Perinatal Risk Factors in Relation to Asthma and Allergic Rhinitis in Children and Adolescents

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Abstract

Objectives: To evaluate the associations between birth-related exposures and postnasal factors and risk for allergic rhinitis and asthma in children and adolescents.

Methods: We conducted a comprehensive search of five literature databases up until May 2023. To estimate the associations between birth-related exposures (birth weight, mode of delivery, prematurity, sex, maternal age, and parental history of allergy) and postnatal factors (birth order, number of siblings, exclusive, and duration of breastfeeding) and allergic disease, we calculated pooled odds ratios with 95% confidence intervals. In addition, we performed subgroup analyses according to allergic disease, birth order, number of siblings, and parental history of allergy. Methodological quality of the included studies was assessed using the Newcastle-Ottawa scale.

Results: This meta-analysis included 31 studies with 218,899 patients. Among the birth-related exposures, low birth weight, maternal age, and prematurity (<37 weeks) showed no significant associations with risk for asthma or allergic rhinitis in childhood or adolescence. On the other hand, male sex, family history of allergy, and cesarean section were related to higher risk for asthma or allergic rhinitis. Among postnatal factors, exclusive breastfeeding, long duration (>6 months) of breastfeeding, birth order second or later, and presence of sibling(s) showed preventive effects against allergic disease in offspring.

Conclusion: The risks for allergic rhinitis and asthma were higher in male patients delivered by cesarean section and with a family history of allergy. By contrast, exclusive and long duration (>6 months) breastfeeding and the presence of sibling(s) reduced the risk of developing respiratory allergic disease.

Keywords: Adolescent; Asthma; Child; Rhinitis, Allergic; Risk factors

HIGHLIGHTS

- Male sex, family history of allergy, and cesarean section were related to higher risk for asthma or allergic rhinitis.
- Exclusive breastfeeding, long duration (>6 months) of breastfeeding showed preventive effects against allergic disease in offspring.
- Birth order second or later, and presence of sibling(s) reduced the risk of developing respiratory allergic disease.

Introduction

There is a common association between asthma and rhinitis involving a predisposition to the development of hypersensitivity reactions to environmental allergens, particularly those present in the air [1]. The increasing prevalence rates of asthma and allergic rhinitis over the past few decades have been well documented [2]. These increases cannot be solely attributed to genetic factors, as environmental changes also significantly contribute to the development of such conditions [3]. There is evidence that exposure during the early stages of life has a significant impact, suggesting that the developing immune system may be more susceptible to improper "programming" during this period [4]. In addition, an atopic phenotype may be programmed in *utero* [5]. The immune system initiates a response to ubiquitous environmental allergens early in development, and there is a possibility of sensitization to allergens even during fetal stages [6]. Therefore, allergen-specific responses of the human immune system may exhibit certain biases from birth and increase with age. Accordingly, assessing and managing pre- and postnatal risk factors with respect to the incidences of asthma and allergic rhinitis in children and adolescents would play an important role in reducing the global health burden of airway disease. Although various studies have been conducted on this topic, as far as we know, no meta-analysis on perinatal risk factors has been reported. Additionally, several conflicting opinions have been reported regarding the effects of several birth-related exposures and postnatal factors on asthma and rhinitis [4,7-36]. Because medical prevention can be more effective than treatment, it is necessary to secure objective and high-level evidence by integrating and analyzing this subject through meta-analysis. It is also important to determine how closely associated each perinatal risk factor is to asthma and rhinitis. Therefore, in this meta-analysis, we investigated the risks for allergic rhinitis and asthma according to a number of birth-related and postnatal factors.

Materials and methods

Study protocol and registration

The necessity for Institutional Review Board (IRB) approval is not mandated by our institution in the case of a systematic review and meta-analysis exclusively reliant on published literature. This systematic review and meta-analysis was prepared in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [37]. This study protocol was prospectively registered in the Open Science Framework (https://osf.io/k7fgy/).

Literature search

Reports were retrieved by searching the PubMed, Scopus, Embase, Web of Science, and Cochrane Central Register of Controlled Trials (CENTRAL) databases until February 2023. The key search Medical Subject Headings (MeSH) terms were as follows: "allergic rhinitis," "hay fever," "allergic rhinoconjunctivitis," "seasonal allergic rhinitis," "asthma," "allergic diseases," "pregnant women," "pregnant," "cesarean section," "c-section," "delivery mode," "abdominal deliveries," "post cesarean section," "adolescent," "child," "breast feeding," and "risk factors." Detailed keywords and search methods retrieved from the database are listed in Supplementary Table 1. Two authors independently reviewed and selected candidate studies based on reviewing the title, abstract, and main text. If the two reviewers differed in their decision whether to include a study, it was decided through discussion with a third reviewer.

Selection criteria

The analysis included cross-sectional, cohort, and case–control studies assessing the associations between birth-related exposures (birth weight, mode of delivery, prematurity, sex, maternal age, and parental history of allergy) and postnasal factors (birth order, number of siblings, and exclusiveness and duration of breastfeeding) and risks for allergic rhinitis and asthma in offspring (children and adolescents). In the literature, if allergic rhinitis or asthma

was not specified, it was collectively referred to as 'allergic diseases'. All study designs except case reports and review articles were included. These studies should have relevant data prediction, including risk ratio (odds ratio [OR]) and 95% confidence interval (CI). All studies were performed in human subjects. Articles with insufficient data for statistical analysis were excluded from the study. The selection strategy is summarized in Figure 1.

Data organization and quality assessment

Data were extracted from selected studies and items were organized in a standardized format [38]. We examined the following items: number of patients, sex, nationality, the presence of allergic rhinitis or asthma, and the OR and corresponding 95% CI to evaluate the relations of the risk factors with prevalence of allergic disease [4,7-36,39]. The risk of bias of the studies included in the analysis was assessed using the Newcastle-Ottawa scale.

Statistical analyses

R version 4.2.2 (R Foundation for Statistical Computing, Vienna, Austria) was used for R version 4.2.2 (R Foundation for Statistical Computing, Vienna, Austria) was used for statistical analysis. OR was used as the effect index. The correlation strengths of birth-related exposures and postnasal factors with respiratory allergic disease in offspring were determined by combining OR and 95% CI. The I^2 test was used to assess heterogeneity. If both multivariate and univariate analyses were used to evaluate the risk factors, the OR and relevant 95% CI derived from multivariate analysis were used. The I^2 test accounts for the rate of variability across studies due to heterogeneity with values ranging from 0 to 100 where higher values correspond to increased heterogeneity. In cases where a notable degree of heterogeneity was observed between the outcomes ($I^2 > 50$), a meta-analysis was conducted using a random-effects model. On the other hand, for outcomes without significant heterogeneity ($I^2 < 50$), a fixed-effects model was used for the analysis. All *p*-values are reported as two-tailed values. Furthermore, sensitivity analyses were performed to assess the influence of individual studies

on the overall findings of the meta-analysis. Potential publication bias for each item was identified using a combination of funnel plot and Egger's test. When publication bias was suspected, the funnel plot asymmetry was corrected and confirmed by adding Duval and Tweedie's trim-and-fill method.

Results

In total, 218,899 patients from 31 studies were included in the analysis. Study characteristics and bias assessment are shown in Table 1 and Supplementary Table 2.

Association of birth related exposures with the risk of allergic rhinitis and asthma

Low birth weight (OR = 0.9644 [0.8004; 1.1622]; I^2 = 49.0%), maternal age > 35 years (0.8827 [0.7052; 1.1049]; I^2 = 61.4%), and prematurity (<37 weeks) (OR = 1.0189 [0.9156; 1.1338]; I^2 = 14.9%) had no significant association with the risks for asthma or allergic rhinitis in childhood or adolescence. By contrast, male sex (OR = 1.4985 [1.3961; 1.6084]; I^2 = 56.0%), family history of allergy (OR = 2.3300 [1.9690; 2.7571]; I^2 = 92.2%), and cesarean section (OR = 1.2252 [1.1543; 1.3004]; I^2 = 50.5%) were related to higher risks for asthma or allergic rhinitis (Supplementary Figure 1).

Begg's funnel plot and Egger's test for prematurity (p = 0.563), male sex (p = 0.8109), and family history of allergy (p = 0.0815) suggested that there was no potential publication bias in these studies. However, those tests for cesarean section (p = 0.004629) indicated potential bias in these studies. Nevertheless, the trim-and-fill test revealed a lack of statistical significance in comparisons of observed and adjusted values (1.2252, p < 0.0001 vs. 1.1626, p < 0.0001). Therefore, we concluded that there was no publication bias in the items included in the analysis. Begg's funnel plot results are presented in Supplementary Figure 2. Analysis of publication bias could not be performed on low birth weight and maternal age > 35 years due to the small number

of included studies (<10).

In subgroup analysis regarding disease type (allergic rhinitis vs. asthma), birth-related exposures (birth weight: allergic rhinitis = 0.8065 [0.6353; 1.0237] vs. asthma = 1.2355 [0.9069; 1.6831], p = 0.4538; c-section: allergic rhinitis = 1.2216 [1.1159; 1.3374] vs. asthma = 1.2270 [1.0991; 1.3698], p = 0.9516; prematurity: allergic rhinitis = 1.0109 [0.9056; 1.1283] vs. asthma = 1.1418 [0.7096; 1.8372], p = 0.7941; sex: allergic rhinitis = 1.5331 [1.4317; 1.6417] vs. asthma = 1.5590 [1.4244; 1.7064], p = 0.3259; maternal age: allergic rhinitis = 0.9273 [0.7139; 1.2044] vs. asthma = 0.7289 [0.3877; 1.3707], p = 0.4901; parental history of allergy: allergic rhinitis = 2.5807 [2.0509; 3.2474] vs. asthma = 1.9223 [1.2784; 2.8904], p = 0.2995) were found to have similar causative or preventive associations with allergic rhinitis and asthma (Supplementary Figure 1).

In subgroup analysis of family history, the risk for allergic disease was higher for maternal than paternal history of allergy (OR = 2.5191 [2.0369; 3.1155] vs. OR = 1.6880 [1.2735; 2.2375], respectively, p = 0.0262). By contrast, there were no significant differences in risk for allergic disease between single-parental history of allergy (OR = 2.1035 [1.8149; 2.4380]) and biparental history of allergy (OR = 2.0901 [1.8113; 2.4119], p = 0.9516) (Supplementary Figure 1).

Association between postnatal factors and risks for allergic rhinitis and asthma

Exclusive breastfeeding (OR = 0.7573 [0.6564; 0.8738]; $I^2 = 73.7\%$) and long duration (>6 months) of breastfeeding (OR = 0.8584 [0.7907; 0.9319]; $I^2 = 67.3\%$), birth order second or later (0.7925 [0.7526; 0.8344]; $I^2 = 66.3\%$), and presence of sibling(s) (0.7836 [0.7300; 0.8412]; $I^2 = 55.9\%$) were negatively associated with offspring allergic disease (Supplementary Figure 3).

Begg's funnel plot and Egger's test for exclusive breastfeeding (p = 0.07949), long duration

(>6 months) of breastfeeding (p = 0.9796), and presence of sibling(s) (p = 0.3667) showed no publication bias in the studies. However, Egger's test (p = 0.004675) and Begg's funnel plot analyses of birth order second or later (p = 0.03244) suggested that there may have been publication bias in the included studies.

In subgroup analysis regarding disease type (allergic rhinitis vs. asthma), postnasal factors (exclusive breastfeeding (AR = 0.7471 [0.6317; 0.8836] vs. asthma = 0.7724 [0.5300; 1.1255], p = 0.8746) and long duration (>6 months) of breastfeeding (AR = 0.8306 [0.7600; 0.9076] vs. asthma a = 0.9374 [0.8047; 1.0920], p = 0.1793) were found to have similar causative or preventive effects on allergic rhinitis and asthma. By contrast, birth order second or later (AR = 0.7369 [0.6796; 0.7989] vs. asthma = 0.8278 [0.6863; 0.9986], p = 0.0048) and presence of sibling(s) (AR = 0.7477 [0.6910; 0.8090] vs. asthma = 0.8618 [0.6735; 1.1026], p = 0.0218) showed greater preventive effects against allergic rhinitis than asthma (Supplementary Figure 3).

With regard to birth order and number of siblings, there were no significant differences in risk for allergic disease between birth order second and 3rd or later (0.8185 [0.7670; 0.8733] vs. 0.7535 [0.6827; 0.8316], respectively, p = 0.1701). In addition, subjects with a single sibling had a reduced risk for allergic disease, which was similar to that of subjects with two or more siblings (0.8341 [0.7515; 0.9257] vs. 0.7659 [0.7020; 0.8357], respectively, p = 0.2187) (Supplementary Figure 3).

Sensitivity analyses

Sensitivity analyses were performed to assess differences in congruency estimates. All of the analyzed results were consistent with the above results.

Discussion

Through meta-analysis, we were able to perform odd ratio analysis by statistically integrating a larger number of patients, thus providing more objective and high-level evidence. Also, we can check how large the odd ratio is for each factor. Among birth-related exposures, family history of allergy showed the highest odds ratio for asthma or allergic rhinitis, followed by male sex and cesarean section. Among family history of allergies, maternal history of allergy was especially important. Among postnatal factors, exclusive breastfeeding was most negatively associated, followed by presence of sibling(s), birth order second or later, and long duration (>6 months) of breastfeeding. Presence of sibling(s) and birth order were particularly more negatively associated with allergic rhinitis. There were reports that allergic rhinitis and asthma were related to low birth weight, high maternal age and prematurity [14,17,21]. However, as shown in the results of this analysis, low birth weight had a low relation with allergic rhinitis, and asthma had a high relationship. There were mixed reports in the case of elderly mothers and prematurity, but through this analysis, it was concluded that the relationship with allergic disease was not clear.

In subgroup analysis, birth order second or later and presence of sibling(s) showed greater preventive effects against allergic rhinitis than asthma. However, all birth-related exposures (birth weight, birth by cesarean section, prematurity, sex, maternal age, parental history of allergy) and other postnasal factors (exclusive or long duration [>6 months] of breastfeeding) were found to have similar causative or preventive effects on allergic rhinitis and asthma.

Allergic rhinitis and asthma were suggested to be influenced by both genetic and environmental factors [40]. Allergic rhinitis and asthma are prevalent allergic diseases with similar etiologies, which frequently occur concomitantly in the same family [41]. Genetic susceptibility to allergic

diseases has been reported, which explains why a family history of the disease can be an important risk factor for the occurrence of allergy in children [42]. Recently, however, the different entities of these two diseases have been discussed more actively, away from the concept of "one-airway-one-disease" [43]. In this study, we confirmed that interactions with siblings were more closely related to allergic rhinitis than asthma. Children who experience familial infections or have exposure to gut commensals are prone to encountering microorganisms for extended periods and potentially in greater quantities, thereby facilitating appropriate immune conditioning. In addition, heightened levels of household crowding have been associated with elevated antigen exposure, potentially contributing to the observed protective influence of crowding [4,35]. It was inferred that continuous exposure to allergens contributes more to the occurrence of allergic rhinitis than asthma, and additional research on this issue is required.

In this study, the risks for allergic rhinitis and asthma were higher in boys during childhood. However, there have been reports that the proportion of females with these allergic diseases increases with age [44]. This may be due to genetic susceptibility and environmental exposure, but it has also been suggested that the influence of hormones, such as estrogen and progesterone, may make women more vulnerable to allergic diseases [44].

A multidisciplinary review yielded identical findings regarding the relations between breastfeeding and the subsequent development of allergic diseases [45]. The plausibility of the allergy-preventive impact of breastfeeding has been investigated using various approaches, including analyzing traces of food proteins ingested by lactating mothers that promote tolerance to these foods, as well as eliminating microbes that trigger inflammatory responses [46].

