.001
Syed AA et al, 2012/Stewart MJ et al, 2013	6.700	0.332	0.110	6.050	7.350	20.203	0.000
Arias A et al, 2013	6.370	0.033	0.001	6.305	6.435	192.076	0.000
Homan M et al, 2015	0.790	0.166	0.027	0.465	1.115	4.764	0.000
Giriens B et al, 2015	2.290	0.480	0.230	1.350	3.230	4.775	0.000
Molina-Infante J et al, 2018	8.090	0.694	0.481	6.730	9.450	11.659	0.000
La Orden Izquierdo E et al, 2018	5.400	0.842	0.709	3.750	7.050	6.414	0.000
Robson J et al, 2018	23.600	1.250	1.563	21.150	26.050	18.880	0.000
Hommeida S et al, 2018 (2005)	15.200	6.378	40.675	2.700	27.700	2.383	0.017
Hommeida S et al, 2018 (2013)	25.100	8.018	64.288	9.385	40.815	3.130	0.002
Hommeida S et al, 2018 (2015)	19.200	7.288	53.121	4.915	33.485	2.634	0.008
Arias A et al, 2019	9.308	0.865	0.749	7.613	11.004	10.758	0.000
Weerasekera K et al, 2019	6.950	0.564	0.318	5.845	8.055	12.327	0.000
Zdanowicz K et al, 2020	2.830	0.480	0.230	1.890	3.770	5.901	0.000
RooiJ WE et al, 2020	0.990	0.079	0.006	0.835	1.145	12.518	0.000
La Orden Izquierdo E et al, 2021	15.100	1.536	2.359	12.090	18.110	9.832	0.000
Melgaard D et al, 2021	5.090	0.332	0.110	4.440	5.740	15.348	0.000
Garber et al, 2022	1.220	0.291	0.085	0.650	1.790	4.195	0.000
Allin et al, 2022	6.500	0.342	0.117	5.830	7.170	19.015	0.000
	5.003	0.028	0.001	4.949	5.057	179.948	0.000

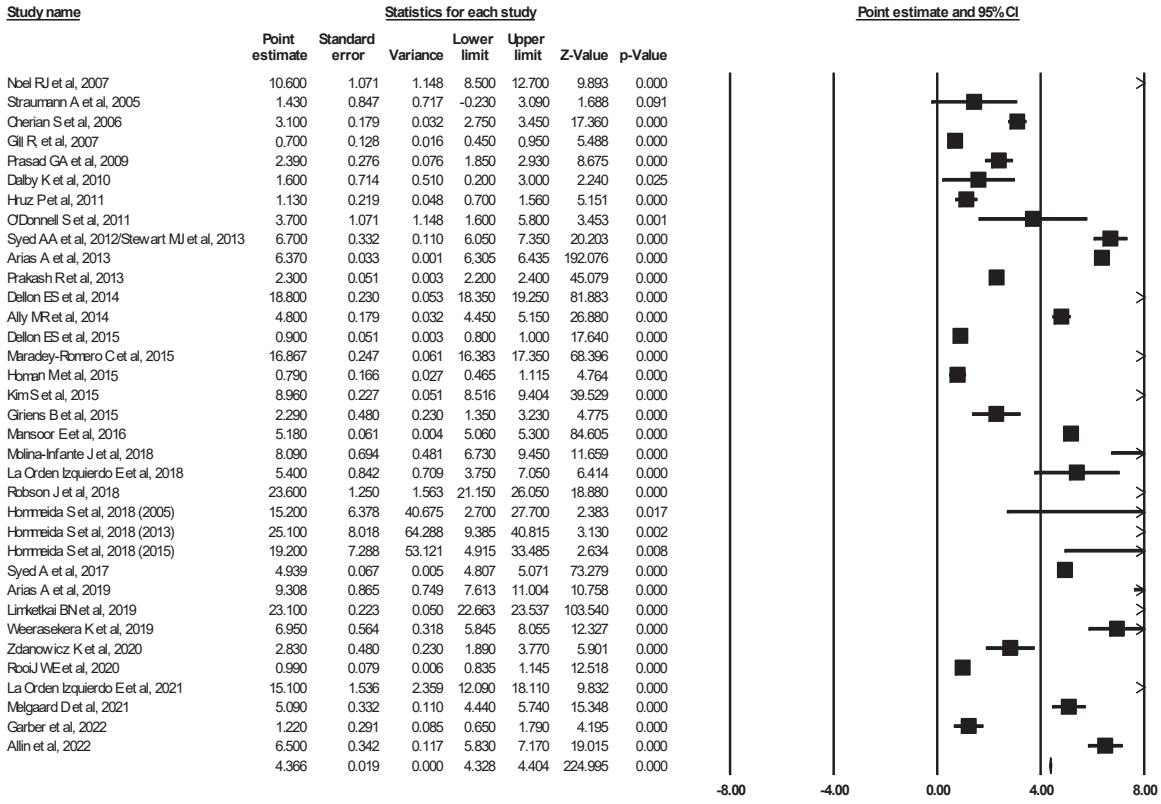


2) Funnel plot



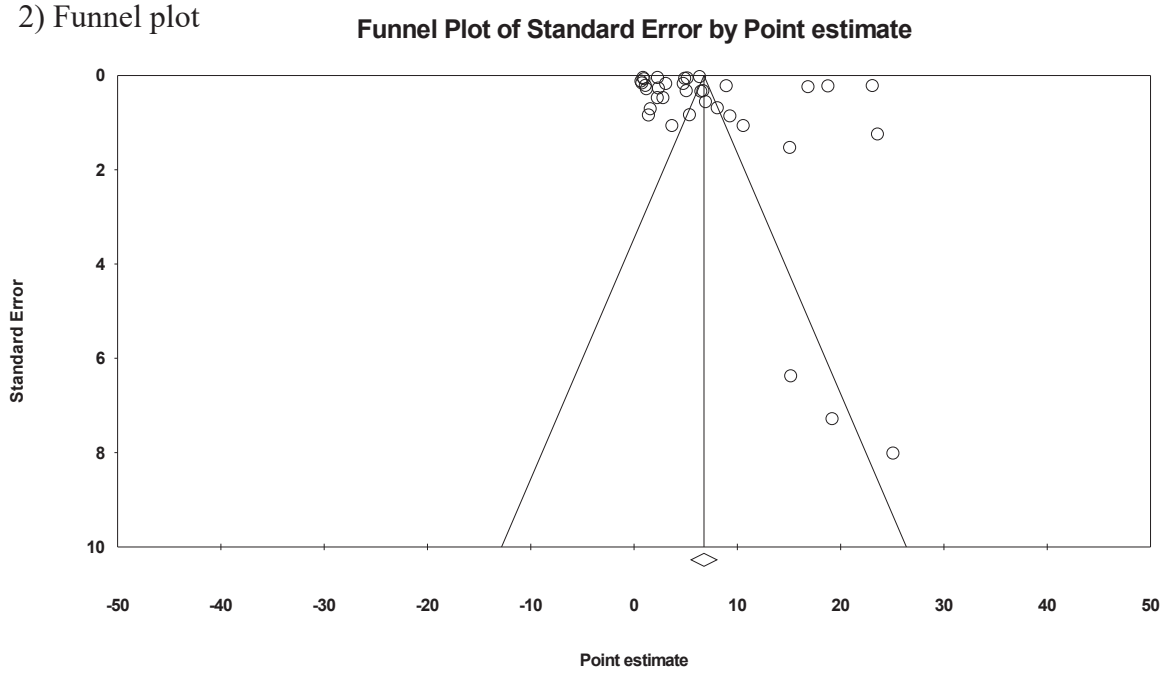
Supplementary Figure 49. High-income countries incidence of EoE included in our systematic review (researcher-validated studies). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot



Study name	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Noel RJ et al, 2007	10.600	1.071	1.148	8.500	12.700	9.893	0.000
Straumann A et al, 2005	1.430	0.847	0.717	-0.230	3.090	1.688	0.091
Cherian S et al, 2006	3.100	0.179	0.032	2.750	3.450	17.360	0.000
Gill R et al, 2007	0.700	0.128	0.016	0.450	0.950	5.488	0.000
Prasad GA et al, 2009	2.390	0.276	0.076	1.850	2.930	8.675	0.000
Dalby K et al, 2010	1.600	0.714	0.510	0.200	3.000	2.240	0.025
Hruz P et al, 2011	1.130	0.219	0.048	0.700	1.560	5.151	0.000
O'Donnell S et al, 2011	3.700	1.071	1.148	1.600	5.800	3.453	0.001
Syed AA et al, 2012/Stewart MJ et al, 2013	6.700	0.332	0.110	6.050	7.350	20.203	0.000
Arias A et al, 2013	6.370	0.033	0.001	6.305	6.435	192.076	0.000
Prakash R et al, 2013	2.300	0.051	0.003	2.200	2.400	45.079	0.000
Dellon ES et al, 2014	18.800	0.230	0.053	18.350	19.250	81.883	0.000
Ally MR et al, 2014	4.800	0.179	0.032	4.450	5.150	26.880	0.000
Dellon ES et al, 2015	0.900	0.051	0.003	0.800	1.000	17.640	0.000
Maradey-Romero C et al, 2015	16.867	0.247	0.061	16.383	17.350	68.396	0.000
Homan M et al, 2015	0.790	0.166	0.027	0.465	1.115	4.764	0.000
Kim S et al, 2015	8.960	0.227	0.051	8.516	9.404	39.529	0.000
Giriens B et al, 2015	2.290	0.480	0.230	1.350	3.230	4.775	0.000
Mansoor E et al, 2016	5.180	0.061	0.004	5.060	5.300	84.605	0.000
Molina-Infante J et al, 2018	8.090	0.694	0.481	6.730	9.450	11.659	0.000
La Orden Izquierdo E et al, 2018	5.400	0.842	0.709	3.750	7.050	6.414	0.000
Robson J et al, 2018	23.600	1.250	1.563	21.150	26.050	18.880	0.000
Hommeida S et al, 2018 (2005)	15.200	6.378	40.675	2.700	27.700	2.383	0.017
Hommeida S et al, 2018 (2013)	25.100	8.018	64.288	9.385	40.815	3.130	0.002
Hommeida S et al, 2018 (2015)	19.200	7.288	53.121	4.915	33.485	2.634	0.008
Syed A et al, 2017	4.939	0.067	0.005	4.807	5.071	73.279	0.000
Arias A et al, 2019	9.308	0.865	0.749	7.613	11.004	10.758	0.000
Limketkai BN et al, 2019	23.100	0.223	0.050	22.663	23.537	103.540	0.000
Weerasekera K et al, 2019	6.950	0.564	0.318	5.845	8.055	12.327	0.000
Zdanowicz K et al, 2020	2.830	0.480	0.230	1.890	3.770	5.901	0.000
Rooij WE et al, 2020	0.990	0.079	0.006	0.835	1.145	12.518	0.000
La Orden Izquierdo E et al, 2021	15.100	1.536	2.359	12.090	18.110	9.832	0.000
Melgaard D et al, 2021	5.090	0.332	0.110	4.440	5.740	15.348	0.000
Garber et al, 2022	1.220	0.291	0.085	0.650	1.790	4.195	0.000
Allin et al, 2022	6.500	0.342	0.117	5.830	7.170	19.015	0.000
	4.366	0.019	0.000	4.328	4.404	224.995	0.000

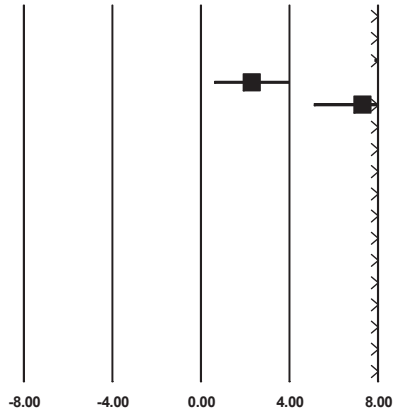
2) Funnel plot



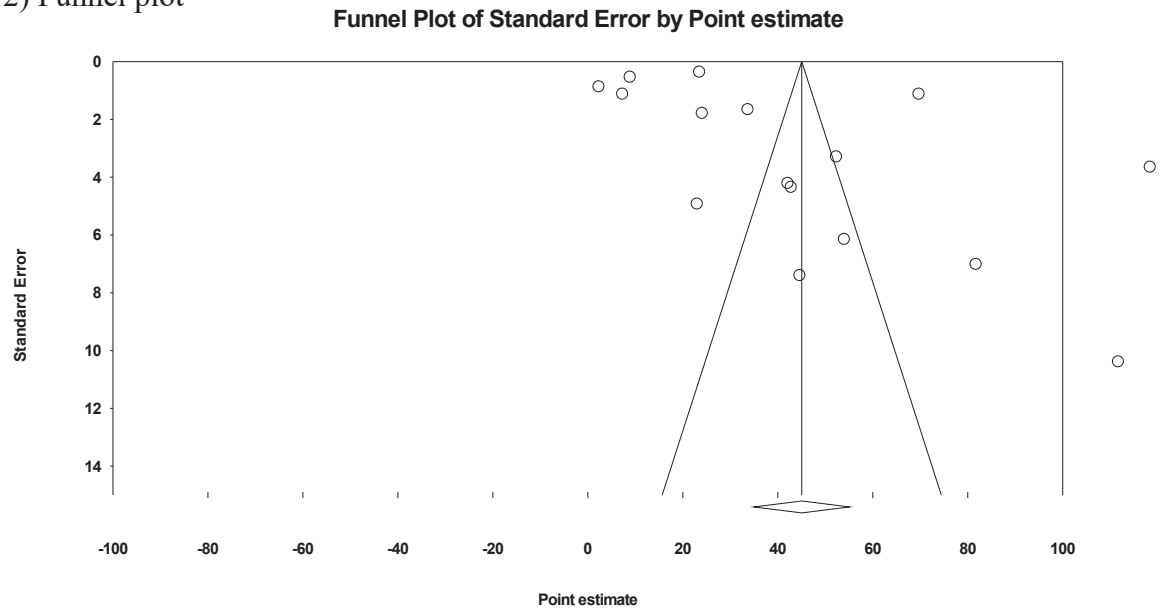
Supplementary Figure 50. High-income countries incidence of EoE included in our systematic review (total study). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot

Study name	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Arias A et al, 2013	44.620	7.398	54.732	30.120	59.120	6.031	0.000
Arias A et al, 2019	111.700	10.383	107.803	91.350	132.050	10.758	0.000
Cherian S et al, 2006	8.900	0.536	0.287	7.850	9.950	16.613	0.000
Dalby K et al, 2010	2.300	0.867	0.752	0.600	4.000	2.652	0.008
Gill R, et al, 2007	7.300	1.122	1.260	5.100	9.500	6.504	0.000
Giriens B et al, 2015	24.080	1.786	3.189	20.580	27.580	13.485	0.000
Hruz P et al, 2011	42.800	4.347	18.897	34.280	51.320	9.846	0.000
La Orden Izquierdo E et al, 2018	52.330	3.291	10.830	45.880	58.780	15.902	0.000
Noel RJ et al, 2007	42.100	4.209	17.718	33.850	50.350	10.002	0.000
Prasad GA et al, 2009	54.000	6.148	37.799	41.950	66.050	8.783	0.000
Robson J et al, 2018	118.400	3.648	13.308	111.250	125.550	32.456	0.000
RooiJ WE et al, 2020	23.500	0.357	0.128	22.800	24.200	65.799	0.000
Straumann A et al, 2005	23.000	4.924	24.241	13.350	32.650	4.671	0.000
Syed AA et al, 2012/Stewart MJ et al, 2013	33.700	1.658	2.750	30.450	36.950	20.323	0.000
Allin et al, 2022	69.700	1.122	1.260	67.500	71.900	62.095	0.000
Molina-Infante J et al, 2018	81.730	7.013	49.181	67.985	95.475	11.654	0.000
	21.128	0.256	0.065	20.628	21.629	82.672	0.000



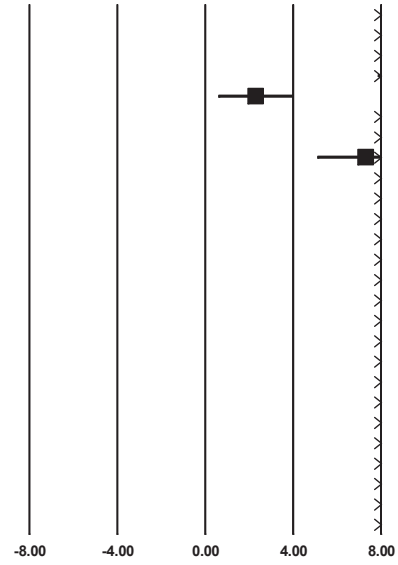
2) Funnel plot



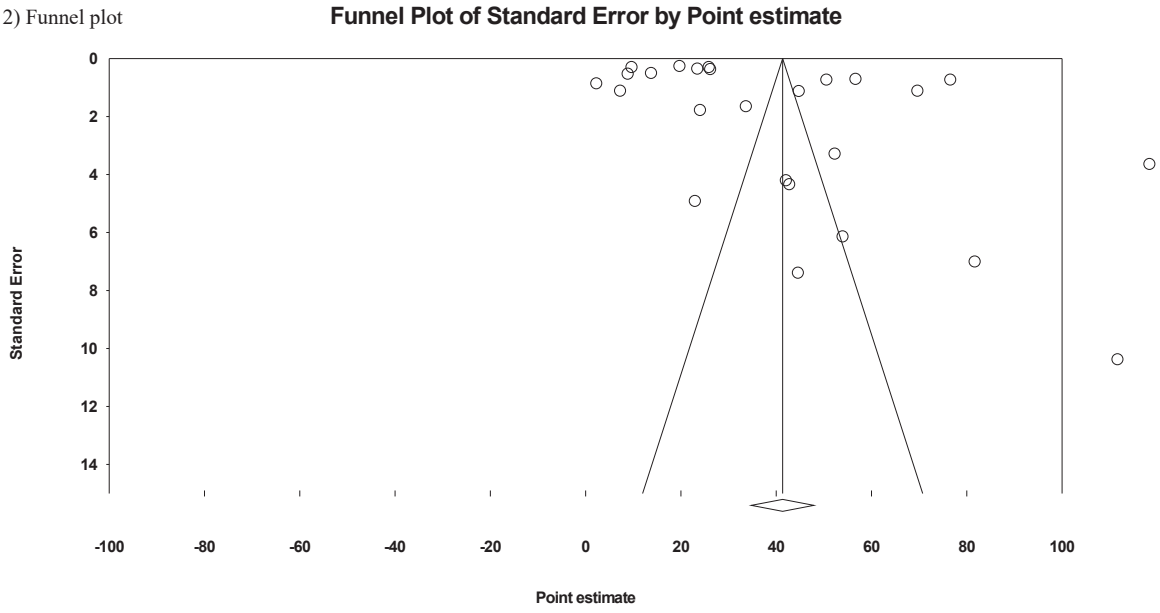
Supplementary Figure 51. High-income countries prevalence of EoE included in our systematic review (researcher-validated studies). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot

Study name	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Ally MR et al, 2014	9.700	0.306	0.094	9.100	10.300	31.686	0.000
Arias A et al, 2013	44.620	7.398	54.732	30.120	59.120	6.031	0.000
Arias A et al, 2019	111.700	10.383	107.803	91.350	132.050	10.758	0.000
Cherian S et al, 2006	8.900	0.536	0.287	7.850	9.950	16.613	0.000
Dalby K et al, 2010	2.300	0.867	0.752	0.600	4.000	2.652	0.008
Dellon ES et al, 2014	56.700	0.714	0.510	55.300	58.100	79.379	0.000
Dellon ES et al, 2015	13.800	0.510	0.260	12.800	14.800	27.048	0.000
Gill R, et al, 2007	7.300	1.122	1.260	5.100	9.500	6.504	0.000
Giriens B et al, 2015	24.080	1.786	3.189	20.580	27.580	13.485	0.000
Hruz P et al, 2011	42.800	4.347	18.897	34.280	51.320	9.846	0.000
Kim S et al, 2015	44.800	1.133	1.284	42.579	47.021	39.529	0.000
La Orden Izquierdo E et al, 2018	52.330	3.291	10.830	45.880	58.780	15.902	0.000
Limketkai BN et al, 2019	76.600	0.740	0.547	75.150	78.050	103.540	0.000
Mansoor E et al, 2016	25.900	0.306	0.094	25.300	26.500	84.605	0.000
Maradey-Romero C et al, 2015	50.600	0.740	0.547	49.150	52.050	68.396	0.000
McGowan EC et al, 2020	26.210	0.377	0.142	25.471	26.949	69.548	0.000
Noel RJ et al, 2007	42.100	4.209	17.718	33.850	50.350	10.002	0.000
Prasad GA et al, 2009	54.000	6.148	37.799	41.950	66.050	8.783	0.000
Robson J et al, 2018	118.400	3.648	13.308	111.250	125.550	32.456	0.000
RooiJ WE et al, 2020	23.500	0.357	0.128	22.800	24.200	65.799	0.000
Straumann A et al, 2005	23.000	4.924	24.241	13.350	32.650	4.671	0.000
Syed A et al, 2017	19.750	0.270	0.073	19.220	20.280	73.036	0.000
Syed AA et al, 2012/Stewart MJ et al, 2013	33.700	1.658	2.750	30.450	36.950	20.323	0.000
Allin et al, 2022	69.700	1.122	1.260	67.500	71.900	62.095	0.000
Molina-Infante J et al, 2018	81.730	7.013	49.181	67.985	95.475	11.654	0.000
	23.511	0.122	0.015	23.273	23.750	193.312	0.000



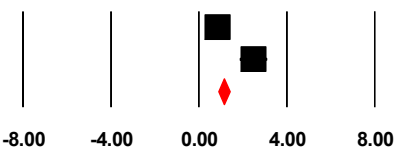
2) Funnel plot



Supplementary Figure 52. High-income countries prevalence of EoE included in our systematic review (total study). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot

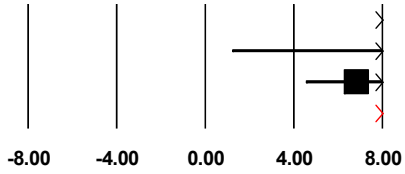
Study name	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
1.000	0.850	0.145	0.021	0.565	1.135	5.846	0.000
2.000	2.480	0.316	0.100	1.860	3.100	7.840	0.000
	1.134	0.132	0.017	0.875	1.393	8.586	0.000



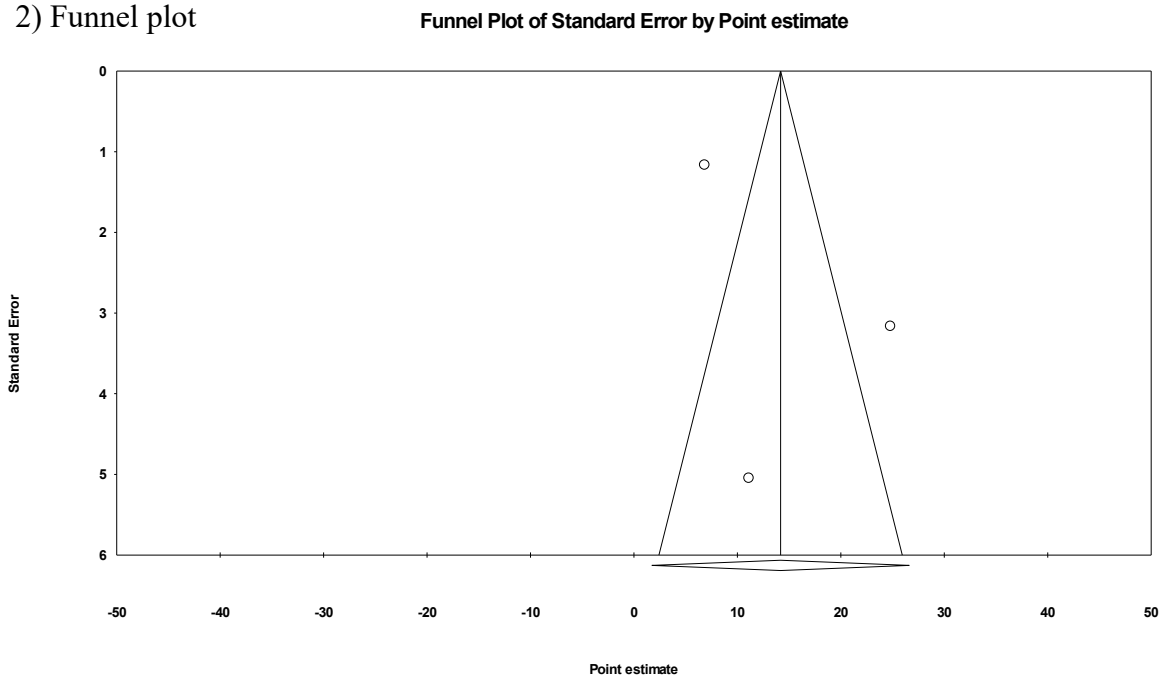
Supplementary Figure 53. Low- or middle-income countries incidence of EoE included in our systematic review (total study). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot

Study name	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
1.000	24.800	3.163	10.007	18.600	31.000	7.840	0.000
2.000	11.110	5.046	25.462	1.220	21.000	2.202	0.028
3.000	6.830	1.163	1.353	4.550	9.110	5.871	0.000
	9.066	1.067	1.139	6.975	11.158	8.496	0.000

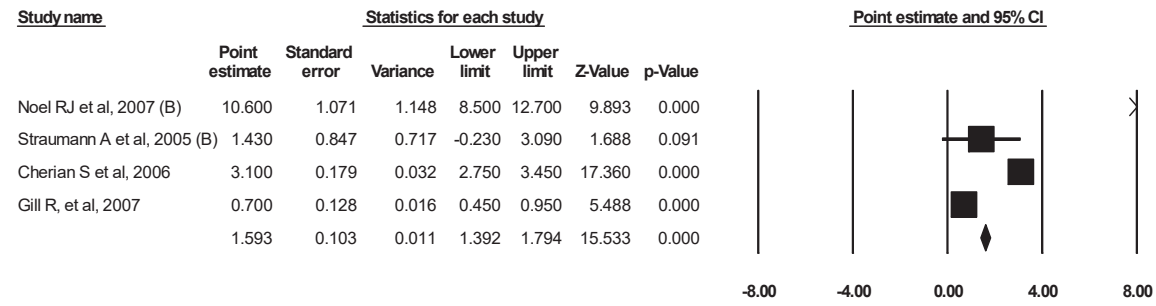


2) Funnel plot

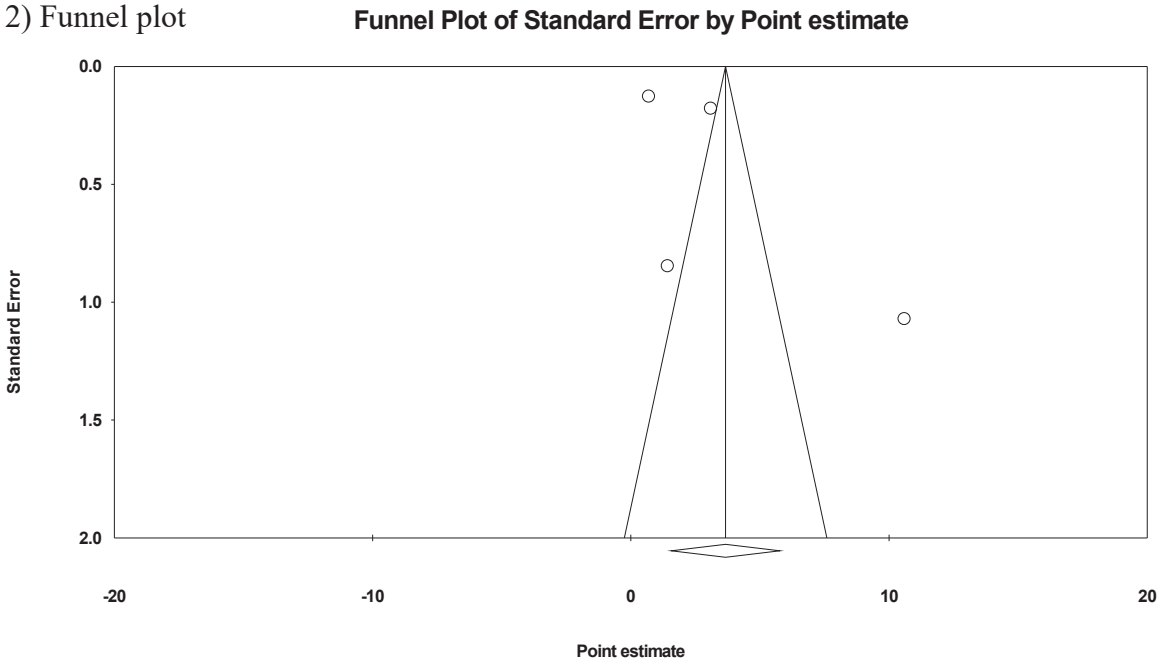


Supplementary Figure 54. Low- or middle-income countries prevalence of EoE included in our systematic review (total study). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot

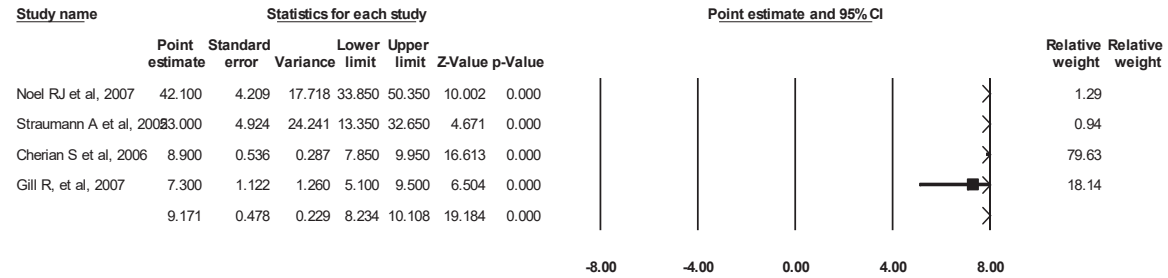


2) Funnel plot

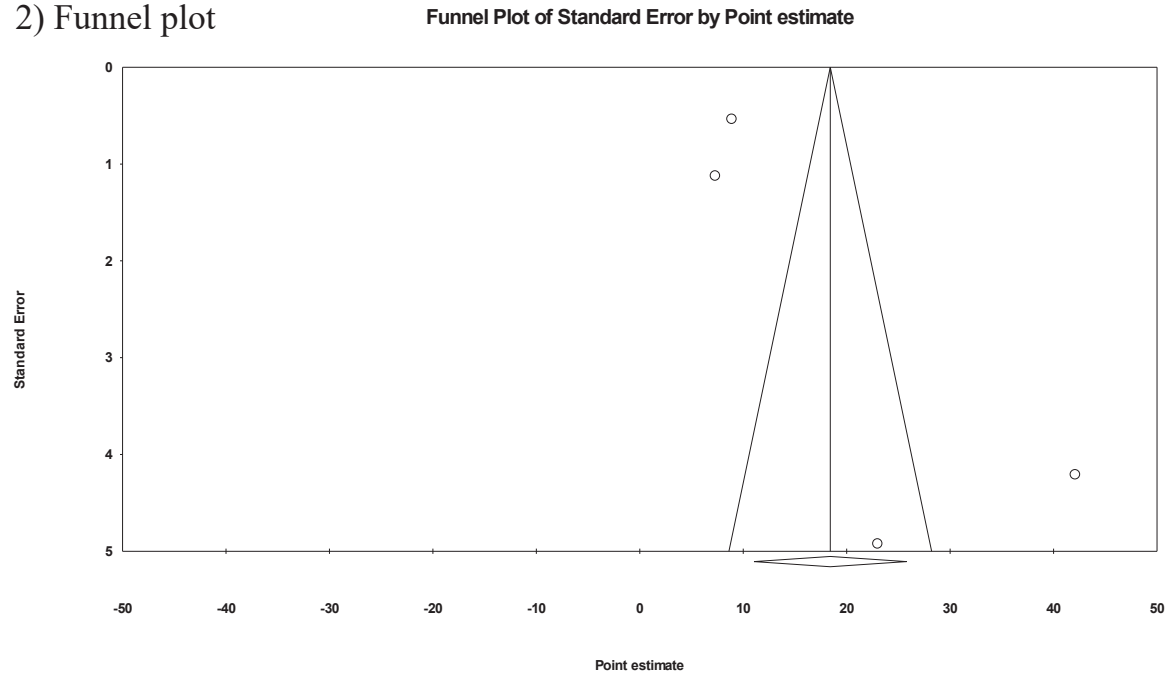


Supplementary Figure 55. Before 2007 consensus incidence of EoE included in our systematic review (total study). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot

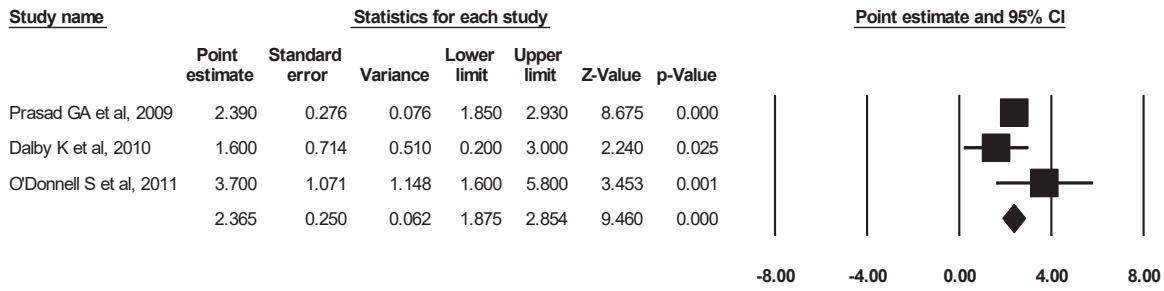


2) Funnel plot

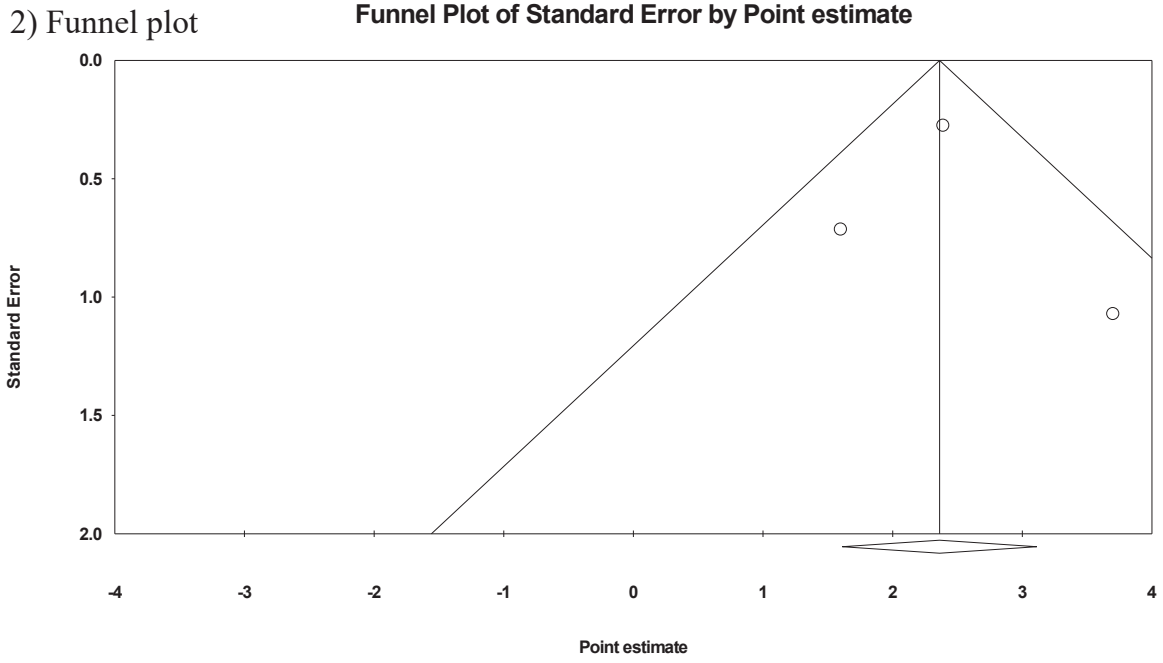


Supplementary Figure 56. Before 2007 consensus prevalence of EoE included in our systematic review (total study). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot

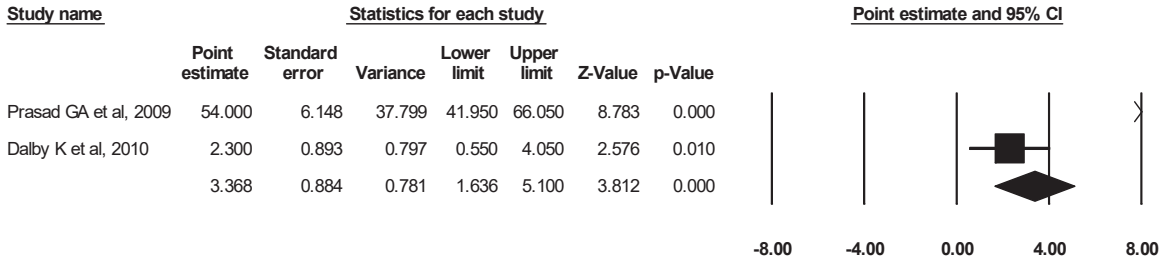


2) Funnel plot

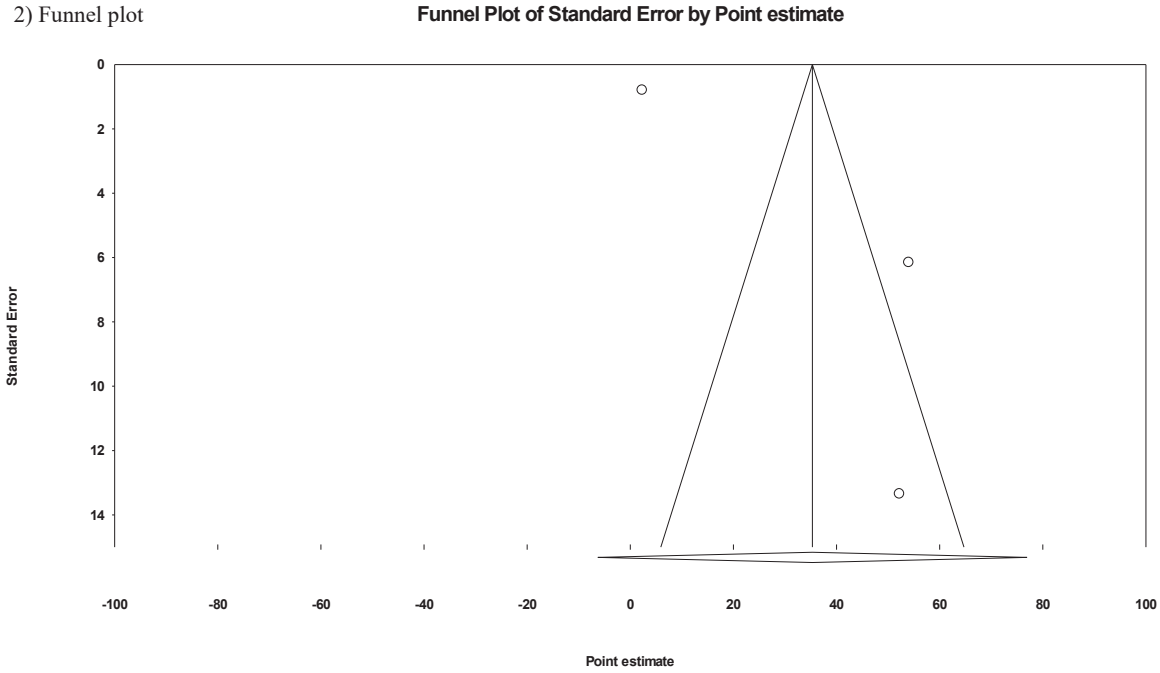


Supplementary Figure 57. After 2007 consensus incidence of EoE included in our systematic review (total study). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot



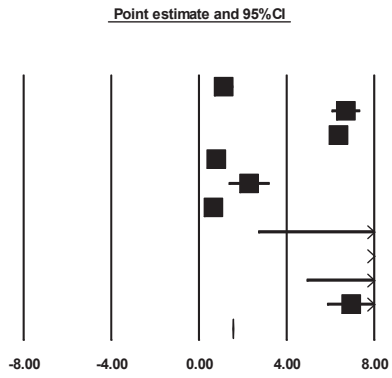
2) Funnel plot



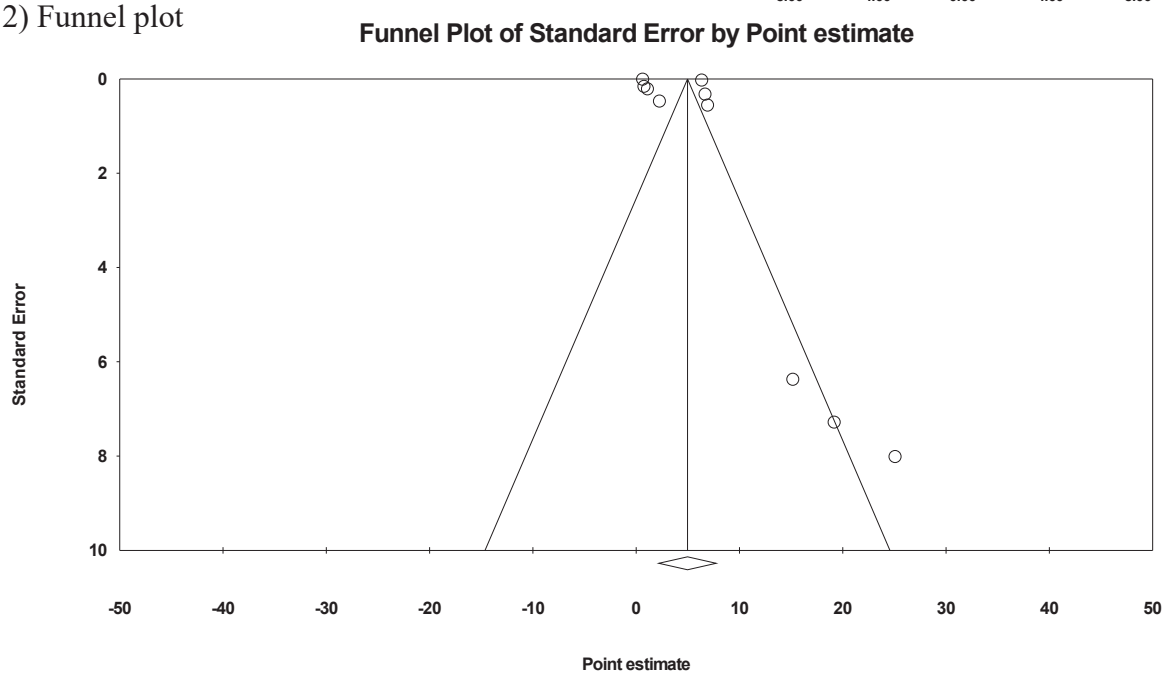
Supplementary Figure 58. After 2007 consensus prevalence of EoE included in our systematic review (total study). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot

Study name	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Hruz P et al, 2011	1.130	0.219	0.048	0.700	1.560	5.151	0.000
Syed AA et al, 2012/Stewart MJ et al, 2013	6.700	0.332	0.110	6.050	7.350	20.203	0.000
Arias A et al, 2013	6.370	0.033	0.001	6.305	6.435	192.076	0.000
Homan M et al, 2015	0.790	0.166	0.027	0.465	1.115	4.764	0.000
Giriens B et al, 2015	2.290	0.480	0.230	1.350	3.230	4.775	0.000
Warner MJ et al, 2017	0.660	0.014	0.000	0.632	0.688	46.615	0.000
Hommeida S et al, 2018 (2005)	15.200	6.378	40.675	2.700	27.700	2.383	0.017
Hommeida S et al, 2018 (2013)	25.100	8.018	64.288	9.385	40.815	3.130	0.002
Hommeida S et al, 2018 (2015)	19.200	7.288	53.121	4.915	33.485	2.634	0.008
Weerasekera K et al, 2019	6.950	0.564	0.318	5.845	8.055	12.327	0.000
	1.546	0.013	0.000	1.520	1.571	119.446	0.000



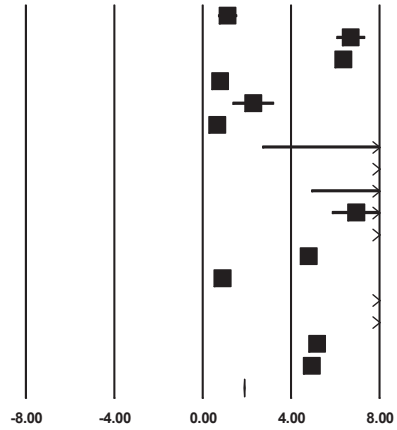
2) Funnel plot



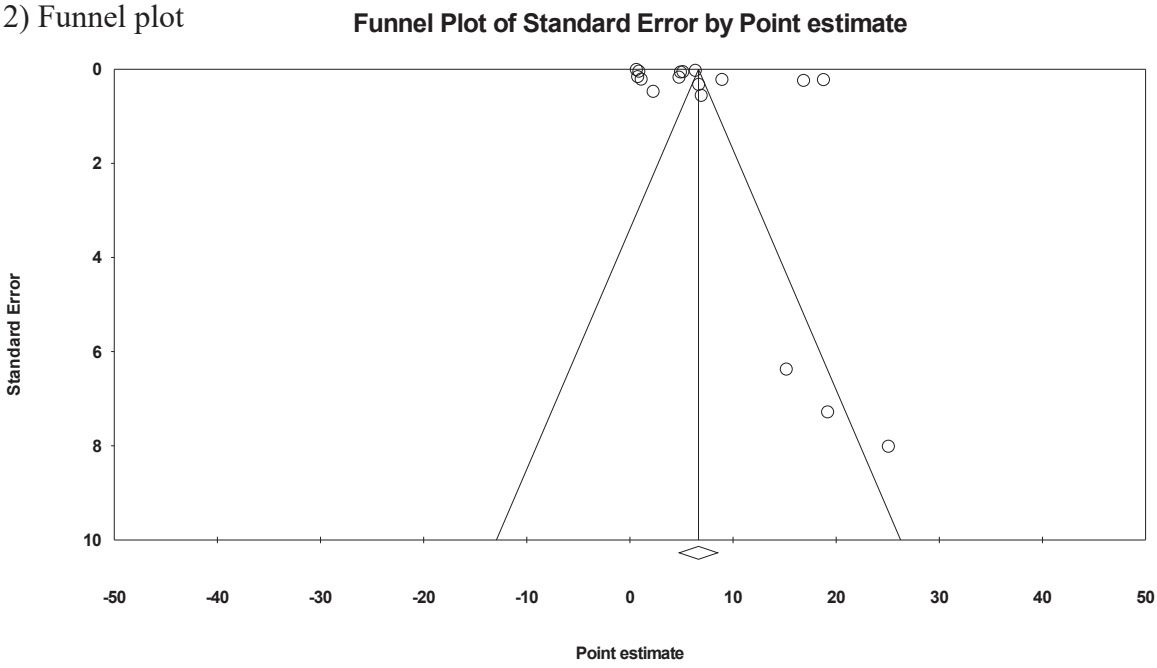
Supplementary Figure 59. After 2011 consensus incidence of EoE included in our systematic review (researcher-validated studies). (*A*) Forest plot; (*B*) Funnel plot.