The effects of cesarean delivery have been compared to those of vaginal delivery, considering factors such as the absence of vaginal compression on the chest of the neonate and reduced

stress during cesarean delivery. The stress and labor during vaginal delivery stimulate the release of catecholamines, cortisol, and pulmonary surfactant, which contribute significantly to normal postnatal lung development [47]. Furthermore, it has been postulated that cesarean section, by not exposing the neonate to maternal vaginal microflora, could potentially impede maturation of the immune system, possibly impacting the balance between Th1 and Th2 lymphocytes in early life [48]. Caesarean section rates, both for medical necessity and nonmedical reasons, continue to increase worldwide [49]. In addition, caesarean section could affect lactogenesis, which makes breastfeeding less likely or may delay the onset of breastfeeding [50]. Therefore, as caesarean section for nonmedical reasons and duration and extent of breastfeeding could affect the development of asthma and allergic rhinitis in children, these points should be included as important components of maternal education.

This study had several limitations. Primarily, the majority of investigations that have examined the associations between pre- or postnatal factors and respiratory allergic status in children and adolescents have relied on retrospective or cross-sectional designs, lacking the inclusion of explicit clinical criteria for maternal or medical decision-making regarding caesarean section, preterm birth, maternal age, breastfeeding, and other relevant factors. Therefore, conclusions regarding cause-and-effect relations are limited. Additional clinical studies that assess the effects of pre- or postnatal factors on respiratory allergic state are needed to overcome this issue. Second, it is necessary to consider that variation in publication domains, duration of study, and approaches employed to address confounding variables may contribute to potential disparities between the reported results and the true underlying status. Furthermore, our analysis encompassed certain enrolled investigations that relied on self-reported diagnoses of allergic rhinitis or asthma, potentially leading to disparity from actual prevalence and consequently diminishing the generalizability of our findings. It is essential to acknowledge that any deviations or inaccuracies present within individual studies could have influenced our overall analysis. Nevertheless, given the robustness of the association between pre- or postnatal factors and respiratory allergic state development, our findings suggest that future randomized trials that explore the potential roles of these factors on respiratory allergic state are warranted.

In summary, allergic rhinitis and asthma showed increased incidence rates among individuals delivered by cesarean section, identified as male at birth, and those with a familial background of allergies. On the other hand, exclusive and long-duration (>6 months) breastfeeding and the presence of siblings were potential protective factors against the development of allergic rhinitis and asthma in children and adolescents.

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Table 1. Characteristics of Included Studies.

Study (year)	Study design	Sample Size	Age (year; mean, range, or standard deviation)	Time line (year; mean, range, or standard deviation)	Sex (Male/F emale)	Nation	Allergic disease diagnosis	Comparison
Nafstad 2000	Cohort	2531	4	4	1298/12 33	Sweden	Physician based	Allergic disease (AR vs asthma), delivary mode (C section vs vaginal delivery), any family member allergy history, single parent allergy history (mother vs father), parent allergy history (single vs both history), gender (male vs female), maternal age at birth (older than 35 vs less than 35), birth order (second vs third or later), number of sibiling (2 vs 3 or more)
Montgomery 2001	Cohort	5519	26	27	NA	UK	Survey based	Any family member allergy history, parent allergy history (single vs both history), birth orde (Second vs third or later), number of sibiling (2 vs 3 or more), exclusive breastfeeding, duration of breastfeeding more than 6 month, delivary mode (C section vs vaginal delivery)
Xu 2001	Cohort	11635	31	31	NA	Finland	Physician based	Delivary mode (C section vs vaginal delivery)
McKeever 2002	Cohort	29238	2.9 (0- 11)	2	NA	UK	Physician based	Allergic disease (AR vs asthma), delivary mode (C section vs vaginal delivery)
Bager 2003	Cohort	9722	25 (20-28)	25	0/9722	Denmark	Physician based	Allergic disease (AR vs asthma), delivary mode (C section vs vaginal delivery), Maternal age at birth older than 35, premature (<37 weeks), number of sibiling (2 vs 3 or more)
Negele 2004	Cohort	2500	2	2	1205/12 95	Germany	Physician based	Allergic disease (AR vs asthma), delivary mode (C section vs vaginal delivery)

Polster 2005	Cohort	7872	3-10	3-10	4001/38 71	USA	Physician based	Gender (male vs female), allergic disease (AR vs asthma), delivary mode (C section vs vaginal delivery), birth order (second vs third or later), number of sibiling (2 vs 3 or more)
Salam 2006	Cohort	2653	10.5±2.2	10.5	NA	USA	Survey based	Delivary mode (C section vs vaginal delivery), allergic disease (AR vs asthma),
Miyake 2007	Cross- sectional	24077	6-15	6-15	12161/1 1916	Japan	Survey based	Allergic disease (AR vs asthma), exclusive breastfeeding, duration of breastfeeding more than 6 months
Westergaard 2007	Cross- sectional	31145	15-43	15-43	All women	Denmark	Physician based	Birth order (Second vs third or later), number of sibiling (2 vs 3 or more)
Ehlayel 2008	Cross- sectional	1278	0-5	0-5	632/646	UK	Physician based	Allergic disease (AR vs asthma), exclusive breastfeeding
Mallen 2008	Cross- sectional	567	18-25	18-25	NA	UK	Physician based	Allergic disease (AR vs asthma), delivary mode (C section vs vaginal delivery), Premature (<37 weeks)
Pistiner 2008	Cohort	432	7.4 (6.5- 10.1)	9	237/195	USA	Physician based	Allergic disease (AR vs asthma), delivary mode (C section vs vaginal delivery)
Park 2010	Cross- sectional	279	4.6±3.8	4.6±3.8	180/99	Korea	Physician based	Allergic disease (AR vs asthma), delivary mode (C section vs vaginal delivery)
Valdivia 2010	Case- control	366	4.02 (2-7)	2-7	172/197	Peru	Physician based	Exclusive breastfeeding, low birth weight (<2500 g), Premature (<37 weeks)
Jelding- Dannemand 2015	Cohort	335	7	7	NA	Denmark	Physician based	Allergic disease (AR vs asthma), exclusive breastfeeding
Li 2015	Cross- sectional	20803	9.19	9.19	10803/1 0000	China	Survey based	Exclusive breastfeeding, delivary mode (C section vs vaginal delivery), gender (male vs female), premature (<37 weeks)
Bion 2016	Cohort	2140	10-18	10	NA	UK	Survey based	Allergic disease (AR vs asthma), exclusive breastfeeding, duration of breastfeeding more than 6 months
Brandão 2016	Cross- sectional	672	6	6	336/336	Brazil	Survey based	Allergic disease (AR vs asthma), delivary mode (C section vs vaginal delivery)

Chu 2017	Cross- sectional	12639	7-10	7-10	NA	China	Survey based	Delivary mode (C section vs vaginal delivery)
Bedolla- Barajas 2018	Cross- sectional	1003	6-7	6-7	474/529	Mexico	Survey based	Allergic disease (AR vs asthma), any family member allergy history, parent allergy history (single vs both history), gender (male vs female)
Krzych-Fałta 2018	Cross- sectional	18617	NA	6-44	8606/10 011	Poland	Physician based	Delivary mode (C section vs vaginal delivery), any family member allergy history
Han 2019	Cohort	1374	4-12	4-12	941/433	Korea	Physician based	Duration of breastfeeding more than 6 months, delivary mode (C section vs vaginal delivery), number of sibiling (2 vs 3 or more)
Kim 2019	Cohort	175	3	3	78/97	Korea	Survey based	Delivary mode (C section vs vaginal delivery), any family member allergy history, parent allergy history (single vs both history), low birth weight (<2500 g), Premature (<37 weeks), gender (male vs female)
Gorris 2020	Cross- sectional	189	8.2±2.7	8.2±2.7	101/88	Austria	Physician based	Allergic disease (AR vs asthma), exclusive breastfeeding, delivary mode (C section vs vaginal delivery), any family member allergy history, single parent allergy history (mother vs father), parent allergy history (single vs both history), Premature (<37 weeks), gender (male vs female)
Lu 2020	Cohort	1344	6.4	6.4	763/581	Taiwan	Physician based	Delivary mode (C section vs vaginal delivery), any family member allergy history, single parent allergy history (mother vs father), parent allergy history (single vs both history), maternal age at birth older than 35, premature (<37 weeks), birth order (second vs third or later), number of sibiling (2 vs 3 or more), gender (male vs female)
Tong 2020	Cross- sectional	5550	6-12	8.79±1.7	2993/25 57	China	Physician based	Duration of breastfeeding more than 6 months, any family member allergy history, Maternal age at birth older than 35, gender (male vs female)
Hu 2021	Cohort	10464	6-12	9.2±2.2	5464/50 00	China	Survey based	Allergic disease (AR vs asthma), duration of breastfeeding more than 6 months, delivary mode

								(C section vs vaginal delivery), any family member allergy history, low birth weight (<2500 g), premature (<37 weeks), gende (male vs female)
Meza-Lopez 2021	Cross- sectional	1003	6-7	6-7	477/526	Mexico	Survey based	Delivary mode (C section vs vaginal delivery)
Tong 2022	Cross- sectional	10757	6-12	8.91±1.78	5809/49 48	China	Survey based	Duration of breastfeeding more than 6 months, delivary mode (C section vs vaginal delivery), any family member allergy history, Maternal age at birth older than 35, gender (male vs female)
Wang 2022	Case- control	2020	5.18±0.99	5.18±0.99	225/179	China	Survey based	Duration of breastfeeding more than 6 months, delivary mode (C section vs vaginal delivery), any family member allergy history, single parent allergy history (mother vs father), parent allergy history (single vs both history), low birth weight (<2500 g), premature (<37 weeks)

NA; Nor available, AR; allergic rhinitis, C section; Cesarean section

Figure Legends

Figure 1. Flow diagram of the article-selection process.

Supplementary Table 1. Search Strategies.

Supplementary Table 2. Risk of Bias Assessment.

Supplementary Figure 1. Odd ratios of birth-related exposures with risks for allergic rhinitis and asthma. (A) Low birth weight. (B) Maternal age > 35 years. (C) Prematurity (<37 weeks). (D) Male sex. (E) Family history of allergy. (F) Birth by cesarean section.

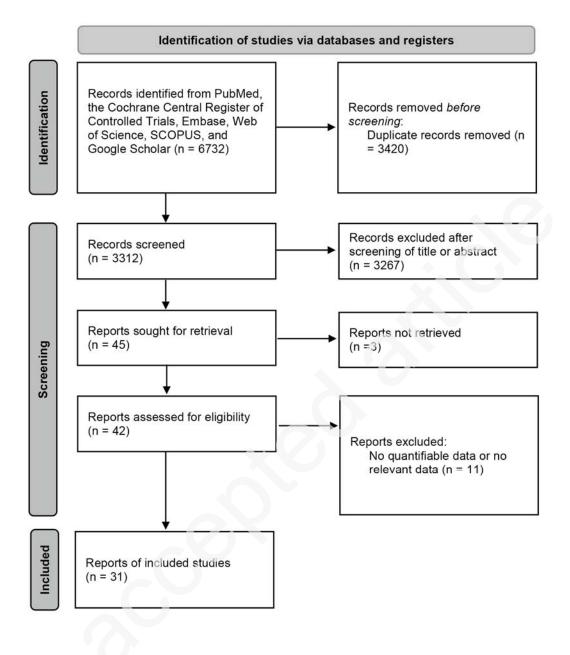
Supplementary Figure 2. Begg's funnel plot. (A) Prematurity. (B) Male sex. (C) Family history of allergy. (D) Birth by cesarean section. (E) Exclusive breastfeeding. (F) Long duration (>6 months) of breastfeeding. (G) Presence of sibling(s). (H) Birth order.

Supplementary Figure 3. Odds ratios of postnatal factors with risks for allergic rhinitis and asthma. (A) Exclusive breastfeeding. (B) Long duration (>6 months) of breastfeeding. (C) Birth order second or later. (D) Presence of sibling(s).

The English in this document has been checked by at least two professional editors, both native speakers of English. For a certificate, please see:

http://www.textcheck.com/certificate/BdyOwT

Figure 1.



Supplementary Table 1. Search Strategies.

Database	Search	Search terms/queries
PubMed	#1	"Child"[Mesh] OR "Child"[TW] OR "Children"[TW]
	#2	"Child, Preschool"[Mesh]
	#3	"Child, Preschoo"[TW] OR "Preschool Child"[TW] OR "Children, Preschool"[TW] OR "Preschool Childrenl"[TW]
	#4	"Adolescent"[Mesh]
	#5	"Adolescent"[TW] OR "Adolescents"[TW] OR "Adolescence"[TW] OR "Teens"[TW] OR "Teen"[TW] OR "Teenagers"[TW] OR "Teenager"[TW] OR "Youth"[TW] OR "Youths"[TW] OR "Adolescents, Female"[TW] OR "Adolescent, Female"[TW] OR "Female Adolescent"[TW] OR "Female Adolescents"[TW] OR "Adolescents, Male"[TW] OR "Adolescent, Male"[TW] OR "Male Adolescent"[TW] OR "Male Adolescents"[TW]
	#6 Combine	#1 OR #2 OR #3 OR #4 OR #5
	#7	"Asthma"[Mesh]
	#8	"Asthma"[TW] OR "Asthmas"[TW] OR "Bronchial Asthma"[TW] OR "Asthma, Bronchial"[TW]
	#9	"Rhinitis, Allergic"[Mesh]
	#10	"Rhinitis, Allergic"[TW] OR "Allergic Rhinitides"[TW] OR "Rhinitides, Allergic"[TW] OR "Allergic Rhinitis"[TW] OR "allergic rhinoconjunctivitis"[TW]
	#11	"Rhinitis, Allergic, Seasonal"[Mesh]
	#12	"Rhinitis, Allergic, Seasonal"[TW] OR "Seasonal Allergic Rhinitis"[TW] OR "Allergic Rhinitides, Seasonal"[TW] OR "Allergic Rhinitis, Seasonal"[TW] OR "Rhinitides, Seasonal Allergic"[TW] OR "Rhinitis, Seasonal Allergic"[TW] OR "Seasonal Allergic Rhinitides"[TW] OR "Pollen Allergy"[TW] OR "Allergies, Pollen"[TW] OR "Allergy, Pollen"[TW] OR "Pollen Allergies"[TW] OR "Pollinosis"[TW] OR "Pollinoses"[TW] OR "Hay Fever"[TW] OR "Fever, Hay"[TW] OR "Hayfever"[TW]
	#13 Combine	#7 OR #8 OR #9 OR #10 OR #11 OR #12
	#14	"Delivery, Obstetric"[Mesh]
	#15	"Delivery, Obstetric"[TW] OR "Deliveries, Obstetric"[TW] OR "Obstetric Deliveries"[TW] OR "Obstetric Delivery"[TW] OR "Delivery"[TW] OR "Delivery mode"[TW] OR "vaginal delivery"[TW]
	#16	"Cesarean Section"[Mesh]
	#17	"Cesarean Section"[TW] OR "Cesarean Sections"[TW] OR "Delivery, Abdominal"[TW] OR "Abdominal Deliveries"[TW] OR "Deliveries, Abdominal"[TW] OR "Caesarean Section"[TW] OR "Caesarean Sections"[TW] OR "Abdominal Delivery"[TW] OR "C-Section (OB)"[TW] OR "C Section (OB)"[TW] OR "C-Sections (OB)"[TW] OR "Postcesarean Section"[TW] OR "C-section"[TW]
	#18	"allergy history"[TW] OR "family member allergy history"[TW] OR "single parent allergy history"[TW] OR "parent allergy history"[TW]