1) Fovrest plot

Study name	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Hruz P et al, 2011	1.130	0.219	0.048	0.700	1.560	5.151	0.000
Syed AA et al, 2012/Stewart MJ et al, 2013	6.700	0.332	0.110	6.050	7.350	20.203	0.000
Arias A et al, 2013	6.370	0.033	0.001	6.305	6.435	192.076	0.000
Homan M et al, 2015	0.790	0.166	0.027	0.465	1.115	4.764	0.000
Giriens B et al, 2015	2.290	0.480	0.230	1.350	3.230	4.775	0.000
Warner MJ et al, 2017	0.660	0.014	0.000	0.632	0.688	46.615	0.000
Hommeida S et al, 2018 (2005)	15.200	6.378	40.675	2.700	27.700	2.383	0.017
Hommeida S et al, 2018 (2013)	25.100	8.018	64.288	9.385	40.815	3.130	0.002
Hommeida S et al, 2018 (2015)	19.200	7.288	53.121	4.915	33.485	2.634	0.008
Weerasekera K et al, 2019	6.950	0.564	0.318	5.845	8.055	12.327	0.000
Dellon ES et al, 2014	18.800	0.230	0.053	18.350	19.250	81.883	0.000
Ally MR et al, 2014	4.800	0.179	0.032	4.450	5.150	26.880	0.000
Dellon ES et al, 2015	0.900	0.051	0.003	0.800	1.000	17.640	0.000
Maradey-Romero C et al, 2015	16.867	0.247	0.061	16.383	17.350	68.396	0.000
Kim S et al, 2015	8.960	0.227	0.051	8.516	9.404	39.529	0.000
Mansoor E et al, 2016	5.180	0.061	0.004	5.060	5.300	84.605	0.000
Syed A et al, 2017	4.939	0.067	0.005	4.807	5.071	73.279	0.000
	1.877	0.012	0.000	1.853	1.900	156.224	0.000



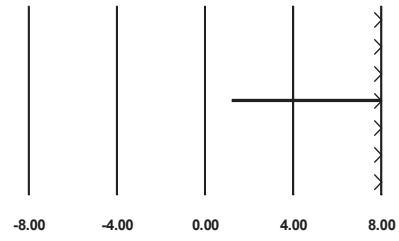
2) Funnel plot



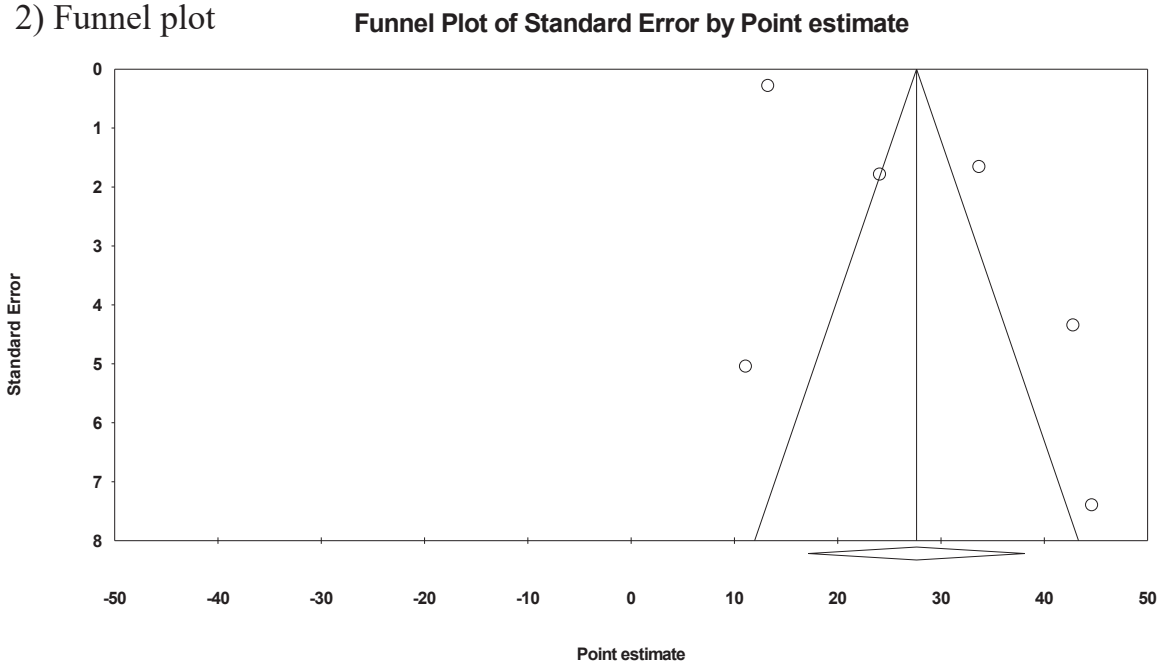
Supplementary Figure 60. After 2011 consensus incidence of EoE included in our systematic review (total study). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot

Study name	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Hruz P et al, 2011	42.800	4.347	18.897	34.280	51.320	9.846	0.000
Syed AA et al, 2012/Stewart MJ et al, 2013	33.700	1.658	2.750	30.450	36.950	20.323	0.000
Arias A et al, 2013	44.620	7.398	54.732	30.120	59.120	6.031	0.000
Ma X et al, 2015	11.110	5.046	25.462	1.220	21.000	2.202	0.028
Giriens B et al, 2015	24.080	1.786	3.189	20.580	27.580	13.485	0.000
Warner MJ et al, 2017	13.260	0.283	0.080	12.705	13.815	46.827	0.000
	14.231	0.275	0.075	13.693	14.770	51.820	0.000



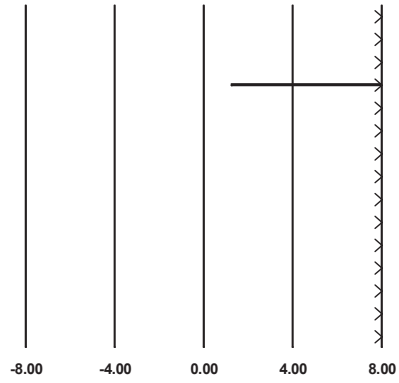
2) Funnel plot



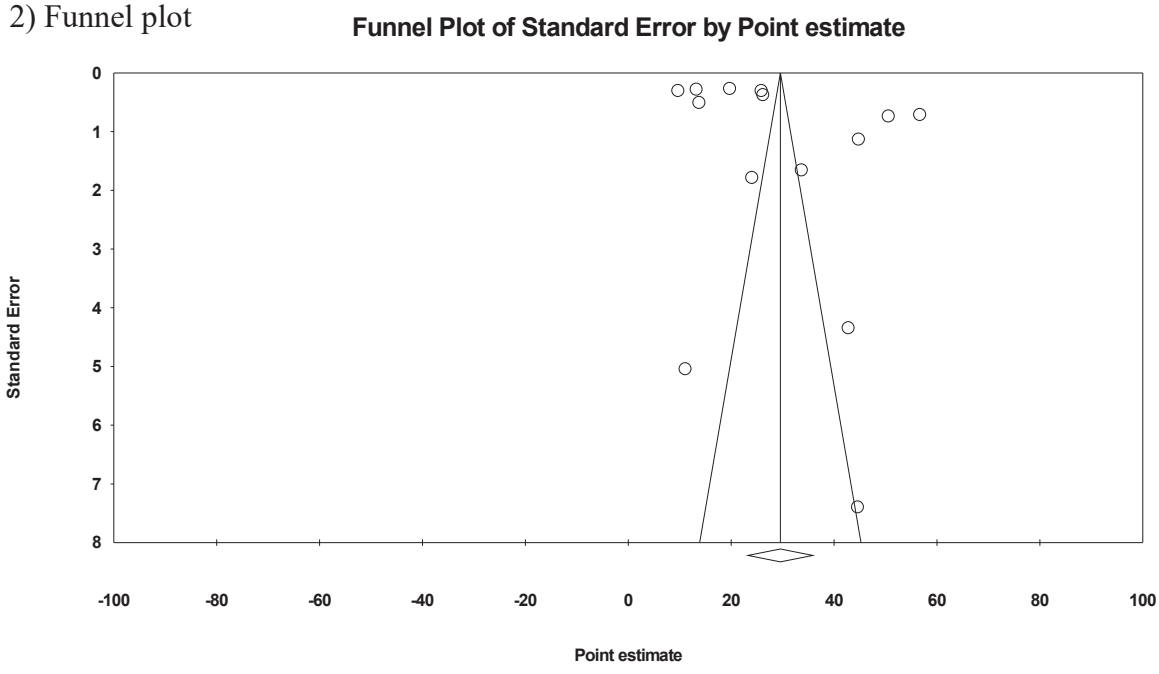
Supplementary Figure 61. After 2011 consensus prevalence of EoE included in our systematic review (researcher-validated studies). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot

Study name	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Hruz P et al, 2011	42.800	4.347	18.897	34.280	51.320	9.846	0.000
Syed AA et al, 2012/Stewart MJ et al, 2013	33.700	1.658	2.750	30.450	36.950	20.323	0.000
Arias A et al, 2013	44.620	7.398	54.732	30.120	59.120	6.031	0.000
Ma X et al, 2015	11.110	5.046	25.462	1.220	21.000	2.202	0.028
Giriens B et al, 2015	24.080	1.786	3.189	20.580	27.580	13.485	0.000
Warner MJ et al, 2017	13.260	0.283	0.080	12.705	13.815	46.827	0.000
Dellon ES et al, 2014	56.700	0.714	0.510	55.300	58.100	79.379	0.000
Ally MR et al, 2014	9.700	0.306	0.094	9.100	10.300	31.686	0.000
Dellon ES et al, 2015	13.800	0.510	0.260	12.800	14.800	27.048	0.000
Maradey-Romero C et al, 2015	50.600	0.740	0.547	49.150	52.050	68.396	0.000
Kim S et al, 2015	44.800	1.133	1.284	42.579	47.021	39.529	0.000
Mansoor E et al, 2016	25.900	0.306	0.094	25.300	26.500	84.605	0.000
Syed A et al, 2017	19.750	0.270	0.073	19.220	20.280	73.036	0.000
McGowan EC et al, 2020	26.210	0.377	0.142	25.471	26.949	69.548	0.000
	20.631	0.125	0.016	20.385	20.876	164.690	0.000

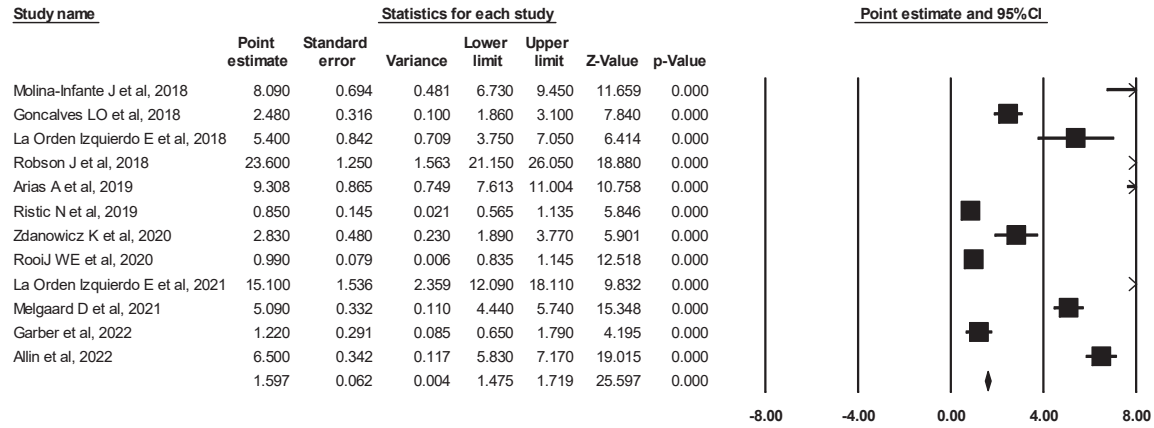


2) Funnel plot

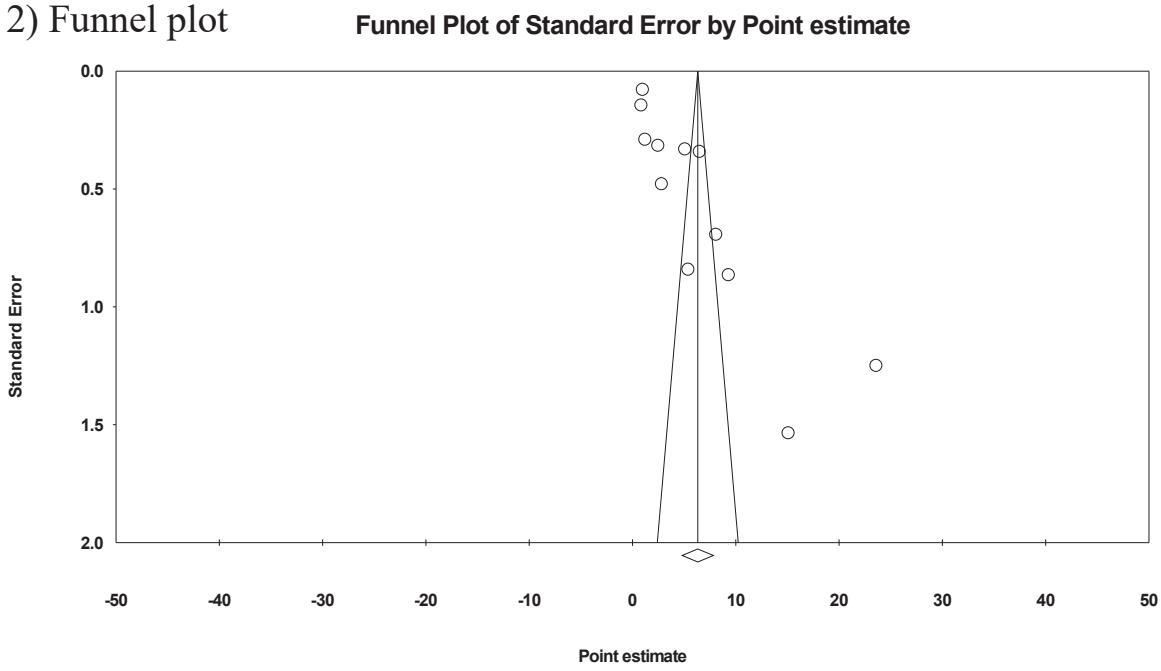


Supplementary Figure 62. After 2011 consensus prevalence of EoE included in our systematic review (total study). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot



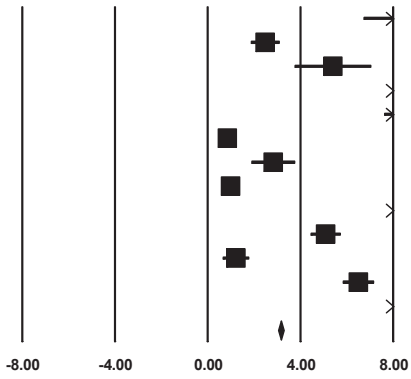
2) Funnel plot



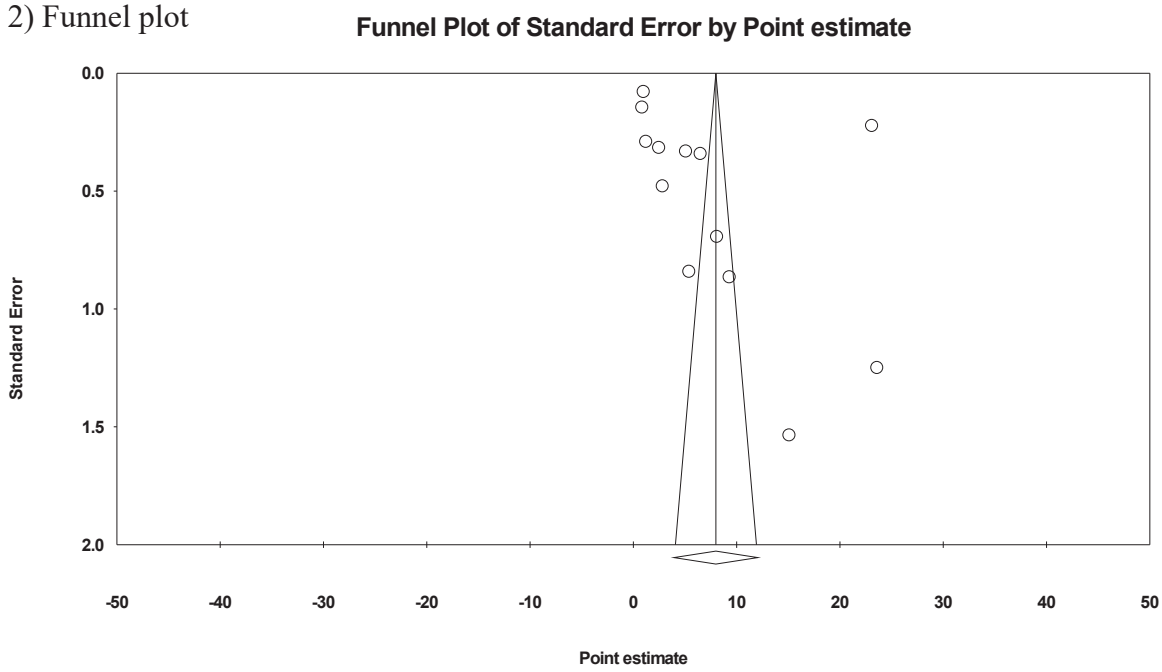
Supplementary Figure 63. After 2018 guidelines incidence of EoE included in our systematic review (researcher-validated studies). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot

Study name	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Molina-Infante J et al, 2018	8.090	0.694	0.481	6.730	9.450	11.659	0.000
Goncalves LO et al, 2018	2.480	0.316	0.100	1.860	3.100	7.840	0.000
La Orden Izquierdo E et al, 2018	5.400	0.842	0.709	3.750	7.050	6.414	0.000
Robson J et al, 2018	23.600	1.250	1.563	21.150	26.050	18.880	0.000
Arias A et al, 2019	9.308	0.865	0.749	7.613	11.004	10.758	0.000
Ristic N et al, 2019	0.850	0.145	0.021	0.565	1.135	5.846	0.000
Zdanowicz K et al, 2020	2.830	0.480	0.230	1.890	3.770	5.901	0.000
RooiJ WE et al, 2020	0.990	0.079	0.006	0.835	1.145	12.518	0.000
La Orden Izquierdo E et al, 2021	15.100	1.536	2.359	12.090	18.110	9.832	0.000
Melgaard D et al, 2021	5.090	0.332	0.110	4.440	5.740	15.348	0.000
Garber et al, 2022	1.220	0.291	0.085	0.650	1.790	4.195	0.000
Allin et al, 2022	6.500	0.342	0.117	5.830	7.170	19.015	0.000
Limketkai BN et al, 2019	23.100	0.223	0.050	22.663	23.537	103.540	0.000
	3.157	0.060	0.004	3.039	3.275	52.537	0.000



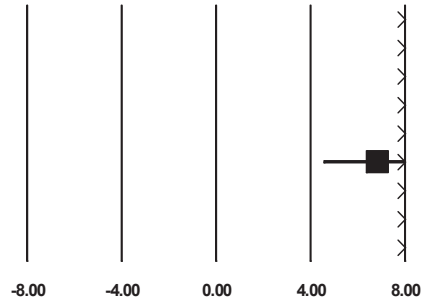
2) Funnel plot



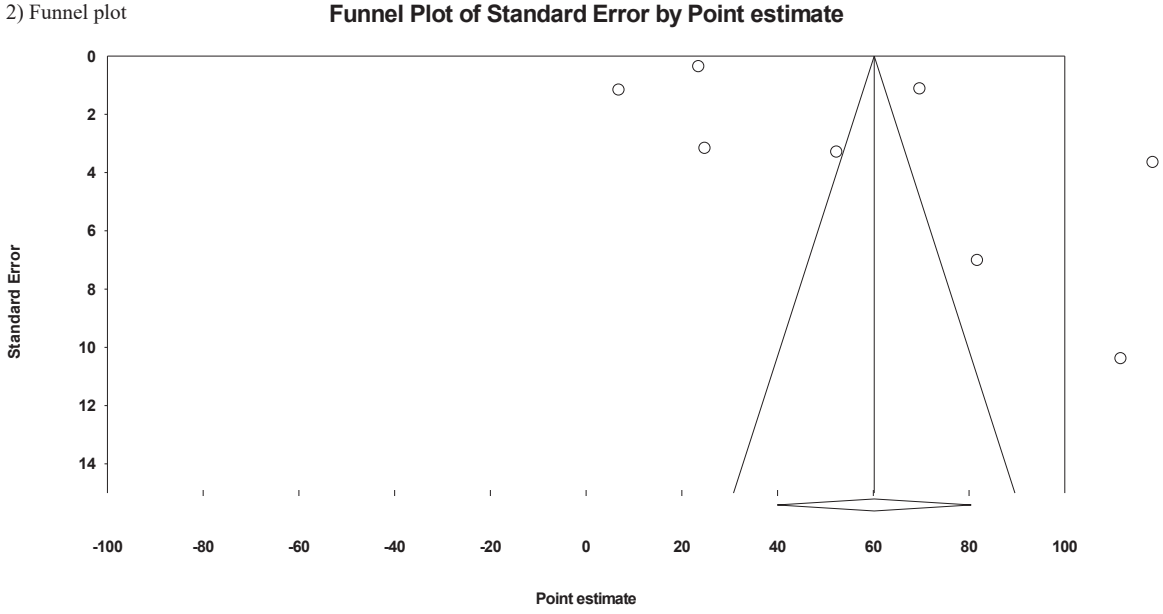
Supplementary Figure 64. After 2018 guidelines incidence of EoE included in our systematic review (total study). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot

Study name	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Molina-Infante J et al, 2018	81.730	7.013	49.181	67.985	95.475	11.654	0.000
Goncalves LO et al, 2018	24.800	3.163	10.007	18.600	31.000	7.840	0.000
La Orden Izquierdo E et al, 2018	52.330	3.291	10.830	45.880	58.780	15.902	0.000
Robson J et al, 2018	118.400	3.648	13.308	111.250	125.550	32.456	0.000
Arias A et al, 2019	111.700	10.383	107.803	91.350	132.050	10.758	0.000
Ristic N et al, 2019	6.830	1.163	1.353	4.550	9.110	5.871	0.000
RooiJ WE et al, 2020	23.500	0.357	0.128	22.800	24.200	65.799	0.000
Allin et al, 2022	69.700	1.122	1.260	67.500	71.900	62.095	0.000
	27.252	0.322	0.103	26.621	27.882	84.740	0.000



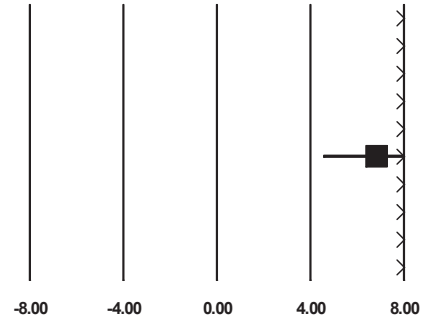
2) Funnel plot



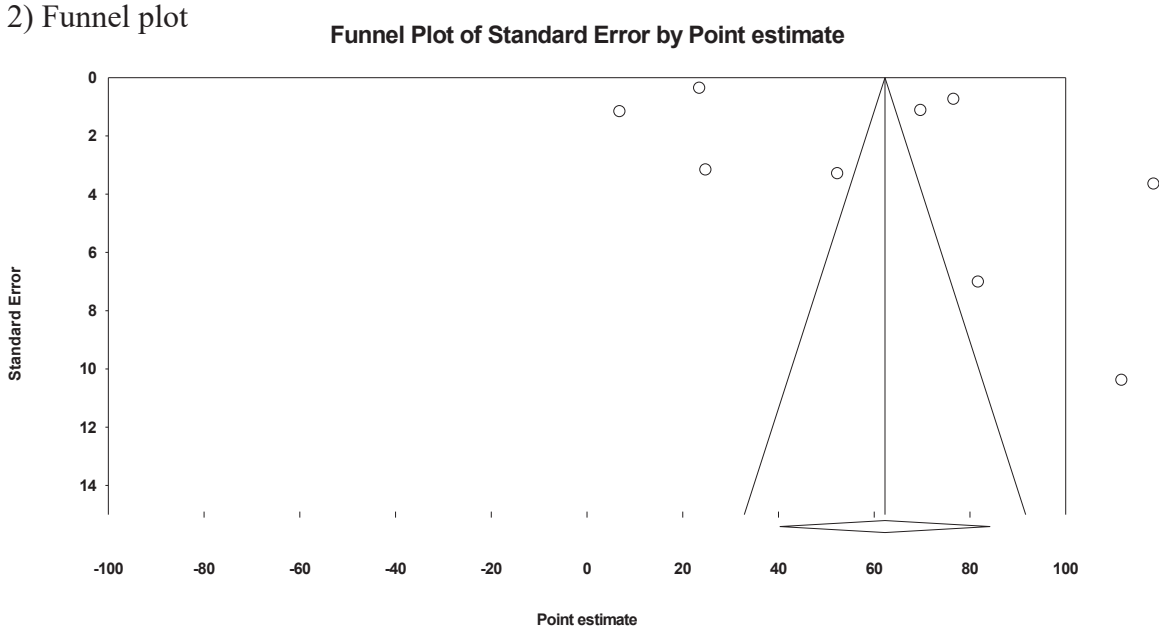
Supplementary Figure 65. After 2018 guidelines prevalence of EoE included in our systematic review (researcher-validated studies). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot

Study name	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Molina-Infante J et al, 2018	81.730	7.013	49.181	67.985	95.475	11.654	0.000
Goncalves LO et al, 2018	24.800	3.163	10.007	18.600	31.000	7.840	0.000
La Orden Izquierdo E et al, 2018	52.330	3.291	10.830	45.880	58.780	15.902	0.000
Robson J et al, 2018	118.400	3.648	13.308	111.250	125.550	32.456	0.000
Arias A et al, 2019	111.700	10.383	107.803	91.350	132.050	10.758	0.000
Ristic N et al, 2019	6.830	1.163	1.353	4.550	9.110	5.871	0.000
RooiJ WE et al, 2020	23.500	0.357	0.128	22.800	24.200	65.799	0.000
Allin et al, 2022	69.700	1.122	1.260	67.500	71.900	62.095	0.000
Limketkai BN et al, 2019	76.600	0.740	0.547	75.150	78.050	103.540	0.000
	35.094	0.295	0.087	34.516	35.672	118.992	0.000

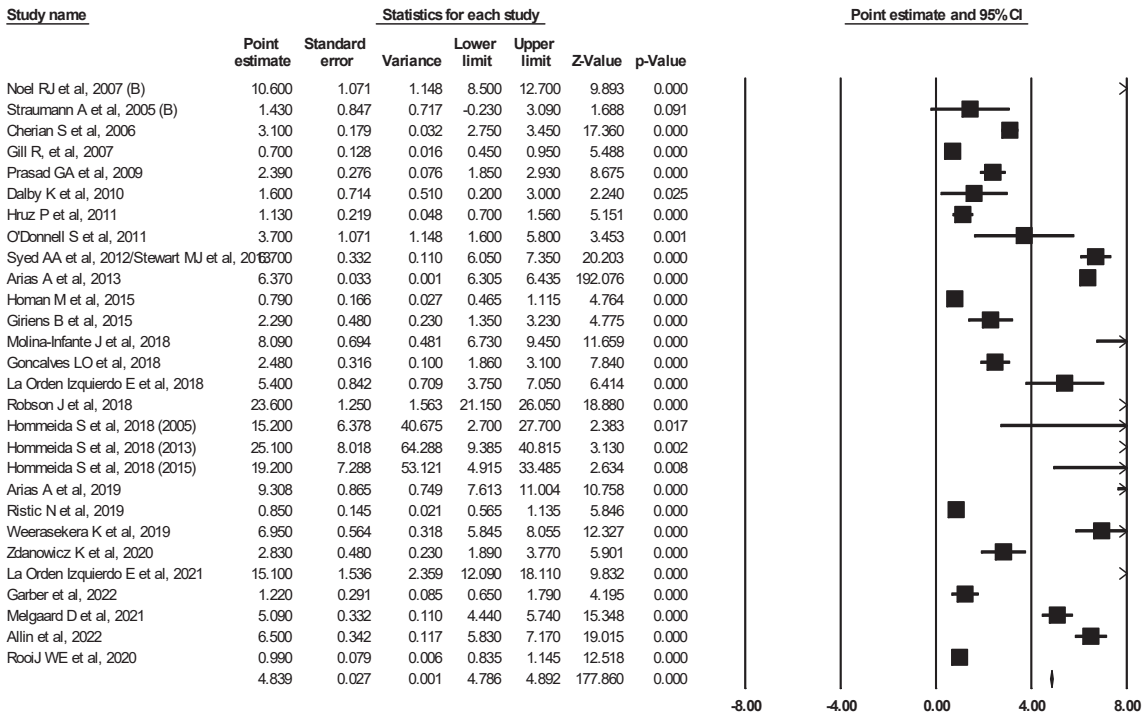


2) Funnel plot



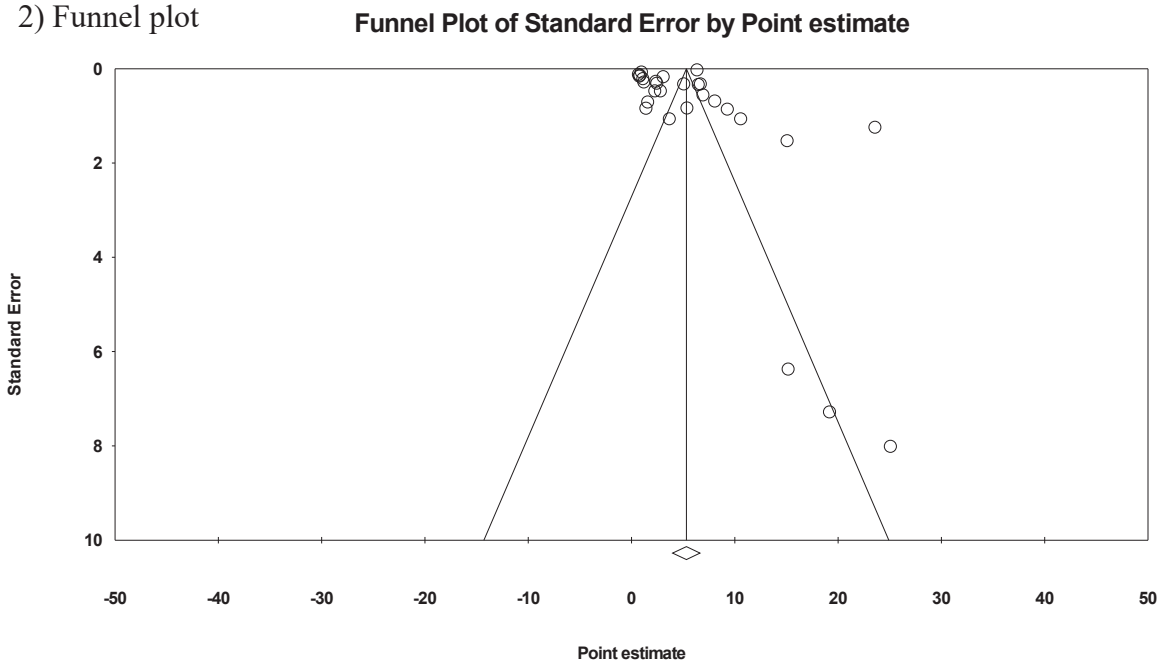
Supplementary Figure 66. After 2018 guidelines prevalence of EoE included in our systematic review (total study). (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot



Study name	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Noel RJ et al, 2007 (B)	10.600	1.071	1.148	8.500	12.700	9.893	0.000
Straumann A et al, 2005 (B)	1.430	0.847	0.717	-0.230	3.090	1.688	0.091
Cherian S et al, 2006	3.100	0.179	0.032	2.750	3.450	17.360	0.000
Gill R, et al, 2007	0.700	0.128	0.016	0.450	0.950	5.488	0.000
Prasad GA et al, 2009	2.390	0.276	0.076	1.850	2.930	8.675	0.000
Dalby K et al, 2010	1.600	0.714	0.510	0.200	3.000	2.240	0.025
Hruz P et al, 2011	1.130	0.219	0.048	0.700	1.560	5.151	0.000
O'Donnell S et al, 2011	3.700	1.071	1.148	1.600	5.800	3.453	0.001
Syed AA et al, 2012/Stewart MJ et al, 2016	6.700	0.332	0.110	6.050	7.350	20.203	0.000
Arias A et al, 2013	6.370	0.033	0.001	6.305	6.435	192.076	0.000
Homan M et al, 2015	0.790	0.166	0.027	0.465	1.115	4.764	0.000
Giriens B et al, 2015	2.290	0.480	0.230	1.350	3.230	4.775	0.000
Molina-Infante J et al, 2018	8.090	0.694	0.481	6.730	9.450	11.659	0.000
Goncalves LO et al, 2018	2.480	0.316	0.100	1.860	3.100	7.840	0.000
La Orden Izquierdo E et al, 2018	5.400	0.842	0.709	3.750	7.050	6.414	0.000
Robson J et al, 2018	23.600	1.250	1.563	21.150	26.050	18.880	0.000
Hommeida S et al, 2018 (2005)	15.200	6.378	40.675	2.700	27.700	2.383	0.017
Hommeida S et al, 2018 (2013)	25.100	8.018	64.288	9.385	40.815	3.130	0.002
Hommeida S et al, 2018 (2015)	19.200	7.288	53.121	4.915	33.485	2.634	0.008
Arias A et al, 2019	9.308	0.865	0.749	7.613	11.004	10.758	0.000
Ristic N et al, 2019	0.850	0.145	0.021	0.565	1.135	5.846	0.000
Weerasekera K et al, 2019	6.950	0.564	0.318	5.845	8.055	12.327	0.000
Zdanowicz K et al, 2020	2.830	0.480	0.230	1.890	3.770	5.901	0.000
La Orden Izquierdo E et al, 2021	15.100	1.536	2.359	12.090	18.110	9.832	0.000
Garber et al, 2022	1.220	0.291	0.085	0.650	1.790	4.195	0.000
Melgaard D et al, 2021	5.090	0.332	0.110	4.440	5.740	15.348	0.000
Allin et al, 2022	6.500	0.342	0.117	5.830	7.170	19.015	0.000
RociJ WE et al, 2020	0.990	0.079	0.006	0.835	1.145	12.518	0.000
	4.839	0.027	0.001	4.786	4.892	177.860	0.000

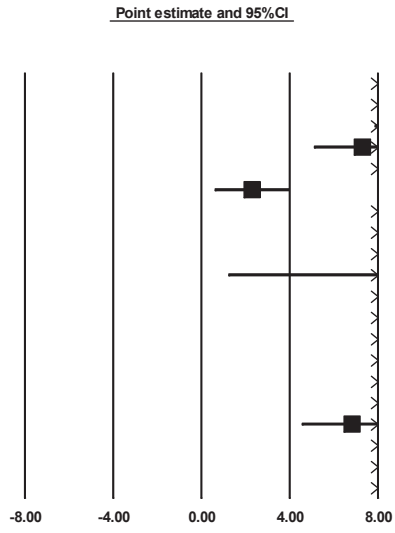
2) Funnel plot



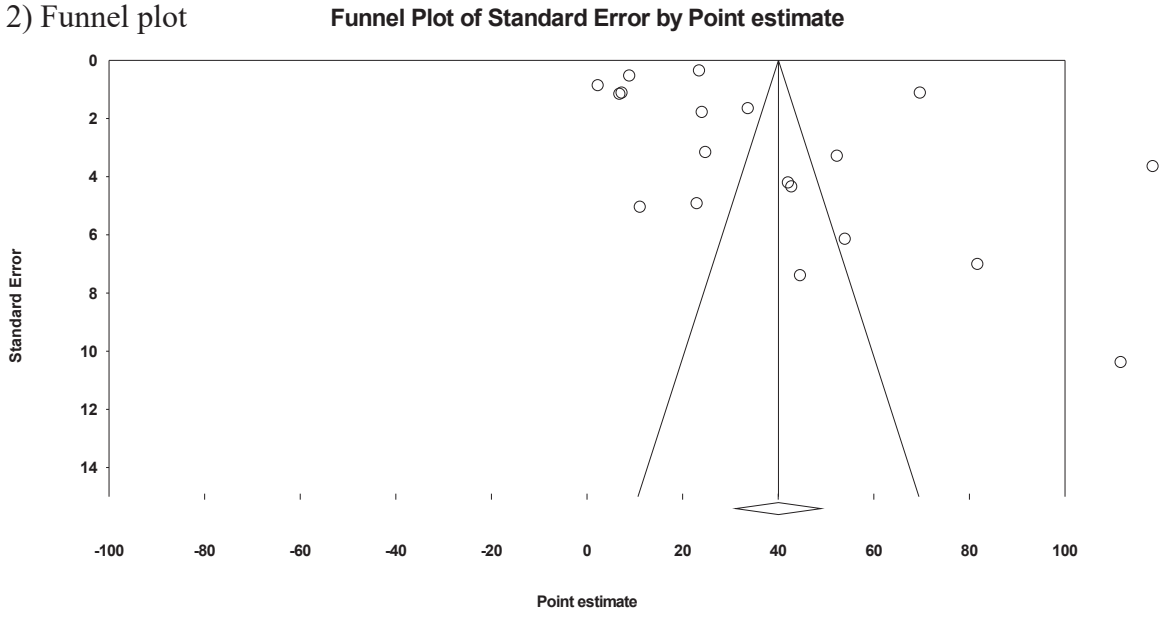
Supplementary Figure 67. Researcher-validated incidence of EoE included in our systematic review. (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot

Study name	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Noel RJ et al, 2007 (A)	42.100	4.209	17.718	33.850	50.350	10.002	0.000
Straumann A et al, 2005 (A)	23.000	4.924	24.241	13.350	32.650	4.671	0.000
Cherian S et al, 2006	8.900	0.536	0.287	7.850	9.950	16.613	0.000
Gill R, et al, 2007	7.300	1.122	1.260	5.100	9.500	6.504	0.000
Prasad GA et al, 2009	54.000	6.148	37.799	41.950	66.050	8.783	0.000
Dalby K et al, 2010	2.300	0.867	0.752	0.600	4.000	2.652	0.008
Hruz P et al, 2011	42.800	4.347	18.897	34.280	51.320	9.846	0.000
Syed AA et al, 2012/Stewart MJ et al, 2013	33.700	1.658	2.750	30.450	36.950	20.323	0.000
Arias A et al, 2013	44.620	7.398	54.732	30.120	59.120	6.031	0.000
Ma X et al, 2015	11.110	5.046	25.462	1.220	21.000	2.202	0.028
Giriens B et al, 2015	24.080	1.786	3.189	20.580	27.580	13.485	0.000
Molina-Infante J et al, 2018	81.730	7.013	49.181	67.985	95.475	11.654	0.000
Goncalves LO et al, 2018	24.800	3.163	10.007	18.600	31.000	7.840	0.000
La Orden Izquierdo E et al, 2018	52.330	3.291	10.830	45.880	58.780	15.902	0.000
Robson J et al, 2018	118.400	3.648	13.308	111.250	125.550	32.456	0.000
Arias A et al, 2019	111.700	10.383	107.803	91.350	132.050	10.758	0.000
Ristic N et al, 2019	6.830	1.163	1.353	4.550	9.110	5.871	0.000
Allin et al, 2022	69.700	1.122	1.260	67.500	71.900	62.095	0.000
RooiJ WE et al, 2020	23.500	0.357	0.128	22.800	24.200	65.799	0.000
	20.474	0.249	0.062	19.987	20.961	82.377	0.000



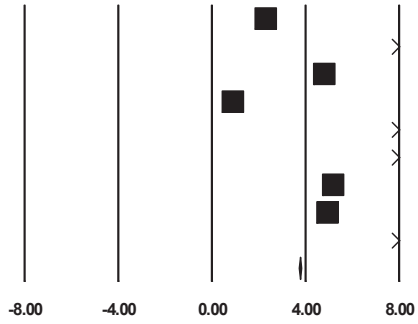
2) Funnel plot



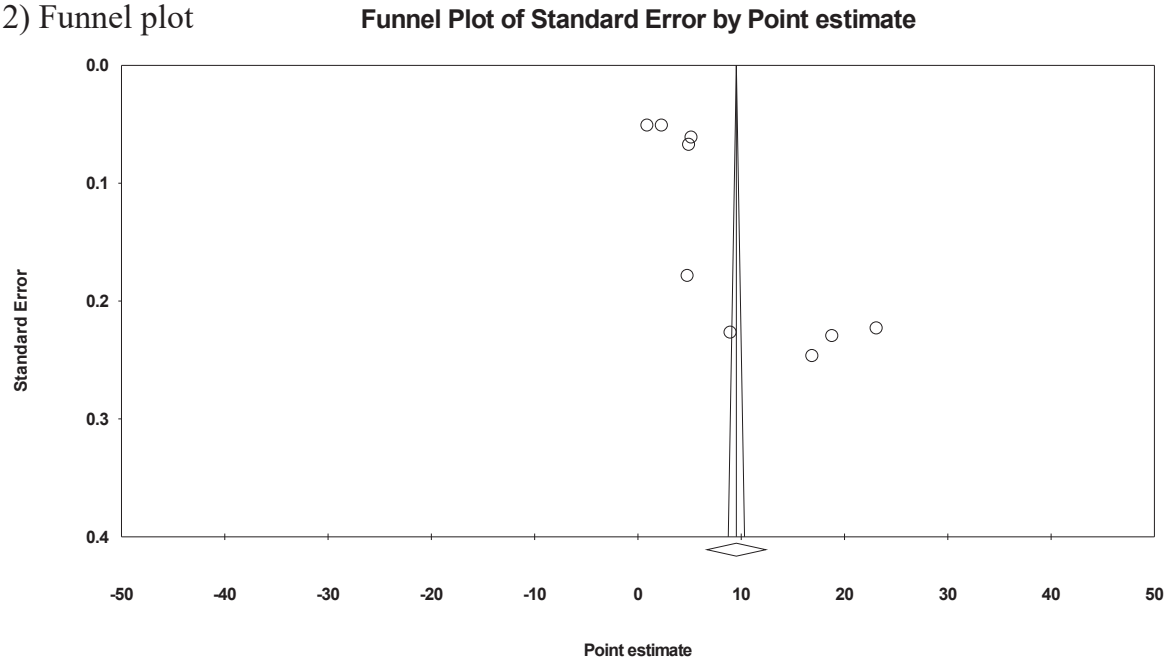
Supplementary Figure 68. Researcher-validated prevalence of EoE included in our systematic review. (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot

Study name	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Prakash R et al, 2013	2.300	0.051	0.003	2.200	2.400	45.079	0.000
Dellon ES et al, 2014	18.800	0.230	0.053	18.350	19.250	81.883	0.000
Ally MR et al, 2014	4.800	0.179	0.032	4.450	5.150	26.880	0.000
Dellon ES et al, 2015	0.900	0.051	0.003	0.800	1.000	17.640	0.000
Maradey-Romero C et al, 2015	16.867	0.247	0.061	16.383	17.350	68.396	0.000
Kim S et al, 2015	8.960	0.227	0.051	8.516	9.404	39.529	0.000
Mansoor E et al, 2016	5.180	0.061	0.004	5.060	5.300	84.605	0.000
Syed A et al, 2017	4.939	0.067	0.005	4.807	5.071	73.279	0.000
Limketkai BN et al, 2019	23.100	0.223	0.050	22.663	23.537	103.540	0.000
	3.761	0.027	0.001	3.708	3.815	138.795	0.000



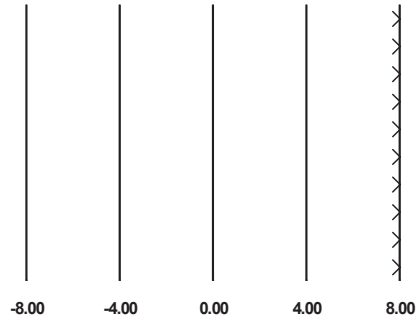
2) Funnel plot



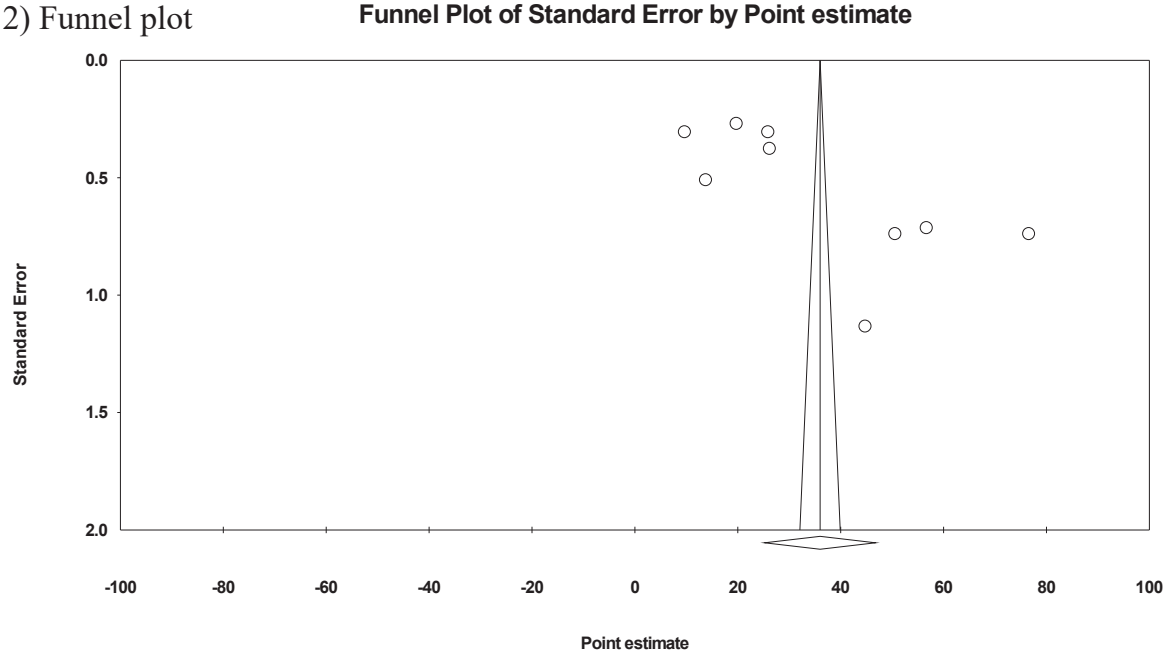
Supplementary Figure 69. Code-based incidence of EoE included in our systematic review. (*A*) Forest plot; (*B*) Funnel plot.