#19	"Maternal Age"[Mesh]
#20	"Maternal Age"[TW] OR "Age, Maternal"[TW] OR "Ages, Maternal"[TW] OR "Maternal Ages"[TW]
#21	"Birth Order"[Mesh]
#22	"Birth Order"[TW] OR "Birth Orders"[TW] OR "First Birth"[TW] OR "Birth, First"[TW] OR "Births, First"[TW] OR "First Births"[TW]
#23	"Siblings"[Mesh]
#24	"Siblings"[TW] OR "Sibling"[TW] OR "Sisters"[TW] OR "Sister"[TW] OR "Brothers"[TW] OR "Brother"[TW] OR "number of sibling"[TW]
#25	"Breast Feeding"[Mesh]
#26	"Breast Feeding"[TW] OR "Breastfed"[TW] OR "Breastfeeding"[TW] OR "Breast Fed"[TW] OR "Milk Sharing"[TW] OR "Sharing, Milk"[TW] OR "Breast Feeding, Exclusive"[TW] OR "Exclusive Breast Feeding"[TW] OR "Breastfeeding, Exclusive"[TW] OR "Exclusive Breastfeeding"[TW] OR "Wet Nursing"[TW] OR "exclusive breastfeeding "[TW] OR "duration of breastfeeding"[TW]
#27	"Premature Birth"[Mesh]
#28	"Premature Birth"[TW] OR "Birth, Premature"[TW] OR "Births, Premature"[TW] OR "Premature Births"[TW] OR "Preterm Birth"[TW] OR "Birth, Preterm"[TW] OR "Births, Preterm"[TW] OR "Preterm Births"[TW]
#29 Combine	#14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28
#30 Combine	#6 AND #13 AND #29

Database	Search	Search terms/queries
EMBASE	#1	"child"/exp OR "Child":ti,ab,kw,de OR "Children":ti,ab,kw,de
	#2	"preschool child"/exp
	#3	"Child, Preschoo":ti,ab,kw,de OR "Preschool Child":ti,ab,kw,de OR "Children, Preschool":ti,ab,kw,de OR "Preschool Childrenl":ti,ab,kw,de
	#4	"adolescent"/exp
	#5	"Adolescent":ti,ab,kw,de OR "Adolescents":ti,ab,kw,de OR "Adolescence":ti,ab,kw,de OR "Teens":ti,ab,kw,de OR "Teen":ti,ab,kw,de OR "Teenagers":ti,ab,kw,de OR "Teenager":ti,ab,kw,de OR "Youth":ti,ab,kw,de OR "Youths":ti,ab,kw,de OR "Adolescents, Female":ti,ab,kw,de OR "Adolescent, Female":ti,ab,kw,de OR "Female Adolescent":ti,ab,kw,de OR "Female Adolescents":ti,ab,kw,de OR "Adolescents, Male":ti,ab,kw,de OR "Adolescent, Male":ti,ab,kw,de OR "Male Adolescent":ti,ab,kw,de OR "Male Adolescents":ti,ab,kw,de
	#6 Combine	#1 OR #2 OR #3 OR #4 OR #5
	#7	"asthma"/exp
	#8	"Asthma":ti,ab,kw,de OR "Asthmas":ti,ab,kw,de OR "Bronchial Asthma":ti,ab,kw,de OR "Asthma, Bronchial":ti,ab,kw,de

#9	"allergic rhinitis"/exp
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#11	"pollen allergy"/exp
#12	"Rhinitis, Allergic, Seasonal":ti,ab,kw,de OR "Seasonal Allergic Rhinitis":ti,ab,kw,de OR "Allergic Rhinitides, Seasonal":ti,ab,kw,de OR "Allergic Rhinitis, Seasonal":ti,ab,kw,de OR "Rhinitides, Seasonal Allergic":ti,ab,kw,de OR "Rhinitis, Seasonal Allergic":ti,ab,kw,de OR "Seasonal Allergic Rhinitides":ti,ab,kw,de OR "Pollen Allergy":ti,ab,kw,de OR "Allergies, Pollen":ti,ab,kw,de OR "Allergy, Pollen":ti,ab,kw,de OR "Pollen Allergies":ti,ab,kw,de OR "Pollinosis":ti,ab,kw,de OR "Pollinoses":ti,ab,kw,de OR "Hay Fever":ti,ab,kw,de OR "Fever, Hay":ti,ab,kw,de OR "Hayfever":ti,ab,kw,de
#13 Combine	#7 OR #8 OR #9 OR #10 OR #11 OR #12
#14	"obstetric delivery"/exp
#15	"Delivery, Obstetric":ti,ab,kw,de OR "Deliveries, Obstetric":ti,ab,kw,de OR "Obstetric Deliveries":ti,ab,kw,de OR "Obstetric Delivery":ti,ab,kw,de OR "Delivery":ti,ab,kw,de OR "Delivery mode":ti,ab,kw,de OR "vaginal delivery":ti,ab,kw,de
#16	"cesarean section"/exp
#17	"Cesarean Section":ti,ab,kw,de OR "Cesarean Sections":ti,ab,kw,de OR "Delivery, Abdominal":ti,ab,kw,de OR "Abdominal Deliveries":ti,ab,kw,de OR "Deliveries, Abdominal":ti,ab,kw,de OR "Caesarean Section":ti,ab,kw,de OR "Caesarean Sections":ti,ab,kw,de OR "Abdominal Delivery":ti,ab,kw,de OR "C-Section (OB)":ti,ab,kw,de OR "C Section (OB)":ti,ab,kw,de OR "C-Sections (OB)":ti,ab,kw,de OR "Postcesarean Section":ti,ab,kw,de OR "C-section":ti,ab,kw,de
#18	"allergy history":ti,ab,kw,de OR "family member allergy history":ti,ab,kw,de OR "single parent allergy history":ti,ab,kw,de OR "parent allergy history":ti,ab,kw,de
#19	"maternal age"/exp
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#21	"birth order"/exp
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	"Breastfeeding, Exclusive":ti,ab,kw,de OR "Exclusive Breastfeeding":ti,ab,kw,de OR "Wet Nursing":ti,ab,kw,de OR "exclusive breastfeeding ":ti,ab,kw,de OR "duration of breastfeeding":ti,ab,kw,de
#27	"prematurity"/exp
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#29 Combine	#14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28
#30 Combine	#6 AND #13 AND #29

	Combine	
Database	Search	Search terms/queries
Cochrane	#1	[mh "Child"] OR "Child":ti,ab,kw OR "Children":ti,ab,kw
Library	#2	[mh "Child, Preschool"]
	#3	"Child, Preschoo":ti,ab,kw OR "Preschool Child":ti,ab,kw OR "Children, Preschool":ti,ab,kw OR "Preschool Childrenl":ti,ab,kw
	#4	[mh "Adolescent"]
	#5	"Adolescent":ti,ab,kw OR "Adolescents":ti,ab,kw OR "Adolescence":ti,ab,kw OR "Teens":ti,ab,kw OR "Teen":ti,ab,kw OR "Teenagers":ti,ab,kw OR "Teenager":ti,ab,kw OR "Youth":ti,ab,kw OR "Youths":ti,ab,kw OR "Adolescents, Female":ti,ab,kw OR "Adolescent, Female":ti,ab,kw OR "Female Adolescent":ti,ab,kw OR "Female Adolescents":ti,ab,kw OR "Adolescents, Male":ti,ab,kw OR "Adolescent, Male":ti,ab,kw OR "Male Adolescent":ti,ab,kw OR "Male Adolescents":ti,ab,kw OR "Male Adolescent":ti,ab,kw OR "Male
	#6 Combine	#1 OR #2 OR #3 OR #4 OR #5
	#7	[mh "Asthma"]
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	#9	[mh "Rhinitis, Allergic"]
	#10	"Rhinitis, Allergic":ti,ab,kw OR "Allergic Rhinitides":ti,ab,kw OR "Rhinitides, Allergic":ti,ab,kw OR "Allergic Rhinitis":ti,ab,kw OR "allergic rhinoconjunctivitis":ti,ab,kw
	#11	[mh "Rhinitis, Allergic, Seasonal"]
	#12	"Rhinitis, Allergic, Seasonal":ti,ab,kw OR "Seasonal Allergic Rhinitis":ti,ab,kw OR "Allergic Rhinitides, Seasonal":ti,ab,kw OR "Allergic Rhinitis, Seasonal":ti,ab,kw OR "Rhinitides, Seasonal Allergic":ti,ab,kw OR "Rhinitis, Seasonal Allergic":ti,ab,kw OR "Seasonal Allergic Rhinitides":ti,ab,kw OR "Pollen Allergy":ti,ab,kw OR "Allergies, Pollen":ti,ab,kw OR "Allergy, Pollen":ti,ab,kw OR "Pollen Allergies":ti,ab,kw OR "Pollinosis":ti,ab,kw OR "Pollen Allergies":ti,ab,kw OR "Fever, Hay":ti,ab,kw OR "Hayfever":ti,ab,kw

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#21	[mh "Birth Order"]
#22	"Birth Order":ti,ab,kw OR "Birth Orders":ti,ab,kw OR "First Birth":ti,ab,kw OR "Birth, First":ti,ab,kw OR "Births, First":ti,ab,kw O "First Births":ti,ab,kw
#23	[mh "Siblings"]
#24	"Siblings":ti,ab,kw OR "Sibling":ti,ab,kw OR "Sisters":ti,ab,kw OR "Sister":ti,ab,kw OR "Brothers":ti,ab,kw OR "Brother":ti,ab,kw OR "number of sibling":ti,ab,kw
#25	[mh "Breast Feeding"]
#26	"Breast Feeding":ti,ab,kw OR "Breastfed":ti,ab,kw OR "Breastfeeding":ti,ab,kw OR "Breast Fed":ti,ab,kw OR "Milk Sharing":ti,ab,kw OR "Sharing, Milk":ti,ab,kw OR "Breast Feeding, Exclusive":ti,ab,kw OR "Exclusive Breast Feeding":ti,ab,kw OR "Breastfeeding, Exclusive":ti,ab,kw OR "Exclusive Breastfeeding":ti,ab,kw OR "Wet Nursing":ti,ab,kw OR "exclusive breastfeeding ":ti,ab,kw OR "duration of breastfeeding":ti,ab,kw
#27	[mh "Premature Birth"]
#28	"Premature Birth":ti,ab,kw OR "Birth, Premature":ti,ab,kw OR "Births, Premature":ti,ab,kw OR "Premature Births":ti,ab,kw OR "Preterm Birth":ti,ab,kw OR "Birth, Preterm":ti,ab,kw OR "Births, Preterm":ti,ab,kw OR "Preterm Births":ti,ab,kw
#29 Combine	#14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28
#30 Combine	#6 AND #13 AND #29

Database	Search	Search terms/queries
Web of Science	#1	TS=("Child" OR "Children" OR "Preschool Child" OR "Adolescent" OR "Teenager" OR "Teen")
	#2	TS=("Asthma" OR "Allergic Rhinitis" OR "Allergic Rhinitides" OR "allergic rhinoconjunctivitis" OR "Seasonal Allergic Rhinitis" OR "Seasonal Allergic Rhinitides" OR "Hay Fever")
	#3	TS=("Obstetric Delivery" OR "Obstetric Deliveries" OR "Delivery" OR "Cesarean Section" OR "C-section" OR "allergy history" OR "Maternal Age" OR "Maternal Ages" OR "Birth Order" OR "First Birth" OR "Siblings" OR "Sister" OR "Brother" OR "number of sibling" OR "Breast Feeding" OR "Premature Birth" OR "Preterm Birth")
	#4 Combine	#1 AND #2 AND #3

Google Scholar#1("Child" OR "Children" OR "Adolescent")#2("Asthma" OR "Allergic Rhinitis" OR "allergic rhinoconjunctivitis" OR "Hay Fever")#3("Cesarean Section" OR "Maternal Age" OR "Birth Order" OR "Siblings" OR "Breast Feeding" OR "Premature Birth")#4("Child" OR "Children" OR "Adolescent") AND ("Asthma" OR "Allergic Rhinitis" OR "allergic rhinoconjunctivitis" OR "Hay Fever") AND ("Combine ("Cesarean Section" OR "Maternal Age" OR "Birth Order" OR "Siblings"	Database	Search	Search terms/queries
#2 ("Astimut OR "Atterge Runnus" OR "anorgie Runnoconjunctivitis" OR "Hay Fever") #3 ("Cesarean Section" OR "Maternal Age" OR "Birth Order" OR "Siblings" OR "Breast Feeding" OR "Premature Birth") #4 ("Child" OR "Children" OR "Adolescent") AND ("Asthma" OR "Allergic Rhinitis" OR "allergic rhinoconjunctivitis" OR "Hay Fever") AND		#1	
 ^{#3} OR "Breast Feeding" OR "Premature Birth") ("Child" OR "Children" OR "Adolescent") AND ("Asthma" OR "Allergic #4 Rhinitis" OR "allergic rhinoconjunctivitis" OR "Hay Fever") AND 	Scholar	#2	
#4 Rhinitis" OR "allergic rhinoconjunctivitis" OR "Hay Fever") AND		#3	
OR "Breast Feeding" OR "Premature Birth")			Rhinitis" OR "allergic rhinoconjunctivitis" OR "Hay Fever") AND ("Cesarean Section" OR "Maternal Age" OR "Birth Order" OR "Siblings"

Supplementary Table 2. Risk of Bias Assessment.	

		Sele	ction ^a		Compa	Comparability ^b		xposu	re ^c	The New York Others See 1
Study (year)	1	2	3	4	5A	5B	6	7	8	. The Newcastle-Ottawa Scale
Nafstad 2000	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	7
Montgomery 2001	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	7
Xu 2001	Yes	No	Yes	Yes	No	No	Yes	Yes	Yes	6
McKeever 2002	Yes	No	Yes	Yes	No	No	Yes	Yes	Yes	6
Bager 2003	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	7
Negele 2004	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	7
Polster 2005	Yes	No	Yes	Yes	No	No	Yes	Yes	Yes	6
Salam 2006	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	7
Miyake 2007	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	7
Westergaard 2007	Yes	No	Yes	Yes	No	No	Yes	Yes	Yes	6
Ehlayel 2008	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	7
Mallen 2008	Yes	No	Yes	Yes	No	No	Yes	Yes	Yes	6
Pistiner 2008	Yes	Yes	Yes	Yes	No	No	Yes	Yes	No	6
Park 2010	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	7

Valdivia 2010	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	7
Jelding-Dannemand 2015	Yes	Yes	Yes	Yes	No	No	Yes	Yes	No	6
Li 2015	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	7
Bion 2016	Yes	No	Yes	Yes	No	No	Yes	Yes	Yes	6
Brandão 2016	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	7
Chu 2017	Yes	No	Yes	Yes	No	No	Yes	Yes	Yes	6
Bedolla-Barajas 2018	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	7
Krzych-Fałta 2018	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	7
Han 2019	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	7
Kim 2019	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	7
Gorris 2020	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	7
Lu 2020	Yes	No	Yes	Yes	No	No	Yes	Yes	Yes	6
Tong 2020	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	7
Hu 2021	Yes	No	Yes	Yes	No	No	Yes	Yes	Yes	6
Meza-Lopez 2021	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	7
Tong 2022	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	7
Wang 2022	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	7

A star rating system was used to indicate the quality of a study, with a maximum of nine stars. A study could be awarded a maximum of one star for each

numbered item within the selection and exposure categories

a: Selection (4 items): adequacy of case definition; representativeness of the cases; selection of controls; and definition of controls.

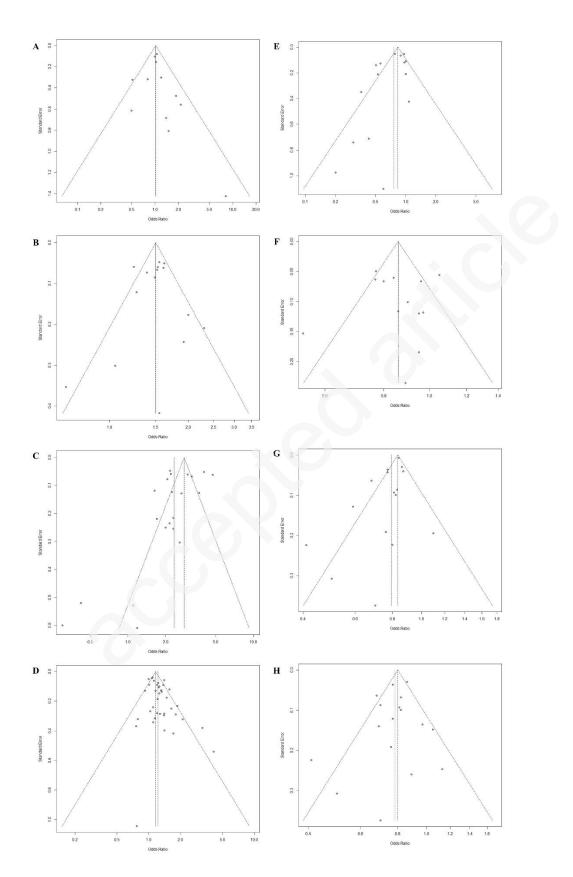
- b:. Comparability (1 item): comparability of cases and controls on the basis of the design or analysis.
- c:. Exposure (3 items): ascertainment of exposure; same method of ascertainment for cases and controls; and non-response rate (same rate for both groups).

Supplementary Figure 1.

A Study		TE	seTE	Odds	Ratio	OR	95	%-CI	Weight (fixed)	Weight (random)
g1 = A	llergic disease	0.70	0.6016			2.00	10.04	0.701	2.5%	5.8%
Rando	effect model om effects model geneity: not applicab	0,10	0.0010			2.08	[0.64; [0.64; [0.64;	6.76]	2.5%	5.8%
Valdivi	llergic rhinitis a 2010		0.3625 -		e	0.55	[0.27;	1.12]	6.9%	13.0%
Hu 202 Wang	21 2022	-0.13 -0.31	0.1447 0.2867		Ē	0.88	[0.66;	1.17]	43.2%	32.6% 17.7%
Rando	effect model om effects model geneity: $l^2 = 0\%$, τ^2 :		0.45	00			[0.64; [0.64;		61.1%	63.3%
Hu 202		0.21	0.1577	ana ata		1.24	[0.91;	1.68]	36.4%	30.9%
Rando	effect model om effects model geneity: not applicab	de		allo de como	00	1.24 1.24	[0.91; [0.91;	1.68] 1.68]	36.4%	30.9%
Fixed Rando Heterog Residu	effect model om effects model geneity: $I^2 = 49\%$, τ^2 al heterogeneity: I^2	² = 0.05 = 0%, p	24, p = 0.10 = 0.45 0.2	0.5	2	0.96 0.93	[0.80; [0.69;	1.16] 1.27]	100.0%	100.0%
Study		TE	seTE	Odds	Ratio	OR	95	%-CI	Weight (fixed)	Weight (random)
g1 = A Nafsta	llergic rhinitis d 2000	-1.20	0.4571			0.30	[0.12;	0.73]	2.1%	5.0%
Bager Lu 202	2003	0.12	0.1593 0.1316	+	# -	1.13	[0.83;	1.54]	17.5%	17.0% 19.0%
Tong 2	020	-0.13	0.1768	-	-		[0.62,	1.24]	14.2%	15.8%
Rando	effect model om effects model geneity: $l^2 = 64\%$, τ^2		0.1484 27, p = 0.03	Ŷ	* *	0,97	[0.91, [0.84; [0.71;	1.12]	79.5%	17.8% 74.6%
g1 = A Nafsta	sthma d 2000	-0.60	0.3071			0.50	[0.27;	0.911	4.7%	9.0%
Bager Fixed Rando	2003 effect model	-0.04	0.1674	A.	+	0.96	[0.69; [0.62; [0.39;	1.33]	15.8% 20.5%	16.4%
Fixed	geneity: $l^2 = 71\%$, τ^2 effect model			4		0.94	[0.82;	1.07]	100.0%	
Heterog Residu	geneity: $I^2 = 61\%$, τ^2 al heterogeneity: I^2	² = 0.05 = 66%,	18, p = 0.02 p = 0.01 0.2	0.5	2	5	. [0.71,	1.10]	-	100.076
Study		TE	seTE	Odds I	₹atio	OR	9	5%-CI	Weight (fixed)	Weight (random)
g1 = All Kim 201	lergic disease 19	0.40 0	8086		_	1.49	[0.31;	7.271	0.5%	0.8%
Fixed e Rando	ffect model m effects model eneity: not applicable			VV		1.49 1.49	[0.31; [0.31;	7.27] 7.27]	0.5%	0.8%
Bager 2	lergic rhinitis	-0.67 0	.3236	-		0.51	[0.27;	0.96]	2.8%	4.6%
Valdivia Li 2015	2010	0.18 0	.3006	-	-	1.20	[0.67;	2.17]	3.3%	5.2% 27.4%
Gorris 2	2020	0.76 0	0.5585	Ŧ		2.13	[0.71;	6.36]	1.0%	1.6%
Lu 2020 Hu 2021	1	0.02 0	0.0806	Ē	1	1.03	[0.76; [0.89;	1.39]	12.5% 45.8%	16.0% 34.8%
	ffect model m effects model eneity: $t^2 = 27\%$, τ^2	-0.70 0 = 0.010		-		0.50 1.01 1.00	[0.15; [0.91; [0.85;	1.66] 1.13] 1.16]	0. 8% 94.5%	1.3% 91.0%
g1 = As Bager 2	2003	-0.22 0	.3170	-		0.80	[0.43;		3.0%	4.7%
Mallen 2 Gorris 2	2020	0.62 0	.6841	1	5	1.86 1.39	[0.36;	5.31]	1.3%	2.2%
Hu 202 Fixed e	1 Iffect model	2.10 1					10 50.4	33.13]	0.1%	0.3%
	2			104	>	- 8.18 1.14 1.28	[0.50; 1 [0.71; [0.67;	1.84] 2.45]	5.0%	8.3%
Fixed e	ffect model	= 0.134	0, <i>p</i> = 0.23		À	1.14 1.28 1.02	[0.71; [0.67;	2.45]	100.0%	8.3%
Fixed e				0.1 1	10	i.14 1.28	[0.71; [0.67; [0.92;	2.45]	100.0%	++
Fixed e Randou Heteroge Residua Study	effect model m effects model eneity: $J^2 = 15\%$, τ^2 il heterogeneity: $J^2 =$			0.1 1 Odds		1.14 1.28 1.02 1.01	[0.71; [0.67; [0.92; [0.88;	2.45] 1.13] 1.17]	100.0% 	8.3%
Fixed e Randou Heteroge Residua Study g1 = A Polster	ffect model m effects model eneity: $I^2 = 15\%, \tau^2$ I heterogeneity: $I^2 =$ litergic disease r 2005	= 0.008 28%, p TE 0.22	3, p = 0.50 = 0.19.01 seTE 0.0592			1.14 1.28 1.02 1.01 100 0R	[0.71; [0.67; [0.92; [0.88; 95	2.45] 1.13] 1.17] %-CI	100.0% 	8.3% 100.0% Weight (random) 10.8%
Fixed e Randoi Heterogi Residua Study g1 = A Polster Kim 20 Fixed Rando	ffect model m effects model eneity: $I^2 = 15\%, \tau^2$ I heterogeneity: $I^2 =$ litergic disease r 2005	= 0.008 28%, p TE 0.22 -0.39	3, p = 0.50 = 0.19.01 seTE 0.0592 0.3537		Ratio	1.14 1.28 1.02 1.01 100 0R 1.24 0.68 1.22	[0.71; [0.67; [0.92; [0.88;	2.45] 1.13] 1.17] %-CI 1.39] 1.36] 1.37]	100.0% 	8.3% 100.0% Weight (random)
Fixed e Randou Heterogy Residua Study g1 = A Polster Kim 22 Fixed Rando Heterog g1 = A	Iffect model m effects model metry: /² = 15%, 3° I heterogeneity: /² = I lergic disease /2005 019 effect model m effects model genety. /² = 64%, 1°	= 0.008 28%, p TE 0.22 -0.39	<pre>i3, p = 0.30 p = 0.19.01 seTE 0.0592 0.3537 62, p = 0.09</pre>		Ratio	1.14 1.28 1.02 1.01 100 0R 1.24 0.68 1.22 1.02	[0.71; [0.67; [0.88; [0.88; 95 [1.10; [0.34; [1.09; [0.58;	2.45] 1.13] 1.17] %-Cl 1.39] 1.36] 1.37] 1.77]	100.0% 	8.3% 100.0% Weight (random) 10.8% 1.0%
Fixed e Randoo Heterogy Residua Study g1 = A Polstei Kim 20 Fixed Heterog g1 = A Nafsta Polstei	Iffect model m effects model metry: / ² = 15%, 2 ² I heterogeneity: / ² = 1 heterogeneity: / ² = 2005 m effects model om effects model genety: / ² = 04%, t ² Illergic rhinitis d 2000	= 0.008 28%, p TE 0.22 -0.39 2 = 0.11 0.83 0.33	3, p = 0.50 = 0.19.01 seTE 0.0592 0.3537 62, p = 0.09 0.2088 0.0734		Ratio	1.14 1.28 1.02 1.01 100 0R 1.24 0.68 0.22 1.02 1.02	[0.71; [0.67; [0.92; [0.88; 95 [1.10; [0.34; [1.09; [0.58; [1.53; [1.20;	2.45] 1.13] 1.17] %-Cl 1.39] 1.36] 1.37] 1.77] 3.46] 1.61]	100.0% Weight (fixed) 12.0% 0.3% 12.4% 	8.3% 100.0% Weight (random) 10.8% 1.0% 11.8% 2.5% 9.4%
Fixed e Randou Heteroge Residua Study g1 = A Polstei Kim 20 Fixed Rando Heteroge g1 = A Nafsta Polstei Li 2015	ffect model m effects model energy: $r^2 = 158, r^2$ I heterogeneity: $r^2 = r^2$ 2005 119 effect model om effects model genety: $r^2 = 649, r^2$ Illergic rhinitis d 2000 5 2020	= 0.008 28%, p TE 0.22 -0.39 2 = 0.11 0.83 0.83 0.44 0.05	3, p = 0.50 = 0.10.01 seTE 0.0592 0.3537 0.0592 0.2088 0.0734 0.0477 0.3014		Ratio	1.14 1.28 1.02 1.01 100 0R 1.24 0.68 1.22 1.02 1.02 1.39 1.55 1.05	[0.71; [0.67; [0.82; [0.88; 95 [1.10; [0.34; [1.09; [0.58; [1.53; [1.20] [1.41]	2.45] 1.13] 1.17] %-Cl 1.39] 1.36] 1.37] 1.37] 3.46] 1.61] 1.70]	100.0% Weight (fixed) 12.0% 0.3% 12.4% 1.0% 7.8% 18.5% 0.5%	8.3% 100.0% Weight (random) 10.8% 1.0% 1.1.8% 2.5% 9.4% 9.4% 1.3%
Fixed e Randou Heteroge Residua g1 = A Polstee Kim 22 Fixed Rando Heterog g1 = A Nafsta Polstee Li 2015 Gorris Lu 202 Tong 2	ffect model m effects model energy: $r^2 = 158, r^2$ I heterogeneity: $r^2 = r^2$ 2005 119 effect model om effects model genety: $r^2 = 649, r^2$ Illergic rhinitis d 2000 5 5 2020	= 0.008 28%, ρ 28%, ρ -0.22 -0.39 2 ² = 0.11 0.83 0.33 0.44 0.05 0.24 0.24	3, p = 0.50 = 0.19.01 seTE 0.0592 0.3537 0.0592 0.0734 0.0474		Ratio	1.14 1.28 1.02 1.01 100 0R 1.24 0.68 1.22 1.02 1.02 1.39 1.55 1.05 1.05	[0.71; [0.67; [0.92; [0.88; 95 [1.10; [0.34; [1.09; [0.58; [1.53; [1.20; [1.41; [0.58];	2.45] 1.13] 1.17] %-Cl 1.39] 1.36] 1.37] 1.77] 3.46] 1.61] 1.70] 1.90] 9.90	100.0% Weight (fixed) 12.0% 0.3% 12.4% 1.0% 7.8% 18.5% 0.5% 2.9% 9.5%	8.3% 100.0% Weight (random) 10.8% 1.0% 9.4% 9.4% 12.1% 5.6% 1.3% 5.6%