1) Forest plot

Study name	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Dellon ES et al, 2014	56.700	0.714	0.510	55.300	58.100	79.379	0.000
Ally MR et al, 2014	9.700	0.306	0.094	9.100	10.300	31.686	0.000
Dellon ES et al, 2015	13.800	0.510	0.260	12.800	14.800	27.048	0.000
Maradey-Romero C et al, 2015	50.600	0.740	0.547	49.150	52.050	68.396	0.000
Kim S et al, 2015	44.800	1.133	1.284	42.579	47.021	39.529	0.000
Mansoor E et al, 2016	25.900	0.306	0.094	25.300	26.500	84.605	0.000
Syed A et al, 2017	19.750	0.270	0.073	19.220	20.280	73.036	0.000
Limketkai BN et al, 2019	76.600	0.740	0.547	75.150	78.050	103.540	0.000
McGowan EC et al, 2020	26.210	0.377	0.142	25.471	26.949	69.548	0.000
	24.209	0.138	0.019	23.938	24.480	175.063	0.000



2) Funnel plot



Supplementary Figure 70. Code-based prevalence of EoE included in our systematic review. (*A*) Forest plot; (*B*) Funnel plot.

Supplementary Table 1. Eligibility Criteria

Cross-sectional studies
Recruited all age groups (children, adults, and elderly)
Participants recruited from the general population or community
Reported incidence or prevalence of EoE (according to appropriate diagnostic guideline)
Sample size of >50 participants
Published only in English

EoE, Eosinophilic esophagitis.

Supplementary Table 2. Global Pooled Incidence of EoE Included in Our Systematic Review (Total Study)

	Number of studies	Number of participants	Pooled estimates (95% CI)[a]	95% prediction interval	I^2, %	*P* value for I^2	Egger *P* value
Overall incidence	38	288,374,448	6.46 (5.26–7.68)	−0.93 to 13.85	99.9	< .0001	.476
Income							
HICs	35	287,710,647	6.77 (5.52–8.02)	−0.67 to 14.21	99.9	< .0001	.404
LMICs	2	663,801	1.64 (0.04–3.24)	NA	95.4	< .0001	NA
Gender							
Male	17	104,285,995	12.44 (7.06–17.83)	−12.18 to 37.06	99.9	< .0001	.872
Female	17	113,908,827	5.18 (2.32–8.04)	−7.86 to 18.22	99.9	< .0001	.954
Age group							
Children	26	50,282,717	7.70 (5.59–9.81)	−3.32 to 18.72	99.8	< .0001	.272
Adults	17	171,165,275	9.18 (7.36–11.00)	0.84 to 17.52	99.9	< .0001	.193
Elderly	4	13,467,465	5.33 (3.82–6.85)	−1.77 to 12.43	98.8	< .0001	.088
Gender and age group							
Male children	3	507,807	18.88 (15.31–22.44)	−4.20 to 41.96	<0.0001	.781	.032
Female children	3	482,621	8.71 (4.69–12.72)	−35.39 to 52.82	62.5	.07	.424
Male adults	3	127,632	13.36 (10.90–15.81)	−10.88 to 37.60	43.7	.169	.789
Female adults	3	131,680	2.22 (0.17–4.26)	−23.17 to 27.61	90.2	< .0001	.259
Race							
White patients	3	36,655,102	12.1 (9.61–14.56)	−19.40 to 43.60	99.6	< .0001	.224
Black patients	3	6,769,395	3.25 (2.21–4.28)	−9.63 to 16.03	96.0	< .0001	.471
Asian patients	2	1,883,938	4.45 (2.06–6.84)	NA	95.4	< .0001	NA
Geographical areas							
North America	16	243,218,920	10.44 (8.01–12.87)	0.24 to 20.65	99.9	< .0001	.070
Europe	18	29,885,240	3.97 (2.36–5.59)	−3.52 to 11.46	99.9	< .0001	.371
Oceania	2	3,669,968	4.99 (1.22–8.76)	NA	97.6	< .0001	NA-
Diagnostic criteria for EoE[a]							
Before 2007 consensus	4	3,598,411	3.67 (1.57–5.77)	−6.26 to 13.60	98.4	< .0001	.421
After 2007 consensus	3	726,164	2.36 (1.61–3.11)	−4.50 to 9.22	26.1	.258	.882
After updated consensus 2011	17	116,744,526	6.65 (4.78–8.51)	−1.34 to 14.64	99.9	< .0001	.055
After 2018 guidelines	13	168,836,127	7.99 (3.93–12.05)	−9.00 to 24.98	99.9	< .0001	.192
Data source							
Researcher validated	29	42,191,506	5.31 (3.98–6.63)	−1.74 to 12.36	99.7	< .0001	.181
Code-based	9	246,182,942	9.53 (6.69–12.38)	−1.32 to 20.38	99.9	< .0001	.005

CI, Confidence interval; EoE, eosinophilic esophagitis; HICs, high-income countries; LMICs, low- or middle-income countries (Serbia and Brazil); NA, not available.
[a]Guideline definition: 2007 consensus definition is considered by its-related symptoms, biopsy findings (≥15 eosinophils/high-power field), and exclusion of other disorders associated with similar clinical, histological, or endoscopic features; Updated 2011 consensus of EoE is inclusion of the word chronic, the term immune or antigen driven, and the term proton pump inhibitor-responsive esophageal eosinophilia; and 2018 guidelines definition of EoE includes symptoms of esophageal dysfunction, biopsy findings (≥15 eosinophils/high-power field), and no significant other causes of symptoms or esophageal eosinophilia with removal of proton pump inhibitor trial requirement.

Supplementary Table 3. Global Pooled Prevalence of EoE Included in Our Systematic Review (Total Study)

	Number of studies	Number of participants	Pooled estimates (95% CI)[a]	95% prediction interval	I^2, %	*P* value for I^2	Egger *P* value
Overall prevalence	29	280,742,705	38.43 (32.23–44.62)	4.17 to 72.69	99.8	< .0001	.094
Income							
HICs	25	280,075,304	41.34 (34.77–47.91)	6.71 to 75.97	99.9	< .0001	.064
LMICs	3	667,401	14.17 (1.73–26.61)	−141.26 to 169.60	93.0	< .0001	.506
Gender							
Male	12	110,444,588	82.22 (60.80–103.63)	−1.38 to 165.82	99.9	< .0001	.967
Female	12	113,908,827	30.00 (17.44–42.55)	−19.55 to 79.55	99.9	< .0001	.991
Age group							
Children	18	68,245,537	35.10 (25.39–44.80)	−9.68 to 79.88	99.8	< .0001	.710
Adults	12	170,588,875	46.91 (34.50–59.32)	−2.90 to 96.72	99.9	< .0001	.167
Elderly	4	13,467,465	36.18 (23.65–48.70)	−24.89 to 97.25	99.7	< .0001	.059
Gender and age group							
Male children	2	9,447,988	95.48 (-37.11–228.10)	NA	87.7	.004	NA
Female children	2	9,021,882	24.69 (-2.98–52.35)	NA	52.2	.148	NA
Male adults	3	126,684	131.40 (78.34–184.47)	−525.91 to 788.71	89.2	< .0001	.513
Female adults	3	130,971	23.01 (-1.08–47.09)	−278.95 to 324.97	92.4	< .0001	.270
Race							
White patients	4	43,186,129	54.68 (43.48–65.88)	0.22 to 109.14	99.7	< .0001	.139
Black patients	4	11,545,171	15.70 (10.86–20.55)	−7.17 to 38.57	97.9	< .0001	.437
Asian patients	3	2,367,558	19.21 (8.98–29.44)	−111.50 to 149.92	96.4	< .0001	.479
Geographical areas							
North America	13	247,311,506	43.20 (33.65–52.75)	3.40 to 83.00	99.9	< .0001	.070
Europe	12	29,885,240	39.31 (29.10–49.53)	−1.38 to 80.00	99.6	< .0001	.377
Diagnostic criteria for EoE*							
Before 2007 consensus	4	3,598,411	18.41 (11.05–25.78)	−15.36 to 52.18	95.8	< .0001	.227
After 2007 consensus	2	376,164	27.79 (-22.87–78.45)	NA	98.6	< .0001	NA
After updated consensus 2011	14	134,729,697	29.56 (23.27–35.85)	3.04 to 56.08	99.8	< .0001	.134
After 2018 guidelines	9	158,329,579	62.25 (40.27–84.22)	−20.89 to 145.39	99.9	< .0001	.289
Data source							
Researcher validated	20	30,377,177	40.04 (31.10–48.97)	−2.00 to 82.08	99.6	< .0001	.167
Code-based	9	250,275,528	35.99 (25.21–46.77)	−5.12 to 77.10	99.9	< .0001	.024

CI, Confidence interval; EoE, eosinophilic esophagitis; HICs, high-income countries; LMICs, low- or middle-income countries (Serbia, China, and Brazil); NA, not available.

[a]Guideline definition: 2007 consensus definition is considered by its related symptoms, biopsy findings (≥15 eosinophils/high-power field), and exclusion of other disorders associated with similar clinical, histological, or endoscopic features; Updated 2011 consensus of EoE is inclusion of the word chronic, the term immune or antigen driven, and the term proton pump inhibitor-responsive esophageal eosinophilia; and 2018 guidelines definition of EoE includes symptoms of esophageal dysfunction, biopsy findings (≥15 eosinophils/high-power field), and no significant other causes of symptoms or esophageal eosinophilia with removal of proton pump inhibitor trial requirement.

Supplementary Table 4. National Pooled Incidence of EoE Included in Our Systematic Review (Researcher-validated Studies)

	Number of studies	Number of participants	Patients with EoE	Pooled estimates (95% CI)
Nation				
Australia	1	3,198,653	285	3.10 (2.80–3.50)
Brazil	1	253,706	63	2.48 (1.94–3.18)
Canada	1	1,250,000	421	6.70 (6.10–7.40)
Denmark	3	6,442,869	4253	4.50 (2.38–6.62)
Ireland	1	350,000	13	3.70 (2.20–6.40)
Netherland	1	16,390,837	4061	0.99 (0.84–1.15)
New Zealand	1	471,315	152	6.95 (5.91–8.12)
Poland	1	254,417	36	2.83 (2.04–3.92)
Serbia	1	410,095	35	0.85 (0.62–1.19)
Slovenia	1	NA	25	0.79 (0.51–1.16)
Spain	5	849,137	696	8.47 (6.45–10.48)
Sweden	1	9,672,131	1412	1.22 (0.65–1.79)
Switzerland	3	933,317	248	1.56 (0.75–2.37)
United States	7	1,314,963	1283	10.76 (6.87–14.65)

CI, Confidence interval; EoE, eosinophilic esophagitis; NA, not available.

Supplementary Table 5. National Pooled Incidence of EoE Included in Our Systematic Review (Total Study)

	Number of studies	Number of participants	Patients with EoE	Pooled estimates (95% CI)
Nation				
Australia	1	3,198,653	285	3.10 (2.80–3.50)
Brazil	1	253,706	63	2.48 (1.94–3.18)
Canada	1	1,250,000	421	6.70 (6.10–7.40)
Denmark	4	11,971,854	5097	3.53 (0.29–6.78)
Ireland	1	350,000	13	3.70 (2.20–6.40)
Netherland	1	16,390,837	4061	0.99 (0.84–1.15)
New Zealand	1	471,315	152	6.95 (5.91–8.12)
Poland	1	254,417	36	2.83 (2.04–3.92)
Serbia	1	410,095	35	0.85 (0.62–1.19)
Slovenia	1	NA	25	0.79 (0.51–1.16)
Spain	5	849,137	696	8.47 (6.45–10.48)
Sweden	1	9,672,131	1412	1.22 (0.65–1.79)
Switzerland	3	933,317	248	1.56 (0.75–2.37)
United States	15	241,968,922	135,124	10.74 (8.20–13.28)

CI, Confidence interval; EoE, eosinophilic esophagitis; NA, not available.

Supplementary Table 6. National Pooled Prevalence of EoE Included in Our Systematic Review (Researcher-validated Studies)

	Number of studies	Number of participants	Patients with EoE	Pooled estimates (95% CI)
Nation				
Australia	1	3,198,653	285	8.90 (7.90–10.00)
Brazil	1	253,706	63	24.80 (19.40–31.80)
Canada	1	1,250,000	421	33.70 (30.60–37.10)
China	1	3600	4	11.10 (2.22–22.00)
Denmark	3	5,862,869	4017	36.00 (-30.10–102.05
Netherland	1	16,390,836	4061	23.50 (22.80–24.20)
Serbia	1	410,095	35	6.83 (4.96–9.52)
Spain	4	849,137	696	71.45 (47.18–95.72)
Switzerland	3	933,317	248	29.91 (17.69–42.13)
United States	4	1,314,963	1283	55.41 (-0.64–111.46)

CI, Confidence interval; EoE, eosinophilic esophagitis.