Fixed e Randol Heterog Residua Study g1 = A Polstei Kim 20 Fixed Rando Heterog g1 = A Nafsta Polstei Li 2011 Gorris Lu 202 Tong 2 Hu 202	ffect model m effects model energy: $r^2 = 15\%$, r^2 l heterogenety: r^2 = 2005 119 effect model effect model effect model effect model 2000 5 5 2020 0 0 0 0 2020 21	= 0.008 28%, p TE 0.22 -0.39 0.83 0.33 0.44 0.05 0.24 0.42 0.42 0.48	3, p = 0.50 = 0 19.01 seTE 0.0592 0.3537 62, p = 0.09 0.2088 0.0734 0.0477 0.3014 0.0477 0.3014 0.0477 0.3014 0.0506		Ratio	1.14 1.28 1.02 1.01 100 0R 1.24 0.68 1.22 1.02 1.23 1.25 1.05 1.05 1.05 1.05 1.62 1.62 1.62	[0.71; [0.67; [0.92; [0.88; 95 [1.10; [0.34] [1.00; [0.58; [0.58; [0.58; [0.58; [1.20] [1.20] [1.20] [1.41] [1.00; [1.34], [1.41]	2.45] 1.13] 1.17] %-Cl 1.39] 1.36] 1.37] 1.77] 3.46] 1.61] 1.70] 1.61] 1.73] 1.73]	100.0% Weight (fixed) 12.0% 0.3% 12.4% 1.0% 7.8% 18.5% 0.5% 18.5%	
Fixed e Randoi Heterog Residua Study g1 = A Polster Kim 22 Fixed Randd Heterog g1 = A Nafsta Polster Li 2019 Gorris Lu 202 Tong 2 Fixed Rando Rando	ffect model m effects model energy: $r^2 = 15\%$, r^2 l heterogenety: r^2 = 2005 119 effect model effect model effect model effect model 2000 5 5 2020 0 0 0 0 2020 21	= 0.008 28%, p TE 0.22 -0.39 2= 0.11 0.83 0.33 0.44 0.05 0.24 0.42 0.48 0.47	3, p = 0.50 = 0.19.01 seTE 0.0592 0.3537 62, p = 0.09 0.0734 0.0477 0.02088 0.0734 0.0471 0.02086 0.0654		Ratio	1.14 1.28 1.02 1.01 100 0R 1.24 0.68 1.22 1.02 1.23 1.25 1.05 1.05 1.05 1.05 1.62 1.62 1.62	[0.71; [0.67; [0.92; [0.88; 95 [1.10; [0.34; [1.09; [0.58; [1.53; [1.20; [1.41; [0.58];	2.45] 1.13] 1.17] %-Cl 1.39] 1.36] 1.37] 1.77] 3.46] 1.61] 1.70] 1.61] 1.73] 1.73]	100.0% Weight (fixed) 12.0% 0.3% 12.4% 1.0% 7.8% 18.5% 0.5% 2.9% 9.5%	8.3% 100.0% Weight (random) 10.8% 1.0% 9.4% 9.4% 12.1% 5.6% 1.3% 5.6%
Fixed e Randoi Heterogy Study g1 = A Polstei Kim 20 Fixed Rando Heterog g1 = A Nafsta Polstei Li 2011 Gorris Lu 202 Tong 2 Fixed Rando Heterog g1 = A Nafsta Rando Heterog g1 = A Nafsta Rando Heterog g1 = A Nafsta Rando Heterog g1 = A Rando Rando Heterog g1 = A Rando Rando Heterog g1 = A Rando	ffect model m effects model energy. <i>P</i> = 15%, 2 ² i heterogenety. <i>P</i> = i largic disease <i>t</i> 2005 effect model metfects model genety. <i>P</i> = 64%, <i>t</i> ² 149 2020 5 5 2020 30 2020 30 2020 30 2020 30 2020 30 2020 30 2020 30 30 2020 30 30 30 30 30 30 30 30 30 30 30 30 30	TE 0.222 -0.39 2 ² = 0.111 0.83 0.33 0.44 0.42 0.42 0.42 0.47 2 ² = 0.000 0.69	3. p = 0.50 = 0.10 01 se TE 0.0592 0.2088 0.0734 0.0506 0.0774 0.0506 0.0774 0.0506 0.0614 33. p = 0.13 0.1768		Ratio	1.14 1.28 1.02 1.01 100 0R 1.28 0.68 0.68 0.68 0.68 0.122 1.02 1.02 1.02 1.02 1.02 1.02 1.0	[0.71; [0.67; [0.92; [0.88; [0.88; [0.88; [0.34] [0.34] [1.00; [0.58; [1.20] [0.58; [1.20] [0.58; [1.00; [1.41] [1.41; [1.43; [1.44]; [1.41]	2.45] 1.13] 1.17] %-Cl 1.39] 1.36] 1.36] 1.37] 1.77] 3.46] 1.37] 1.70] 1.90] 1.61] 1.73] 1.73] 1.73] 1.62] 1.64]	100.0% Weight (fixed) 12.0% 0.3% 12.4% - - - - - - - - - - - - - - - - - - -	8.3% 100.0% Weight (random) 10.8% 1.0% 11.8% 5.6% 10.1% 11.8% 10.6% 63.3%
Fixed e Randoi Heterogy Residua Study g1 = A Poistei Kim 22 Fixed Rando Heteroy g1 = A Nafsta Li 2011 Li 202 Tong 2 Fixed Heteroy g1 = A Nafsta Lu 202 Tong 2 Fixed Heteroy g1 = A Nafsta Lu 202 Fixed Heteroy g1 = A Nafsta Lu 202 Fixed Heteroy g1 = A Nafsta Lu 202 Fixed Heteroy g1 = A Study Heteroy g1 = A State Heteroy g1 = A States State States States State States States States Sta	ffect model m effects model energy. /* a 15%, 2* i heterogenety. /* a literogenety. /* a literogenety. /* a literogenety. /* a effect model m effects model genety. /* a 64%, r* literogic nhinitis d 2000 2 2005 5 2020 0 2020 0 2021 m effects model m effects model m effects model m effects model m effects model m effects model m effects model a 2000 0 2 2005 5 2 2020 0 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2	= 0.008 28%, p 7E 0.22 -0.39 2 = 0.11 0.83 0.33 0.44 0.05 2 = 0.00 0.49 0.47 0.47 0.44 0.47 0.44 0.47 0.44 0.47 0.44 0.47 0.44 0.44	3, p = 0.50 = 0.10 01 se TE 0.0592 0.2088 0.0734 0.0507 0.00506 0.0614 33, p = 0.13 0.1768 0.0843 0.0788		Ratio	1.14 1.28 1.02 1.01 100 OR 1.24 0.68 0.68 0.68 0.68 0.68 0.68 1.22 1.02 1.02 1.02 1.03 1.24 1.02 1.0	[0.71; [0.92; [0.98; 95 95 [1.10; [0.38; [0.58; [1.00; [1.	2.45] 1.13] 1.17] %-Cl 1.39] 1.36] 1.37] 1.37] 1.37] 1.37] 1.37] 1.37] 1.36] 1.37] 1.37] 1.36] 1.37] 1.36] 1.37] 1.38] 1.48] 1.4	100.0% Weight (fixed) 12.0% 0.3% 12.4% - - - - - - - - - - - - - - - - - - -	8.3% Weight (random) 10.8% 1.0% 1.0% 5.6% 5.6% 5.6% 5.6% 5.6% 5.6% 5.6% 5.6
Fixed e Randoi Heterogy Residua g1 = A Polstei Kim 22 Fixed Rando Heterog g1 = A Nafsta Lu 202 Tong 2 Hu 200 Tong 2 Fixed Rando Rando Rando Heterog g1 = A Rafsta Rando Hu 20 Tong 2 Hu 20 Hu 20 Hu 20 Hu 20 Hu 20 Hu 20 Hu 20	ffect model m effects model energy. $r^2 = 15\%$, r^2 i heterogenety. $r^2 = 10\%$, r^2 lifergic disease r 2005 effect model m effects model genety. $r^2 = 64\%$, r^2 lifergic r hinitis d 2000 lifergic r hinitis d 2000 2020 effect model m effects mod	TE 28%, p 7E 0.22 0.39 2 = 0.11 0.83 0.33 0.44 0.42 0.44 0.44 0.44 0.44	3, p = 0.50 = 0.10.01 se TE 0.0592 0.3537 0.0734 0.0477 0.3014 0.0614 0.0505 0.0614 33, p = 0.13 0.1768 0.04173 0.2426 0.4173		Ratio	1.14 1.28 1.02 1.01 100 OR 124 0.68 1.22 1.02 1.02 1.01 1.01 0 OR 1.24 1.02 1.01 1.01 0 0 0 0 0 0 0 0 0 0 0 0 0	[0.71; [0.67; [0.92; [0.88; 95 95 95 95 95 95 95 11.00; [0.34; [1.00; [0.34; [1.00; [0.58; 11.20; [0.58; 11.20; [0.58; 11.20; [0.54]; [1.20; [1.41]; [1.41]; [1.42]; [1.41]; [1.42]; [2.45] 1.13] 1.17] %-Cl 1.39] 1.36] 1.37] 1.36] 1.37] 1.36] 1.37] 1.36] 1.37] 1.36] 1.37] 1.36] 1.37] 1.36] 1.37] 1.36] 1.37] 1.36] 1.37] 1.36] 1.37] 1.36] 1.37] 1.36] 1.37] 1.36] 1.37] 1.36] 1.37] 1.36] 1.37] 1.36] 1.37] 1.36] 1.37] 1.36] 1.37] 1.36] 1.37] 1.48] 1.4	100.0% Weight (fixed) 12.0% 0.3% 12.4% 7.8% 12.4% 0.5% 0.5% 0.5% 67.8% 	8.3% 100.0% Weight 10.8% 1.0% 2.5% 5.6% 10.1% 5.6% 10.1% 5.6% 10.1% 5.6% 10.5% 5.6% 10.5% 5.6% 10.5% 5.6% 10.5% 10
Fixed e Randod Residua Study g1 = A Polste Kim 22 Fixed Randod Randod Heteroy g1 = A Nafsia Randod Heteroy g1 = A Nafsia Randod Heteroy g1 = A Randod Heteroy g1 = A Randod Randod Heteroy g1 = A Randod Rando	ffect model m effects model energy. $r^2 = 15\%$, r^2 i heterogenety. $r^2 = 10\%$, r^2 lifergic disease r 2005 effect model m effects model genety. $r^2 = 64\%$, r^2 lifergic r hinitis d 2000 lifergic r hinitis d 2000 2020 effect model m effects mod	= 0.008 28%, p TE 0.22 -0.39 2 = 0.11 0.83 0.33 0.44 0.45 0.48 0.47 2 = 0.00 0.69 0.40 0.65 0.44 0.43	3, p = 0.50 = 0.10 01 se TE 0.0592 0.2088 0.0734 0.0505 0.0614 33, p = 0.13 0.1768 0.0542 0.0545 0.0564 0.0564 0.0564 0.0564 0.0564 0.0564 0.0564 0.0564 0.0565 0.0564 0.0564 0.0565 0.0564 0.0565 0.0564 0.0565 0.0564 0.0565 0.0564 0.0565 0.0565 0.0564 0.0565 0.0545 0.0555 0.0545 0.05555 0.05555 0.0555 0.0555 0.0555		Ratio	1.14 1.28 1.02 1.01 100 OR 124 0.68 1.22 1.02 1.01 100 OR 1.24 0.68 1.22 1.02 1.01 1.01 1.01 0	[0.71; [0.92; [0.98; 95 95 [1.10; [0.38; [0.58; [1.00; [1.	2.45] 1.13] 1.17] %-Cl 1.39] 1.36] 1.37] 1.36] 1.37] 1.36] 1.37] 1.36] 1.37] 1.73] 1.61] 1.73] 1.61] 1.73] 1.62] 1.64] 2.83] 1.161] 1.73] 1.62] 1.64] 2.83] 1.17]	100.0% Weight (fixed) 12.0% 0.3% 12.4% - - - - - - - - - - - - - - - - - - -	8.3% Weight (random) 10.8% 1.0% 1.0% 5.6% 5.6% 5.6% 5.6% 5.6% 5.6% 5.6% 5.6