Supplementary Table 7. National Pooled Prevalence of EoE Included in Our Systematic Review (Total Study)

	Number of studies	Number of participants	Patients with EoE	Pooled estimates (95% CI)
Nation				
Australia	1	3,198,653	285	8.90 (7.90–10.00)
Brazil	1	253,706	63	24.80 (19.40–31.80)
Canada	1	1,250,000	421	33.70 (30.60–37.10)
China	1	3600	4	11.10 (2.22–22.00)
Denmark	3	11,391,854	4861	28.59 (−3.70 to 60.88)
Netherland	1	16,390,836	4061	23.50 (22.80–24.20)
Serbia	1	410,095	35	6.83 (4.96–9.52)
Spain	4	849,137	696	71.45 (47.18–95.72)
Switzerland	3	933,317	248	29.91 (17.69–42.13)
United States	12	246,061,506	135,278	44.00 (34.02–53.99)

CI, Confidence interval; EoE, eosinophilic esophagitis.

Supplementary Table 8. Time Trends in EoE Pooled Incidence Included in Our Systematic Review (Researcher-validated Studies)

	Number of studies	Number of participants	Patients with EoE	Pooled estimates (95% CI)	I^2, %	*P* value for I^2
Time trends, year						
<2001	12	22,610,944	331	0.31 (0.19–0.42)	94.873	< .0001
2002–2004	14	5,530,276	255	0.79 (0.55–1.03)	95.613	< .0001
2005–2007	22	5,814,352	520	1.53 (1.15–1.91)	95.681	< .0001
2008–2010	27	10,872,251	260	4.10 (2.66–5.55)	99.441	< .0001
2011–2013	33	16,884,921	1155	6.95 (5.60–8.30)	96.702	< .0001
2014–2016	25	187,479,694	110,938	8.42 (7.23–9.61)	97.114	< .0001
2017–2022	6	23,614,613	1235	6.81 (2.32–11.31)	98.467	< .0001
P_{trend} value						.002

CI, Confidence interval; EoE, eosinophilic esophagitis.

Supplementary Table 9. Time Trends in EoE Pooled Incidence Included in Our Systematic Review (Total Study)

	Number of studies	Number of participants	Patients with EoE	Pooled estimates (95% CI)
Time trends, year				
<2001	13	28,139,929	338	0.26 (0.16–0.36)
2002–2004	14	5,530,276	255	0.79 (0.55–1.03)
2005–2007	22	5,814,352	520	1.53 (1.15–1.91)
2008–2010	29	32,621,983	7760	4.79 (3.17–6.42)
2011–2013	38	77,003,155	17,606	6.95 (5.74–8.15)
2014–2016	27	187,479,694	110,938	9.64 (7.83–11.45)
2017–2022	6	23,614,613	1235	6.81 (2.32–11.31)
P_{trend} value				.004

CI, Confidence interval; EoE, eosinophilic esophagitis.

Supplementary Table 10. Time Trends in EoE Pooled Prevalence Included in Our Systematic Review (Researcher-validated Studies)

	Number of studies	Number of participants	Patients with EoE	Pooled estimates (95% CI)	I^2, %	*P* value for I^2
Time trends, year						
<2001	4	90,000	46	8.18 (3.67–12.69)	52.183	.099
2002–2004	5	399,758	85	27.64 (11.04–44.23)	96.694	< .001
2005–2007	3	1,506,164	427	20.74 (−3.85 to 45.32)	99.315	< .001
2008–2010	2	89,642	40	43.27 (35.92–50.61)	0.000	.832
2011–2013	3	6,835,377	94	32.36 (20.24–44.49)	97.530	< .001
2014–2016	3	1,066,425	360	70.44 (0.74–140.14)	99.326	< .001
2017–2022	4	22,992,504	1216	74.42 (39.66–109.19)	99.812	< .001
P_{trend} value						.004

CI, Confidence interval; EoE, eosinophilic esophagitis.

Supplementary Table 11. Time Trends in EoE Pooled Prevalence Included in Our Systematic Review (Total Study)

	Number of studies	Number of participants	Patients with EoE	Pooled estimates (95% CI)
Time trends, year				
<2001	4	90,000	46	8.18 (3.67–12.69)
2002–2004	5	399,758	85	27.64 (11.04–44.23)
2005–2007	3	1,506,164	427	20.74 (−3.85 to 45.32)
2008–2010	4	21,839,374	7540	38.36 (5.91–70.81)
2011–2013	8	65,439,492	16,701	31.50 (24.12–38.87)
2014–2016	5	165,381,401	110,248	62.70 (29.98–95.41)
2017–2022	4	22,992,504	1216	74.42 (39.66–109.19)
P_{trend} value				.003

CI, Confidence interval; EoE, eosinophilic esophagitis.

Supplementary Table 12. Subgroup Differences in Incidence of EoE (Researcher-validated Studies)

	Number of studies	Group A	Pooled estimates of group A (95% CI)	Group B	Pooled estimates of group B (95% CI)	Mean difference between group A and B, % (95% CI)	*P*-value
Income	28	HICs	5.31 (3.98–6.64)	LMICs	1.64 (0.04–3.24)	**3.67 (1.59–5.75)**	**< .001**
Gender	12	Male	9.38 (7.49–11.28)	Female	2.83 (2.05–3.62)	**6.55 (4.50–8.60)**	**< .001**
Age	24	Adults	7.20 (4.84–9.56)	Children	4.95 (3.91–5.98)	2.25 (−0.33 to 4.83)	.087
Geographical area	25	North America	10.02 (6.53–13.52)	Europe	4.16 (2.47–5.86)	**5.86 (1.98–9.74)**	**.003**
Data source	37	Researcher-validated	5.31 (3.98–6.63)	Code-based	9.53 (6.69–12.38)	**−4.22 (−7.36 to −1.08)**	**.008**

CI, Confidence interval; EoE, eosinophilic esophagitis; HICs, high-income countries; LMICs, low- or middle-income countries (Serbia, China, and Brazil). Boldface values indicate a significant difference (*P*-value $< .05$).

Supplementary Table 13. Subgroup Differences in Incidence of EoE (Total Study)

	Number of studies	Group A	Pooled estimates of group A (95% CI)	Group B	Pooled estimates of group B (95% CI)	Mean difference between group A and B, % (95% CI)	*P*-value
Income	37	HICs	6.77 (5.52–8.02)	LMICs	1.64 (0.04–3.24)	**5.13 (3.10–7.16)**	**< .001**
Gender	17	Male	12.44 (7.06–17.83)	Female	5.18 (2.32–8.04)	**7.26 (1.16–13.36)**	**.020**
Age	30	Adults	9.18 (7.36–11.00)	Children	7.70 (5.59–9.81)	1.48 (−1.31 to 4.27)	.298
Race	3	White	12.1 (9.61–14.56)	Black	3.25 (2.21–4.28)	**8.85 (6.17 to 11.53)**	**< .001**
Race	3	White	12.1 (9.61–14.56)	Asian	4.45 (2.06–6.84)	**7.65 (4.21–11.09)**	**< .001**
Geographical area	34	North America	10.44 (8.01–12.87)	Europe	3.97 (2.36–5.59)	**6.47 (3.55–9.39)**	**< .001**
Data source	37	Researcher validated	5.31 (3.98–6.63)	Code based	9.53 (6.69–12.38)	**−4.22 (−7.36 to −1.08)**	**.008**

CI, Confidence interval; EoE, eosinophilic esophagitis; HICs, high-income countries; LMICs, low- or middle-income countries (Serbia, China, and Brazil). Boldface values indicate a significant difference (*P*-value $< .05$).

Supplementary Table 14. Subgroup Differences in Prevalence of EoE (Researcher-validated Studies)

	Number of studies	Group A	Pooled estimates of group A (95% CI)	Group B	Pooled estimates of group B (95% CI)	Mean difference between group A and B, % (95% CI)	*P*-value
Income	19	HICs	45.05 (34.97–55.12)	LMICs	14.17 (1.73–26.61)	**30.88 (14.87–46.89)**	**< .001**
Gender	6	Male	111.09 (84.70–137.47)	Female	32.83 (14.16–51.50)	**78.26 (45.94–110.58)**	**< .001**
Age	14	Adults	52.95 (21.95–83.96)	Children	32.90 (22.69–43.12)	20.05 (−12.59 to 52.69)	.229
Geographical area	16	North America	50.99 (18.95–83.03)	Europe	42.49 (29.04–55.93)	8.50 (−26.25 to 43.25)	.632
Data source	29	Researcher validated	40.04 (31.10–48.97)	Code based	35.99 (25.21–46.77)	4.05 (-9.95 to 18.05)	0.571

CI, Confidence interval; EoE, eosinophilic esophagitis; HICs, high-income countries; LMICs, low- or middle-income countries (Serbia, China, and Brazil). Boldface values indicate a significant difference (*P*-value $<$ .05).

Supplementary Table 15. Subgroup Differences in Prevalence of EoE (Total Study)

	Number of studies	Group A	Pooled estimates of group A (95% CI)	Group B	Pooled estimates of group B (95% CI)	Mean difference between group A and B, % (95% CI)	*P*-value
Income	28	HICs	41.34 (34.77–47.91)	LMICs	14.17 (1.73–26.61)	**27.17 (13.10–41.24)**	**<0.001**
Gender	12	Male	82.22 (60.80–103.63)	Female	30.00 (17.44–42.55)	**52.22 (27.40–77.04)**	**<0.001**
Age	22	Adults	46.91 (34.50–59.32)	Children	35.10 (25.39–44.80)	11.81 (−3.94 to 27.56)	.142
Race	4	White	54.68 (43.48–65.88)	Black	15.70 (10.86–20.55)	**38.98 (26.78–51.18)**	**< .001**
Race	4	White	54.68 (43.48–65.88)	Asian	19.21 (8.98–29.44)	**35.47 (20.30–50.64)**	**< .001**
Geographical area	25	North America	43.20 (33.65–52.75)	Europe	39.31 (29.10–49.53)	3.89 (−10.09 to 17.87)	.586
Data source	29	Researcher-validated	40.04 (31.10–48.97)	Code-based	35.99 (25.21–46.77)	4.05 (−9.95 to 18.05)	.571

CI, Confidence interval; EoE, eosinophilic esophagitis; HICs, high-income countries; LMICs, low- or middle-income countries (Serbia, China, and Brazil). Boldface values indicate a significant difference (*P*-value $<$ .05).

Supplementary Table 16. Quality Assessment Checklist for Prevalence Studies (Adapted From Hoy et al[a])

Study	Was the study's target population a close representation of the national population in relation to relevant variables (eg, age, sex, occupation)?	Was the sampling frame a true or close representation of the target population?	Was some form of random selection used to select the sample, or was a census undertaken?	Was the likelihood of non-response bias minimal?	Were data collected directly from the subjects (as opposed to a proxy)?	Was an acceptable case definition used in the study?	Was the study instrument that measured the parameter of interest (eg, prevalence of low back pain) shown to have reliability and validity (if necessary)?	Was the same mode of data collection used for all subjects?	Were the numerator(s) and denominator(s) for the parameter of interest appropriate?	Summary on the overall risk of study bias
Noel RJ et al, 2007	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low
Straumann A et al, 2005	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Low
Cherian S et al, 2006	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low
Gill R, et al, 2007	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low
Prasad GA et al, 2009	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low
Dalby K et al, 2010	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low
DeBrosse CW et al, 2010	No	No	No	No	Yes	No	No	Yes	Yes	High
Spergel JM et al, 2011	Yes	No	No	No	No	No	No	No	Yes	High
Hruz P et al, 2011	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low
O'Donnell S et al, 2011	No	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Low
Van Rhijn BD et al, 2013	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Low
Syed AA et al, 2012	No	Yes	No	Yes	Yes	Yes	No	No	Yes	Moderate
Stewart MJ et al, 2013	No	Yes	No	Yes	Yes	Yes	No	No	Yes	Moderate
Arias A et al, 2013	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low
Prakash R et al, 2013	Yes	Yes	No	Yes	Yes	No	No	No	Yes	Moderate
Dellon ES et al, 2014	Yes	Yes	No	Yes	Yes	No	No	No	Yes	Moderate
Ally MR et al, 2014	No	Yes	Yes	Yes	No	No	No	Yes	Yes	Moderate
Ma X et al, 2015	No	Yes	Yes	No	Yes	Yes	No	Yes	Yes	Low
Dellon ES et al, 2015	Yes	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Low

Supplementary Table 16. Continued

Study	Was the study's target population a close representation of the national population in relation to relevant variables (eg, age, sex, occupation)?	Was the sampling frame a true or close representation of the target population?	Was some form of random selection used to select the sample, or was a census undertaken?	Was the likelihood of non-response bias minimal?	Were data collected directly from the subjects (as opposed to a proxy)?	Was an acceptable case definition used in the study?	Was the study instrument that measured the parameter of interest (eg, prevalence of low back pain) shown to have reliability and validity (if necessary)?	Was the same mode of data collection used for all subjects?	Were the numerator(s) and denominator(s) for the parameter of interest appropriate?	Summary on the overall risk of study bias
Maradey-Romero C et al, 2015	Yes	Yes	No	Yes	Yes	Yes	No	Yes	No	Low
Homan M et al, 2015	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Low
Kim S et al, 2015	No	Yes	Yes	No	No	No	No	Yes	No	Moderate
Giriens B et al, 2015	No	Yes	Yes	No	No	Yes	No	Yes	No	Moderate
Mansoor E et al, 2016	Yes	Yes	No	Yes	Yes	Yes	No	Yes	No	Low
Benninger MS et al, 2017	Yes	No	No	No	Yes	No	No	No	Yes	High
Warner MJ et al, 2017	Yes	Yes	No	Yes	Yes	No	No	Yes	Yes	Low
Molina-Infante J et al, 2018	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low
Goncalves LO et al, 2018	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	Low
La Orden Izquierdo E et al, 2018	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Low
Robson J et al, 2018	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low
Hommeida S et al, 2018	No	Yes	Yes	No	Yes	Yes	Yes	Yes	No	Low
Syed A et al, 2017	Yes	Yes	Yes	No	Yes	Yes	No	Yes	No	Low
Arias A et al, 2019	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low
Ristic N et al, 2019	No	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Low
Limketkai BN et al, 2019	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Low
Weerasekera K et al, 2019	No	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Low
Cianferoni A et al, 2020	No	No	No	No	No	No	No	No	Yes	High

Supplementary Table 16. Continued

Study	Was the study's target population a close representation of the national population in relation to relevant variables (eg, age, sex, occupation)?	Was the sampling frame a true or close representation of the target population?	Was some form of random selection used to select the sample, or was a census undertaken?	Was the likelihood of non-response bias minimal?	Were data collected directly from the subjects (as opposed to a proxy)?	Was an acceptable case definition used in the study?	Was the study instrument that measured the parameter of interest (eg, prevalence of low back pain) shown to have reliability and validity (if necessary)?	Was the same mode of data collection used for all subjects?	Were the numerator(s) and denominator(s) for the parameter of interest appropriate?	Summary on the overall risk of study bias
McGowan EC et al, 2020	Yes	Yes	No	No	Yes	No	No	Yes	Yes	Moderate
Zdanowicz K et al, 2020	No	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Low
RooiJ WE et al, 2020	Yes	Yes	No	No	Yes	No	Yes	Yes	Yes	Low
La Orden Izquierdo E et al, 2021	No	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Low
Melgaard D et al, 2021	No	Yes	No	Yes	Yes	Yes	Yes	Yes	No	Low
Garber et al, 2022	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Low
Allin et al, 2022	Yes	Yes	No	Yes	Yes	Yes	Yes	No	No	Low
Hollaender et al, 2022	No	No	No	No	Yes	No	Yes	No	No	High

[a]Hoy D, Brooks P, Woolf A, et al. Assessing risk of bias in prevalence studies: modification of an existing tool and evidence of interrater agreement. J Clin Epidemiol 2012;65:934–939.