E	Study	TE seTE	Odds Ratio	OR	95%-CI	Weight (fixed)	Weigh (random
	g1 = Allergic disease Krzych-Falta 2018	0.77 0.0480		2.17	[1.98; 2.38]	18.2%	6.49
	Krzych-Falta 2018	0.79 0.0590	10	2.20	[1.96; 2.47] [0.39; 3.10]	12.1%	6.49 1.99
	Kim 2019 Kim 2019	0.10 0.5288 0.17 0.6085		1.10 1.18	[0.36; 3.89]	0.2%	1.59
	Fixed effect model Random effects mode	1	0	2.17	[2.02; 2.33] [2.02; 2.33]	30.5%	16.2%
	Heterogeneity: $l^2 = 0\%$, τ^2 g1 = Allergic rhinitis						
	Nafstad 2000 Nafstad 2000	0.83 0.2547 0.69 0.2502		2.00	[1.40; 3.79] [1.22; 3.27] [1.77; 2.40]	0.7%	4.29
	Montgomery 2001 Bedolla-Barajas 2018	0.72 0.0777 0.95 0.3037		2.06 2.58	[1.42; 4.68]	7.0%	6.29
	Gorris 2020 Lu 2020	-1.20 0.5999		0.30	[0.09; 0.97] [1.76; 2.85]	0.1%	1.69
	Lu 2020	0.49 0 1194		1.63	[1.29, 2.06] [2.82, 3.68]	2.9%	5.89
	Tong 2020 Hu 2021	1.17 0.0682 1.39 0.0520		3.22 4.02	[2.82; 3.68] [3.63; 4.45]	9.0% 15.6%	6.39 6.49
	Tong 2022	1.55 0.0618		4.73	[4.19; 5.34]	11.0%	6.39
	Wang 2022 Wang 2022	0.98 0.1283 1.31 0.1271	1 1-	2.67 3.70	[2.08; 3.43] [2.88; 4.75]	2.5% 2.6%	5.79
	Fixed effect model Random effects mode Heterogeneity: 1 ² = 93%, 1	d.	*	3.25 2.58	[3.08; 3.43] [2.05; 3.25]	55.3%	61.9%
	Heterogeneity: I ² = 93%, 1 g1 = Asthma	r ² = 0.1329, p < 0.01					
	Nafstad 2000 Nafstad 2000	0.83 0.2162		2.30 1.70	[1.51; 3.51] [1.11; 2.61]	0.9%	4.6%
	Bedolla-Barajas 2018	0.77 0.2356		2.15	[1.35; 3.41]	0.8%	4.49
	Gorris 2020 Hu 2021	-0.87 0.5196 1.10 0.0606		0.42	[0.15; 1.16] [2.66; 3.37]	0.2%	1.99
	Fixed effect model Random effects mode		*	2.73	[2.45; 3.04] [1.28; 2.89]	14.1%	21.9%
	Heterogeneity: $l^2 = 81\%$,	$t^2 = 0.1567, \mu < 0.01$					
	Fixed effect model Random effects mode	1 2 = 0.1124 p < 0.01	*	2.80	[2.69; 2.92] [1.97; 2.76]	100.0%	100.0%
	Heterogeneity: / ² = 92%, - Residual heterogeneity: / ²	² = 90%, p < 0.010.1	0.5 1 2	10			
F	Study	TE SeTE	Odds Ratio	OR	95%-CI	Weight	Weigh (random
				UR			
	g1 = Allergic disease		e e e				
	g1 = Allergic disease Polster 2005 Salam 2006	0.21 0.0764	u u u u u u u u u u u u u u u u u u u	1.23 1.26	[1.06; 1.43]	4.9%	5.1
	g1 = Allergic disease Polster 2005 Salam 2006 Pistiner 2008	0.23 0.1009 0.74 0.3229	uur 1990 1990	1.23 1.26 2.10	[1.06; 1.43] [1.03; 1.54] [1.12; 3.95]	4.9% 2.8% 0.3%	5.1° 4.1° 0.8°
	g1 = Allergic disease Polster 2005 Salam 2006 Pistiner 2008 Chu 2017 Krzych-Falta 2018	0.23 0.1009 0.74 0.3229 0.49 0.2490 0.18 0.0887		1.23 1.26 2.10 1.64 1.20	[1.06; 1.43] [1.03; 1.54] [1.12; 3.95] [1.01; 2.67] [1.01; 1.43]	4.9% 2.8% 0.3% 0.5% 3.6%	5.1 4.1 0.8 1.2 4.6
	g1 = Allergic disease Polster 2005 Salam 2006 Pistiner 2008 Chu 2017 Krzych-Fata 2018 Kim 2019	0.23 0.1009 0.74 0.3229 0.49 0.2490		1.23 1.26 2.10 1.64 1.20 0.79	[1.06; 1.43] [1.03; 1.54] [1.12; 3.95] [1.01; 2.67] [1.01; 1.43] [0.42; 1.48]	4.9% 2.8% 0.3% 0.5% 3.6% 0.3%	5.1° 4.1° 0.8° 1.2° 4.6°
	g1 = Allergic disease Polster 2005 Salam 2006 Pistiner 2008 Chu 2017 Krzych-Falta 2018	0.23 0.1009 0.74 0.3229 0.49 0.2490 0.18 0.0887 -0.24 0.3213		1.23 1.26 2.10 1.64 1.20 0.79 1.24	[1.06; 1.43] [1.03; 1.54] [1.12; 3.95] [1.01; 2.67] [1.01; 1.43]	4.9% 2.8% 0.3% 0.5% 3.6% 0.3% 12.4%	5.19 4.19 0.89 1.29 4.69 0.89
	g1 = Allergic disease Polster 2005 Salam 2006 Pistiner 2008 Chu 2017 Krzych-Falta 2018 Kim 2019 Fixed effect model Random effects model Refergementy: \vec{r} = 18% r, r g1 = Allergic thintits	$\begin{array}{c} 0.23 & 0.1009 \\ 0.74 & 0.3229 \\ 0.49 & 0.2490 \\ 0.18 & 0.0887 \\ -0.24 & 0.3213 \end{array}$	una fai fai fai fai fai fai fai fai fai fa	1.23 1.26 2.10 1.64 1.20 0.79 1.24 1.25	[1.06; 1.43] [1.03; 1.54] [1.12; 3.95] [1.01; 2.67] [1.01; 1.43] [0.42; 1.48] [1.13; 1.37] [1.12; 1.40]	4.9% 2.8% 0.3% 0.5% 3.6% 0.3% 12.4%	5.1' 4.1' 0.8' 1.2' 4.6' 0.8'
	91 - Allergic disease Polstir 2005 Salam 2006 Pistinar 2008 Chu 2017 Krzych-Fata 2018 Kim 2019 Fixed effect model Random effects model Random effects model Random effects model Nafstad 2000 Nafstad 2000	0.23 0.1009 0.74 0.3229 0.49 0.2490 0.18 0.0887 -0.24 0.3213 $\frac{1}{2}^2 = 0.0036, \rho = 0.30$ 0.18 0.2803 0.19 0.1858		1.23 1.26 2.10 1.64 1.20 0.79 1.24 1.25	[1.06; 1.43] [1.03; 1.54] [1.12; 3.95] [1.01; 2.67] [1.01; 1.43] [0.42; 1.48] [1.13; 1.37] [1.12; 1.40] [0.69; 2.08] [0.84; 1.74]	4.9% 2.8% 0.3% 0.3% 3.6% 0.3% 12.4%	5.1 4.1 0.8 1.2 4.6 0.8 16.7 1.0 2.0
	g1 - Allergic disease Polstic 2005 Salam 2006 Pistiner 2008 Chu 2017 Krzych-Fata 2018 Kim 2019 Fixed effect model remogenety: ℓ^2 = 16%, t g1 = Allergic rhinitis Nafstad 2000 Montgomery 2001 Xu 2001	0.23 0.1009 0.74 0.3229 0.49 0.2490 0.18 0.0887 -0.24 0.3213 1 2 = 0.0036, p = 0.30 0.18 0.2803 0.19 0.1858 0.25 0.2860		1.23 1.26 2.10 1.64 1.20 0.79 1.24 1.25 1.20 1.21 1.28	[1.06; 1.43] [1.03; 1.54] [1.12; 3.95] [1.01; 2.67] [1.01; 1.43] [0.42; 1.48] [1.13; 1.37] [1.12; 1.40] [0.69; 2.08] [0.84; 1.74] [0.73; 2.24]	4.9% 2.8% 0.3% 0.3% 3.6% 0.3% 12.4% 	5.11 4.19 0.88 1.22 4.69 16.79 1.09 2.00
	g1 - Allergic disease Polstic 2005 Salam 2006 Pistiner 2008 Chu 2017 Krzych-Fata 2018 Kim 2019 Fixed effect model restrogenety. <i>P</i> = 18%, y g1 = Allergic thintils Nafstad 2000 Montgomery 2001 Xu 2001 McKsever 2002 Bager 2003	$\begin{array}{c} 0.23 \ 0.1009 \\ 0.74 \ 0.3229 \\ 0.49 \ 0.2490 \\ 0.18 \ 0.0887 \\ -0.24 \ 0.3213 \\ \end{array}$		1.23 1.26 2.10 1.64 1.20 0.79 1.24 1.25 1.20 1.21 1.28 1.01 1.16	[1.06; 1.43] [1.03; 1.54] [1.12; 3.95] [1.01; 2.67] [1.01; 1.43] [0.42; 1.48] [1.13; 1.37] [1.12; 1.40] [0.69; 2.08] [0.84; 1.74] [0.84; 1.74] [0.85; 1.21] [0.90; 1.49]	4.9% 2.8% 0.3% 0.5% 3.6% 0.3% 12.4% 0.8% 0.4% 3.5% 1.7%	5.11 4.14 0.8 1.2 4.6 0.8 16.7 1 1.0 2.0 1.0 4.5 5 3.2
	91 - Allergic disease Poktor 2005 Salam 2006 Pistiner 2008 Chu 2017 Krzych-Fata 2018 Kim 2019 Fixed effect model Random effects model R	$\begin{array}{c} 0.23 \ 0.1009 \\ 0.74 \ 0.3229 \\ 0.49 \ 0.2490 \\ 0.18 \ 0.0887 \\ -0.24 \ 0.3213 \\ \end{array}$		1.23 1.26 2.10 1.64 1.20 0.79 1.24 1.25 1.20 1.21 1.28 1.01 1.16 1.40	[1.06, 1.43] [1.03, 1.54] [1.01, 2.67] [1.01, 2.67] [1.01, 1.43] [0.42, 1.48] [1.13, 1.37] [1.12, 1.40] [0.69, 2.08] [0.84, 1.74] [0.84, 1.24] [0.85, 1.21] [0.90, 1.49] [0.80, 2.44]	4.9% 2.8% 0.3% 0.5% 3.6% 0.3% 12.4% 0.8% 0.4% 3.5% 1.7% 0.4%	5.11 4.12 4.6 0.8 16.7 16.7 1.0 2.0 1.0 4.5 3.2 2 1.0
	91 - Allergic disease Poktor 2005 Salam 2006 Pistiner 2008 Chu 2017 Krzych-Fata 2018 Kim 2019 Fixed effect model Random effects model R	$\begin{array}{c} 0.23 & 0.1009 \\ 0.74 & 0.3229 \\ 0.49 & 0.2490 \\ 0.18 & 0.0687 \\ -0.24 & 0.3213 \\ \end{array} \\ \begin{array}{c} 1 \\ p^2 = 0.0038, p = 0.30 \\ \hline 0.18 & 0.2803 \\ 0.19 & 0.1858 \\ 0.25 & 0.2860 \\ 0.01 & 0.0901 \\ 0.15 & 0.1286 \\ 0.34 & 0.2845 \\ 0.34 & 0.0912 \\ 0.45 & 0.1207 \end{array}$		1.23 1.26 2.10 1.64 1.20 0.79 1.24 1.25 1.20 1.21 1.28 1.01 1.16 1.40 1.37 1.57	[1.06; 1.43] [1.03; 1.54] [1.12; 3.95] [1.01; 2.67] [1.01; 2.67] [1.01; 1.43] [0.42; 1.48] [0.42; 1.48] [0.42; 1.40] [0.84; 1.74] [0.85; 2.28] [0.84; 1.74] [0.85; 1.21] [0.90; 1.49] [0.80; 2.44] [1.15; 1.64] [1.24; 1.99]	4.9% 2.8% 0.3% 0.5% 3.6% 12.4% 0.8% 0.4% 3.5% 1.7% 0.4% 3.4% 2.0%	5.11 4.11 0.8 1.2 4.6 0.8 16.7 10 2.0 1.0 2.0 1.0 2.0 1.0 5 3.2 1.0 4.5 3.2 5 3.5 5
	g1 - Allergic disease Polstic 2005 Salam 2006 Pistiner 2008 Chu 2017 Krzych-Fata 2018 Kim 2019 Fixed effect model remogenety. <i>P</i> = 18%, t g1 = Allergic thintils Nafstad 2000 Montgomery 2001 Xu 2001 McKeever 2002 Bager 2003 Negele 2004 Polster 2005	0.23 0.1009 0.74 0.3229 0.49 0.2490 0.18 0.0887 -0.24 0.3213 1 2 = 0.0036, p = 0.30 0.18 0.2803 0.19 0.1858 0.25 0.2860 0.01 0.0901 0.15 0.1286 0.34 0.2845 0.34 0.0941		1.23 1.26 2.10 1.64 1.20 0.79 1.24 1.25 1.20 1.21 1.28 1.01 1.16 1.40 1.37	[1.06; 1.43] [1.03; 1.54] [1.12; 3.95] [1.01; 2.67] [1.01; 2.67] [1.042; 1.43] [0.42; 1.48] [0.42; 1.48] [0.42; 1.40] [0.69; 2.08] [0.84; 1.74] [0.73; 2.24] [0.85; 1.21] [0.90; 1.49] [0.85; 2.24] [1.15; 1.64]	4.9% 2.8% 0.3% 0.5% 3.6% 12.4% 0.8% 0.4% 3.5% 1.7% 0.4% 3.4% 2.0%	5.11 4.12 4.6 0.8 1.2 4.6 0.8 16.7 1.0 2.0 1.0 2.0 1.0 4.5 3.2 2 1.0 4.5 3.5 0.1 1
	g1 - Allergic disease Polstic 2005 Salam 2006 Pistiner 2008 Chu 2017 Krzych-Fala 2018 Krzych-Fala 2018 Fiside difect model Random effects model Random effects model Nafstad 2000 Morigomery 2001 Xu 2001 McKeever 2002 Bager 2003 Negels 2005 Salam 2006 Pistiner 2008 Pistre 2008 Pistre 2008 Pistre 2008 Pistre 2008 Pistre 2008	$\begin{array}{c} 0.23 & 0.1009 \\ 0.74 & 0.3229 \\ 0.49 & 0.2490 \\ 0.18 & 0.0687 \\ -0.24 & 0.3213 \\ 1 \\ r \\ = 0.0036, p = 0.30 \\ 0.19 & 0.1858 \\ 0.25 & 0.2860 \\ 0.01 & 0.0912 \\ 0.31 & 0.0912 \\ 0.45 & 0.1207 \\ -0.26 & 1.0441 \\ -0.28 & 0.2854 \\ 0.13 & 0.3154 \\ \end{array}$		1.23 1.26 2.10 1.64 1.20 0.79 1.24 1.25 1.20 1.21 1.28 1.01 1.16 1.40 1.37 1.57 0.77 1.80 1.14	[1.06; 1.43] [1.03; 1.54] [1.12; 3.95] [1.01; 2.67] [1.01; 1.43] [0.42; 1.48] [1.13; 1.37] [1.12; 1.40] [0.69; 2.08] [0.84; 1.74] [0.90; 2.44] [0.85; 1.21] [0.90; 2.44] [1.13; 1.64] [1.24; 1.99] [0.10; 5.96] [1.02; 3.17] [0.64; 2.12]	4.9% 2.8% 0.5% 3.6% 0.3% 12.4% 0.4% 3.5% 1.7% 0.4% 3.5% 1.7% 0.4% 0.0% 0.0% 0.3%	5.14 4.11 0.8 1.22 4.6 0.8 16.7 10 1.0 1.0 1.0 4.5 5 3.2 1.0 4.5 5 3.5 5 0.1 1 1.0 9 4.5 3.5 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0
	g1 - Allergic disease Poktri 2005 Salam 2006 Pistiner 2008 Chu 2017 Krzych-Falta 2018 Krzych-Falta 2018 Random effects model Random effects Random effect	$\begin{array}{c} 0.23 & 0.1009 \\ 0.74 & 0.3229 \\ 0.49 & 0.2490 \\ 0.18 & 0.0887 \\ -0.24 & 0.3213 \\ \end{array}\\ \begin{array}{c} \\ \end{array}\\ \begin{array}{c} \\ \end{array} \\ \begin{array}{c} \\ 0.18 & 0.0887 \\ 0.24 & 0.3213 \\ \end{array}\\ \begin{array}{c} \\ 0.18 & 0.2803 \\ 0.19 & 0.1858 \\ 0.25 & 0.2680 \\ 0.15 & 0.1858 \\ 0.25 & 0.2680 \\ 0.15 & 0.1858 \\ 0.11 & 0.2805 \\ 0.11 & 0.2805 \\ 0.11 & 0.2805 \\ 0.11 & 0.2805 \\ 0.11 & 0.2805 \\ 0.11 & 0.2805 \\ 0.11 & 0.2805 \\ 0.11 & 0.2805 \\ 0.11 & 0.2805 \\ 0.11 & 0.2805 \\ 0.11 & 0.2805 \\ 0.11 & 0.2805 \\ 0.11 & 0.2805 \\ 0.11 & 0.2805 \\ 0.11 & 0.2320 \\ \end{array}$		1.23 1.26 2.10 1.64 1.20 0.79 1.24 1.25 1.20 1.21 1.28 1.01 1.16 1.40 1.57 0.77 1.80 1.14 1.107 1.84	[1.06; 1.43] [1.03; 1.54] [1.03; 1.54] [1.01; 1.43] [0.42; 1.48] [1.13; 1.37] [1.12; 1.40] [0.69; 2.08] [0.84; 1.74] [0.90; 2.44] [0.68; 1.21] [0.90; 2.44] [0.90; 2.44] [1.12; 1.40] [0.80; 2.44] [1.02; 1.64] [1.24; 1.99] [1.12; 1.64] [1.24; 1.99] [1.12; 3.17] [0.64; 2.12] [0.96; 1.17] [1.18; 2.93]	4.9% 2.8% 0.5% 3.6% 0.3% 12.4% 0.4% 0.8% 0.4% 3.5% 1.7% 0.4% 3.4% 0.0% 0.3% 14.6% 0.3%	5.11 4.12 4.66 0.8 16.7 ⁴ 1.0 2.0 1.0 4.55 3.2 3.5 3.5 3.5 0.1 1.0 4.5 5.5 3.5 3.5 1.4 ⁴
	g1 - Allergic disease Potstir 2005 Salam 2006 Pistiner 2008 Chu 2017 Krzych-Fata 2018 Kim 2019 Fixed effect model Random effects model Random effects model Natistal 2000 Morgomery 2001 Morgomery 2001 McKseever 2002 Bager 2003 Negele 2004 Potster 2005 Salam 2006 Malen 2008 Patstor Patstor Versitier 2005 Patstor Patstor Potstor Patstor Pat	$\begin{array}{c} 0.23 & 0.1009 \\ 0.74 & 0.3229 \\ 0.49 & 0.2490 \\ 0.18 & 0.0687 \\ 0.24 & 0.0213 \\ \end{array} \\ \begin{array}{c} \\ \\ \\ \\ \\ \\ \end{array} \\ \begin{array}{c} \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\$		1.23 1.26 2.10 1.64 1.20 0.79 1.24 1.25 1.20 1.21 1.28 1.01 1.40 1.37 1.57 0.77 1.80 1.14 1.07 1.86 1.26	[1.06; 1.43] [1.03; 1.54] [1.03; 1.54] [1.01; 2.67] [1.01; 1.43] [0.42; 1.48] [1.13; 1.37] [1.12; 1.40] [0.69; 2.08] [0.84; 1.74] [0.85; 1.21] [0.90; 1.49] [0.80; 2.44] [1.25; 1.64] [1.02; 3.17] [0.61; 2.12] [0.09; 1.41] [1.02; 3.17] [1.18; 2.93] [0.94; 1.68]	4.9% 2.8% 0.5% 3.6% 0.3% 12.4% 0.8% 0.4% 3.5% 1.7% 0.4% 3.4% 2.0% 0.4% 3.4% 2.0% 0.4% 1.4% 0.5% 1.3%	5.11 4.12 4.6 0.8 16.7 10 2.0 1.0 1.0 4.5 3.2 1.0 4.5 3.5 5 0.1 1 1.0 4.5 3.5 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0
	g1 - Allergic disease Polstic 2005 Salam 2006 Pistiner 2008 Chu 2017 Krzych-Fata 2018 Kim 2019 Fixed effect model Random effects model Random effects model Valergic rhinitis Nafstad 2000 Mongomery 2001 Xu 2001 Negale 2003 Pelster 2005 Palstar 2006 Malen 2006 Palstar 2005 Palstar 2006 Malen 2006 Palstar 2005 Palstar 2005 Palstar 2005 Palstar 2006 Malen 2008 Palstar 2008 Palstar 2008 Palstar 2008 Palstar 2008 Palstar 2008 Palstar 2019 Gortis 2020	$\begin{array}{c} 0.23 & 0.1009 \\ 0.74 & 0.3229 \\ 0.49 & 0.2490 \\ 0.18 & 0.0687 \\ 0.24 & 0.0213 \\ \end{array} \\ \begin{array}{c} \\ \\ \\ \end{array} \\ \begin{array}{c} \\ \\ \end{array} \\ \begin{array}{c} \\ \end{array} \\ \begin{array}{c} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \\ \end{array} \\ \begin{array}{c} \\ \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \\ \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \\ \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \\ \end{array} \\ $		1.23 1.26 2.10 1.64 1.20 0.79 1.24 1.25 1.21 1.26 1.21 1.26 1.01 1.16 1.37 1.57 0.77 1.80 1.14 1.07 1.80 1.16 1.26 1.07 1.26 1.10 1.27 1.20 1.21 1.20 1.21 1.20 1.21 1.25	[1.06; 1.43] [1.03; 1.54] [1.01; 2.67] [1.01; 2.67] [1.01; 2.67] [1.01; 1.43] [1.12; 1.40] [0.84; 1.74] [0.85; 1.21] [0.86; 1.21] [0.80; 2.44] [1.15; 1.64] [1.15; 1.64] [1.15; 1.64] [1.15; 1.64] [1.15; 1.64] [1.00; 5.16] [1.00; 5.16] [1.00	4.9% 2.8% 0.5% 3.6% 0.3% 12.4% 0.4% 0.4% 3.5% 1.7% 0.4% 0.0% 0.0% 0.3% 1.4% 0.3% 1.3% 0.2% 1.3%	5.11 0.8% 1.22 1.00 2.00 1.00 1.00 1.00 1.00 1.00
	91 - Allergic disease Pokter 2005 Salam 2006 Pistiner 2008 Chu 2017 Krzych-Fata 2018 Krzych-Fata 2018 Kam 2019 Fixed effect model Random effects model Random effects model Nafsdad 2000 G1 - Allergic enhibits Nafsdad 2000 Montgomery 2001 Xu 2001 McKsever 2002 Bager 2003 Mallen 2008 Mallen 2008	$\begin{array}{c} 0.23 & 0.1009 \\ 0.74 & 0.3229 \\ 0.49 & 0.2490 \\ 0.18 & 0.0687 \\ -0.24 & 0.3213 \\ \end{array} \\ \begin{array}{c} \bullet \\ \bullet $		1.23 1.26 2.10 0.79 1.24 1.25 1.20 1.21 1.28 1.21 1.28 1.21 1.28 1.21 1.28 1.21 1.26 1.40 1.40 1.40 1.41 1.66 1.40 1.40 1.42 1.00 2.10 1.00 1.20 1.20 1.20 1.20 1.2	[1.06, 1.43] [1.03, 1.54] [1.03, 1.54] [1.01, 2.67] [1.01, 2.67] [1.01, 2.67] [1.02, 2.143] [1.12; 1.40] [0.69, 2.08] [0.84, 1.74] [0.69, 2.08] [0.85, 1.21] [0.98, 2.44] [1.12, 1.64] [1.24, 1.99] [0.10, 5.96] [1.24, 1.99] [0.10, 5.96] [1.24, 1.99] [0.10, 5.96] [1.24, 1.99] [0.63, 5.42] [1.24, 1.99] [0.63, 5.42] [1.24, 1.99] [0.63, 5.42] [1.24, 1.99] [0.63, 5.42] [1.24, 1.99] [0.63, 5.42] [1.24, 1.99] [1.24, 1.99] [1.2	4 9% 2 8% 0 3% 0 5% 3 6% 0 3% 12.4% 12.4% 0 3% 0 4% 3 5% 0 4% 3 5% 0 4% 0 3% 0 3% 0 3% 0 3% 0 3% 0 3%	5.11 4.11 0.8% 1.22 4.6% 0.8% 1.6.7% 1.0% 4.5% 3.2% 1.0% 4.5% 3.5% 1.0% 4.5% 3.5% 1.0% 4.5% 3.5% 1.0% 4.5% 3.5% 1.0% 8.6% 5% 1.0% 8.6% 3.2% 1.0% 8.6% 1.0% 8.6% 1.0% 8.6% 1.0% 8.6% 1.0% 8.6% 1.0% 8.6% 1.0% 8.6% 1.0% 1.0% 1.0% 1.0% 1.0% 1.0% 1.0% 1.0
	91 - Allergic disease Pokter 2005 Salam 2006 Pistiner 2008 Chu 2017 Krzych-Fata 2018 Krzych-Fata 2018 Krandom effects model Random effects model Random effects model Random effects model Nafsdad 2000 G = Allergic enthilis Nafsdad 2000 G = Allergic enthilis Nafsdad 2000 Bager 2003 NcKeever 2002 Bager 2003 NcKeever 2002 Bager 2003 Polster 2005 Balam 2006 Mallen 2008 Paistiner 2008	$\begin{array}{c} 0.23 & 0.1009 \\ 0.74 & 0.3229 \\ 0.49 & 0.2490 \\ 0.18 & 0.0887 \\ -0.24 & 0.3213 \\ \end{array} \\ \begin{array}{c} \bullet & 0.0038, \ \rho = 0.30 \\ 0.18 & 0.2803 \\ 0.19 & 0.1859 \\ 0.25 & 0.2806 \\ 0.19 & 0.1859 \\ 0.25 & 0.2806 \\ 0.11 & 0.0261 \\ 0.31 & 0.2845 \\ 0.31 & 0.2845 \\ 0.31 & 0.2845 \\ 0.31 & 0.2845 \\ 0.31 & 0.2845 \\ 0.31 & 0.2845 \\ 0.31 & 0.3154 \\ 0.07 & 0.0444 \\ 0.00 & 0.0567 \\ 0.044 & 0.0464 \\ 0.07 & 0.0444 \\ 0.0$		1.23 1.26 2.10 0.79 1.24 1.25 1.20 1.21 1.28 1.24 1.21 1.28 1.24 1.41 1.40 1.37 1.57 1.80 1.41 1.40 1.41 1.40 1.40 1.41 1.40 1.40	[1.06, 1.43] [1.03, 1.54] [1.01, 2.67] [1.01, 2.67] [1.01, 2.67] [1.01, 2.67] [1.02, 1.43] [0.42, 1.48] [0.42, 1.48] [0.42, 1.48] [0.69, 2.08] [0.69, 2.08] [0.69, 2.08] [0.69, 2.08] [0.69, 2.08] [0.69, 2.08] [0.69, 2.08] [0.69, 2.08] [1.12, 1.40] [0.69, 2.08] [1.12, 1.40] [0.69, 2.08] [1.12, 1.40] [1.12, 1.13] [1.12, 1.13] [1.12, 1.13] [1.12, 1.13] [1.12, 1.13] [1.12, 1.13] [1.12, 1.13] [1.12, 1.13]	4 9% 2 8% 3 6% 0.5% 3 6% 0.3% 0.3% 12.4% 0.3% 0.3% 0.3% 0.3% 0.4% 0.4% 0.3% 0.3% 0.3% 0.3% 0.3% 0.3% 0.3% 0.3	5.11 4.11 10.8 0.8 16.7 10 1.0 0.8 10 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0
	g1 - Allergic disease Potstir 2005 Salam 2006 Pistiner 2008 Chu 2017 Krzych-Fata 2018 Kim 2019 Fixed effect model Random effects model Random effects model Narsdad 2000 Morigomery 2001 Xu 2001 McKsever 2002 Bager 2003 Poister 2005 Paistar 2006 Malano 2008 Paistar 2005 Paistar 2005 Bagar 2016 Li 2015 Brandao 2016 Han 2019 Gorins 2020 Han 2019 Gorins 2021 Hu 2021 MezaL opez 2021 MezaL opez 2021 Yang 2022 Pixed effect model	$\begin{array}{c} 0.23 & 0.1009 \\ 0.74 & 0.3229 \\ 0.49 & 0.2490 \\ 0.18 & 0.0887 \\ -0.24 & 0.3213 \\ \end{array} \\ \begin{array}{c} \bullet & 0.0036, \ p = 0.30 \\ 0.18 & 0.2803 \\ 0.19 & 0.1859 \\ 0.25 & 0.2860 \\ 0.19 & 0.1859 \\ 0.25 & 0.2860 \\ 0.01 & 0.0901 \\ 0.11 & 0.0901 \\ 0.11 & 0.0901 \\ 0.11 & 0.0901 \\ 0.11 & 0.0901 \\ 0.11 & 0.0901 \\ 0.11 & 0.0901 \\ 0.11 & 0.0901 \\ 0.11 & 0.0155 \\ 0.21 & 0.0245 \\ 0.31 & 0.03154 \\ 0.13 & 0.3154 \\ 0.13 & 0.3154 \\ 0.13 & 0.3154 \\ 0.13 & 0.3154 \\ 0.13 & 0.3154 \\ 0.13 & 0.3154 \\ 0.13 & 0.3154 \\ 0.13 & 0.3154 \\ 0.13 & 0.3154 \\ 0.13 & 0.3154 \\ 0.13 & 0.3154 \\ 0.13 & 0.3154 \\ 0.13 & 0.3154 \\ 0.34 & 0.3969 \\ -0.08 & 0.1296 \\ 0.00 & 0.0567 \\ 0.33 & 0.02685 \\ 0.27 & 0.1258 \end{array}$		1.23 1.26 2.10 1.64 1.20 1.24 1.25 1.20 1.21 1.28 1.01 1.26 1.20 1.27 1.28 1.01 1.26 1.40 1.37 1.80 1.37 1.80 1.26 1.20 0.79 1.24 1.25	[1.06, 1.43] [1.03, 1.54] [1.01, 2.67] [1.01, 2.67] [1.01, 2.67] [1.02, 1.43] [0.69, 2.06] [0.84, 1.74] [0.69, 2.06] [0.84, 1.74] [0.65, 1.21] [0.67, 2.24] [1.02, 1.74] [1.02, 3.17] [1.02, 3.17] [1.02, 3.17] [1.02, 3.17] [1.02, 3.17] [1.02, 1.57] [1.02, 1.57] [1.02, 1.57] [1.02, 1.57] [1.02, 1.57]	4 9% 2 8% 0 3% 0 5% 12.4% 0 4% 3 5% 0 4% 3 5% 0 4% 3 5% 0 4% 3 5% 0 4% 3 5% 1.7% 1.2% 0 4% 3 5% 0 4% 0 4% 0 4% 0 4% 0 4% 0 4% 0 4% 0 4	5.11 4.11 10.8 0.8 16.7 10 1.0 0.8 10 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0
	g1 - Allergic disease Polstic 2005 Salam 2006 Pistiner 2008 Chu 2017 Krzych-Fata 2018 Kim 2019 Fixed effect model Random effects model Random effects model Valergic rhinitis Nafstad 2000 Morigomery 2001 Xu 2001 McKeever 2002 Salam 2006 Pistiner 2008 Paistad 2006 Maller 2008 Paistad 2001 Liz 2015 Brandao 2016 Diado 2015 Brandao 2016 Goris 2020 Hu 2021 Meza-Lopez 2021 Yang 2022	$\begin{array}{c} 0.23 & 0.1009 \\ 0.74 & 0.3229 \\ 0.49 & 0.2490 \\ 0.18 & 0.0687 \\ -0.24 & 0.3213 \\ \end{array} \\ \begin{array}{c} ^{2} = 0.0036, \ \rho = 0.30 \\ 0.18 & 0.2803 \\ 0.19 & 0.1858 \\ 0.25 & 0.2860 \\ 0.01 & 0.0912 \\ 0.45 & 0.1206 \\ 0.31 & 0.0912 \\ 0.45 & 0.1207 \\ -0.26 & 1.0441 \\ 0.79 & 0.2481 \\ 0.07 & 0.0444 \\ 0.07 & 0.044 \\ 0.07 & 0.0444 \\ 0.07 & 0.0444 \\ 0.07 & 0.0444 \\ 0.07 & 0.0444 \\ 0$		1.23 1.26 2.10 1.64 1.20 1.24 1.25 1.20 1.21 1.28 1.01 1.26 1.20 1.27 1.28 1.01 1.26 1.40 1.37 1.80 1.37 1.80 1.26 1.20 0.79 1.24 1.25	[1.06, 1.43] [1.03, 1.54] [1.01, 2.67] [1.01, 2.67] [1.01, 2.67] [1.01, 2.67] [1.02, 1.43] [0.42, 1.48] [0.42, 1.48] [0.42, 1.48] [0.69, 2.08] [0.69, 2.08] [0.69, 2.08] [0.69, 2.08] [0.69, 2.08] [0.69, 2.08] [0.69, 2.08] [0.69, 2.08] [1.12, 1.40] [0.69, 2.08] [1.12, 1.40] [0.69, 2.08] [1.12, 1.40] [1.12, 1.13] [1.12, 1.13] [1.12, 1.13] [1.12, 1.13] [1.12, 1.13] [1.12, 1.13] [1.12, 1.13] [1.12, 1.13]	4 9% 2 8% 0 3% 0 5% 12.4% 0 4% 3 5% 0 4% 3 5% 0 4% 3 5% 0 4% 3 5% 0 4% 3 5% 1.7% 1.2% 0 4% 3 5% 0 4% 0 4% 0 4% 0 4% 0 4% 0 4% 0 4% 0 4	5.11 4.11 10.8 0.8 16.7 10 0.2 0.2 0.2 0.0 10 0.2 0.2 0.2 0.2 0.0 10 0.2 0.2 0.2 0.2 0.2 0.2 0.2 0.2 0.2 0.
	91 - Allergic disease Poktic 2005 Salam 2006 Pistiner 2008 Chu 2017 Krzych-Fala 2018 Krzych-Fala 2018 Krised effect model Random effects Random Research 2003 Pistiner 2008 Pistiner 200	$\begin{array}{c} 0.23 & 0.1009 \\ 0.74 & 0.3229 \\ 0.49 & 0.2490 \\ 0.18 & 0.0687 \\ -0.24 & 0.0283 \\ \end{array} \\ \begin{array}{c} & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & $		123 126 2164 120 124 120 124 125 120 121 128 121 128 120 121 128 120 121 128 120 121 128 120 121 128 120 121 128 120 129 124 128 128 128 128 128 128 128 128 128 128	[1.06, 1.43] [1.03, 1.54] [1.01, 2.67] [1.01, 2.67] [1.01, 2.67] [1.02, 1.43] [0.69, 2.06] [0.84, 1.74] [0.69, 2.06] [0.84, 1.74] [0.65, 1.21] [0.67, 2.24] [1.02, 1.74] [1.02, 3.17] [1.02, 3.17] [1.02, 3.17] [1.02, 3.17] [1.02, 3.17] [1.02, 1.57] [1.02, 1.57] [1.02, 1.57] [1.02, 1.57] [1.02, 1.57]	4 9% 2 8% 0 3% 0 5% 3 6% 0 3% 12.4% 12.4% 0 4% 3 5% 17% 0 4% 3 5% 17% 0 4% 3 5% 17% 0 3% 16% 0 3% 13% 6 5% 13% 6 5% 12.4% 13.5% 13	5.11 4.1 0.8 12 2.4 6 0.8 10.7 10 0.2 0.2 10 0.2 0.2 10 0.2 0.2 10 0.2 10 0.4 5 3.5 2.2 6 3.5 3.5 3.5 3.5 3.5 3.5 3.5 3.5 3.5 3.5
	g1 - Allergic disease Poter 2005 Salam 2006 Pistiner 2008 Chu 2017 Krzych-Fata 2018 Kim 2019 Fixed effect model nemogenety / ² = 16% v. 2 91 = Allergic Inhilis Nafstad 2000 Malen 2008 Bager 2003 Negele 2004 Poter 2005 Bager 2004 Poter 2005 Park 2016 Li 2015 Brandao 2016 Han 2019 Goris 2020 Li 2015 Brandao 2016 Han 2019 Goris 2020 Li 2020 Pister 2020 Pister 2020 Pister 2008 Park 2019 Goris 2020 Li 2015 Fished effect model Randon effects model Heterogenety. <i>P</i> = 59% t g1 = Astma Nafstad 2000 Xu 2001	$\begin{array}{c} 0.23 & 0.1009 \\ 0.74 & 0.3229 \\ 0.49 & 0.2490 \\ 0.18 & 0.0687 \\ 0.24 & 0.0213 \\ \end{array} \\ \begin{array}{c} z \\ z $		1233 126 2100 164 1200 124 125 120 121 121 126 121 121 126 121 126 127 127 120 121 121 126 127 120 127 127 120 127 127 120 127 127 120 127 127 127 127 127 127 127 127 127 127	[1.06; 1.43] [1.03; 1.54] [1.01; 2.67] [1.01; 2.67] [1.01; 2.67] [1.01; 1.43] [0.69; 2.08] [0.69; 2.08] [0.69; 2.08] [0.69; 2.28] [0.69; 2.28] [0.69; 2.28] [0.69; 2.28] [0.69; 2.28] [0.69; 2.28] [0.69; 2.28] [0.69; 2.28] [0.69; 1.28] [0.69; 1.28] [0.69; 1.28] [1.12; 1.40] [0.99; 1.17] [1.12; 1.34] [0.69; 1.76] [1.12; 1.34] [0.69; 1.76] [1.53; 6.76]	4 9% 4 9% 28% 03% 12.4% 0.4% 0.5% 0.5% 0.5% 0.5% 0.5% 0.5% 0.5% 0.5% 0.5% 0.5% 0.5% 0.2%	5.11 4.14 0.81 120 120 100 100 100 100 100 100 100 10
	g1 - Allergic disease Potetri 2005 Salam 2006 Pistiner 2008 Chu 2017 Krzych-Fata 2018 Kim 2019 Fixed effect model Random effects model Random effects model Nardstad 2000 Mortgomey 2001 Xu 2001 McKseever 2002 Bager 2003 Negele 2004 Poister 2005 Salam 2006 Mallen 2008 Paistiner 2008 Paister 2005 Brandao 2016 Hu 2021 Gortis 2020 Hu 2021 Prode affect model Heardogenety /* 59%, og G1 = Alstman Natsdad 2000 Malea 2020 Paistiner 2008 Paistiner 2008 Paistad flect model Handom effect model Heardogenety /* 59%, og Gal = Asthma Natsdad 2000 Mekseever 2002 Poster 2003	$\begin{array}{c} 0.23 & 0.1009 \\ 0.74 & 0.3229 \\ 0.49 & 0.2490 \\ 0.18 & 0.0887 \\ 0.24 & 0.0213 \\ \end{array}$		1233 126 2100 164 1200 124 125 120 121 121 125 120 121 121 125 120 121 121 125 120 121 121 125 120 121 125 120 121 125 120 127 125 120 127 127 126 127 127 127 127 127 127 127 127 127 127	[1.06; 1.43] [1.03; 1.54] [1.01; 2.67] [1.01; 2.67] [1.01; 2.67] [1.01; 2.67] [1.01; 1.43] [0.69; 2.08] [0.84; 1.74] [0.73; 2.24] [0.98; 1.21] [0.98; 1.21] [0.98; 1.21] [0.98; 1.21] [0.98; 1.21] [0.98; 1.21] [0.98; 1.21] [0.98; 1.21] [1.02; 3.17] [1.18; 2.93] [0.94; 1.64] [1.22; 1.99] [1.02; 3.17] [1.18; 2.93] [0.94; 1.64] [1.22; 1.57] [1.11; 1.12] [1.11; 1.12] [1.11; 1.12] [1.13; 3.64] [1.53; 6.64] [1.53; 6.64] [1.02; 1.74]	4 9% 2 8% 0 3% 12.4% 0 4% 0 4% 0 5% 17% 12.4% 0.4% 3.5% 17% 112% 0.3% 0.3% 0.3% 0.3% 0.4% 3.5% 17% 112% 0.4% 0.3% 0.3% 0.5% 0	5.11 0.8 1.20 1.00 1
	91 - Allergic disease Pokter 2005 Salam 2006 Pistiner 2008 Chu 2017 Krzych-Falta 2018 Krzych-Falta 2018 Krzych-Falta 2018 Montgomety / e- 198, v 91 - Allergic rhinitis Nafstad 2000 Montgomety 2001 Xu 2001 McKsever 2002 Bage 2003 Negele 2004 Poster 2005 Brandao 2016 Han 2019 Gorris 2020 Hu 2021 Randoo 2016 Han 2019 Gorris 2020 Lu 2020 Hu 2021 Randao 2016 Han 2019 Gorris 2020 Lu 2020 Hu 2021 Randao 2016 Han 2019 Gorris 2020 Lu 2020 Hu 2021 Randao et dictu model Heatogenety / e- 50%, v 91 = Astma	$\begin{array}{c} 0.23 & 0.1009 \\ 0.74 & 0.3229 \\ 0.49 & 0.2490 \\ 0.18 & 0.0687 \\ -0.24 & 0.0213 \\ \end{array} \\ \begin{array}{c} = 0.0038, \ \rho = 0.30 \\ 0.18 & 0.2803 \\ 0.19 & 0.1858 \\ 0.25 & 0.2860 \\ 0.01 & 0.1858 \\ 0.25 & 0.2860 \\ 0.01 & 0.0912 \\ 0.45 & 0.1207 \\ 0.25 & 0.1208 \\ 0.01 & 0.0912 \\ 0.45 & 0.1207 \\ 0.26 & 1.0441 \\ 0.090 & 0.2886 \\ 0.31 & 0.0912 \\ 0.45 & 0.1207 \\ 0.26 & 1.0441 \\ 0.07 & 0.0444 \\ 0.07 & 0.0240 \\ 0.03 & 0.0567 \\ 0.05 & 0.0567 \\ 0.05 & 0.0567 \\ 0.05 & 0.0567 \\ 0.05 $		1233 126 2100 164 1200 121 128 121 128 101 140 121 128 101 140 121 128 101 140 121 128 128 101 140 121 128 128 101 140 129 120 121 128 128 101 144 125 100 121 110 144 125 100 121 110 144 125 100 121 110 144 125 100 121 110 144 125 100 121 110 144 125 100 121 110 144 125 100 121 110 144 125 100 121 110 144 125 100 121 110 144 125 100 109 124 126 100 109 124 115 100 109 124 115 100 109 124 115 100 109 124 115 100 109 100 109 100 100 100 100 100 100	[1.06; 1.43] [1.03; 1.54] [1.01; 2.67] [1.02; 2.67] [1.04] [1.01; 2.67] [1.04] [1.04]; 1.43] [1.04]; 1.43] [1.04]; 1.43] [1.05]; 1.43] [1.08]; 1.43] [1.12]; 1.53] [1.12]; 1.53] [1.03]; 1.64] [1.13]; 1.64] [1.14]; 1.64] [1.16]; 1.64] [1.16]; 1.64] [1.12]; 1.54] [1.14]; 1.24] [1.14]; 1.24] [1.15]; 1.24] [1.14]; 1.24]\\[1.14]; 1.24]\\[1.14]; 1.24]\\[1.14];	4 9% 4 9% 28% 0.3% 12.4% 0.4% 0.4% 3.5% 0.4% 3.5% 0.4% 3.5% 0.4% 3.5% 0.3% 14.6% 0.3% 14.6% 0.3% 14.6% 0.3% 1.1% 0.3% 1.1% 0.3% 1.1% 0.5	5.11' 0.8' 12' 4.6' 0.8' 16.7' 10' 20' 20' 20' 20' 20' 20' 20' 20' 20' 2
	91- Allergic disease Pokter 2005 Salam 2006 Pistiner 2008 Chu 2017 Krzych-Fata 2018 Kim 2019 Fixed effect model Random effects model National Character and National Character and Nati	$\begin{array}{c} 0.23 & 0.1009 \\ 0.74 & 0.3229 \\ 0.49 & 0.2490 \\ 0.18 & 0.0887 \\ -0.24 & 0.3213 \\ \end{array} \\ \begin{array}{c} = 0.0038, \ p = 0.30 \\ 0.18 & 0.2803 \\ 0.19 & 0.1858 \\ 0.29 & 0.1858 \\ 0.25 & 0.2860 \\ 0.01 & 0.0912 \\ 0.25 & 0.2860 \\ 0.01 & 0.0912 \\ 0.45 & 0.1207 \\ 0.26 & 1.0441 \\ 0.70 & 0.248 \\ 0.031 & 0.0912 \\ 0.45 & 0.1207 \\ 0.26 & 1.0441 \\ 0.09 & 0.2868 \\ 0.03 & 0.3154 \\ 0.07 & 0.0444 \\ 0.07 &$		123 126 210 164 120 079 122 121 128 121 128 141 140 137 157 167 147 168 141 141 161 161 121 121 128 109 133 131 124 109 133 131 124 129 109 133 131 124 129 129 129 129 129 129 129 129 129 129	[1.06; 1.43] [1.03; 1.54] [1.01; 2.67; [1.01; 2.67; [1.01, 2.67; [1.01, 1.43] [0.69; 2.08] [0.69; 1.69] [0.71; 1.69] [0.71; 1.69] [1.12; 1.57] [1.02; 1.68] [1.14; 1.24] [1.14; 1.24] [1.14	4 9% 28% 0.3% 0.5% 0.3% 12.4% 0.4% 2.0% 0.4% 2.0% 0.4% 2.0% 0.3% 1.7% 0.4% 2.0% 0.3% 2.0% 0.3% 1.2% 1.7% 0.4% 2.8% 0.3% 1.7% 0.4% 2.8% 0.3% 0.3% 1.2.4% 0.4% 0.3%	5.11 0.1 10.0 20.0 20.0 20.0 20.0 20.0 20
	91 - Allergic disease Polstic 2005 Salam 2006 Pistiner 2008 Chu 2017 Kracht Pia Kracht Pia Auf 2018 Kracht Pia Nafstad 2000 Montgomery 2001 Xu 2001 McKeever 2002 Bager 2003 Bager 2003 Bager 2005 Salam 2006 Pistiner 2008 Pistiner 2008	$\begin{array}{c} 0.23 & 0.1009 \\ 0.74 & 0.3229 \\ 0.49 & 0.2490 \\ 0.18 & 0.0887 \\ -0.24 & 0.0213 \\ \end{array} \\ \begin{array}{c} & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & $		123 126 210 164 127 120 122 120 121 125 125 120 121 125 120 121 125 120 121 125 120 121 125 120 121 125 120 121 125 120 121 125 120 121 125 120 121 125 120 121 125 120 121 125 120 121 125 120 121 125 120 121 125 120 121 125 120 121 125 120 121 125 120 120 121 125 120 120 120 120 120 120 120 120 120 120	[1.06; 1.43] [1.03; 1.54] [1.01; 2.63] [1.01; 2.63] [1.01; 2.63] [1.01; 2.63] [1.01; 2.63] [1.02; 2.63] [1.02; 1.46] [1.13; 1.37] [1.12; 1.40] [0.69; 2.08] [0.69; 2.08] [1.13; 1.40] [1.15; 1.64] [1.15; 1.64] [1.15; 1.64] [1.15; 1.64] [1.15; 1.64] [1.15; 1.64] [1.15; 1.64] [1.12; 1.57] [1.12; 1.57] [1.12; 1.68] [1.12; 1.68] [1.11; 1.13] [1.55; 6.68] [1.11; 1.16] [1.55; 6.68] [1.11; 1.63] [1.55; 6.68] [1.11; 1.63] [1.55; 6.68] [1.11; 1.63] [1.55; 6.68] [1.11; 1.63] [1.55; 6.68] [1.11; 1.64] [1.55; 6.68] [1.11; 1.24] [1.55; 6.68] [1.55; 6.58] [1.55; 6.58] [1.55	4 9% 0 3% 0 5% 3 6% 0 5% 3 6% 12.4% 12.4% 12.4% 12.4% 12.4% 12.4% 0.3% 12.4% 0.3% 12.4% 0.3% 12.4% 0.4% 3.5% 0.4% 0.5% 0.3% 12.4% 0.4% 3.5% 0.4% 0.5% 0.3% 12.4% 0.4% 0.5% 0.3% 12.4% 0.5% 0.3% 0.5% 0.3% 0.5% 0.3% 0.5% 0.3% 0.5% 0.3% 0.4% 0.3% 0.3% 0.4% 0.3% 0.3% 0.4% 0.3% 0.4% 0.3% 0.5% 0.3% 0.4% 0.3% 0.5% 0.3% 0.5% 0.3% 0.5% 0.3% 0.5% 0.3% 0.5%	511' 41' 08' 12' 10' 20' 20' 20' 20' 20' 20' 20' 20' 20' 2
	91- Allergic disease Poktri 2005 Salam 2006 Pistiner 2008 Chu 2017 Krzych-Falta 2018 Krzych-Falta 2018 Krzych-Falta 2018 Krzych-Falta 2018 Anton effects model Random effects model Random effects model Random effects model Salar 2003 Mickeever 2002 Bager 2003 Negete 2004 Pistiner 2008 Pistiner 2008	$\begin{array}{c} 0.23 & 0.1009 \\ 0.74 & 0.3229 \\ 0.49 & 0.2490 \\ 0.18 & 0.0887 \\ -0.24 & 0.0213 \\ \end{array} \\ \begin{array}{c} & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & $		123 126 210 164 1200 124 125 125 125 125 125 125 125 125 125 125	[1.06; 1.43] [1.03; 1.54] [1.01; 2.67] [1.01; 2.67] [1.01; 2.67] [1.01; 2.67] [1.02; 2.68] [0.69; 2.08] [0.69; 2.08] [0.69; 2.08] [0.69; 2.08] [0.69; 2.08] [0.69; 2.08] [0.69; 2.08] [0.69; 2.08] [0.69; 2.08] [1.13; 1.37] [0.90; 1.49] [0.90; 1.49] [0.90; 1.49] [0.90; 1.49] [0.90; 1.49] [0.90; 1.49] [0.90; 1.49] [0.90; 1.49] [0.91; 2.48] [1.16; 2.487] [1.18; 2.93] [0.94; 1.68] [1.11; 1.68] [1.12; 1.68] [1.11; 1.12] [1.12; 1.34] [1.12; 1.34] [1.12; 1.34] [1.12; 1.34] [1.12; 1.29] [1.12; 1.29] [1.1	4 9% 28% 0.3% 36% 0.5% 3.6% 0.3% 12.4% 0.3% 0.3% 0.3% 0.4% 3.4% 3.4% 3.4% 3.4% 3.4% 3.4% 5.2% 0.3% 0.3% 0.3% 0.3% 0.3% 0.3% 0.4% 3.4% 0.4% 3.4% 0.4% 3.4% 0.4% 3.4% 0.4% 3.4% 0.4% 3.4% 0.4% 3.4% 0.4% 3.4% 0.4% 3.4% 0.4% 3.4% 0.4% 3.4% 0.4% 0.4% 3.4% 0.4% 0.4% 0.4% 0.4% 0.4% 0.4% 0.4% 0	5.11 0.1 10.0 20.0 15.3 22 10.0 20.0 15.3 22 10.0 20.0 15.3 22 10.0 8 5.3 5.3 5.3 5.3 5.3 5.3 5.3 5.3 5.3 5.3
	g1 - Allergic disease Potsti 2005 Salam 2006 Pistiner 2008 Chu 2017 Krzych-Fata 2018 Krzych-Fata 2018 Karzych-Fata 2018 Karzych-Fata 2018 Karzych-Fata 2018 Karzych-Fata 2018 Karzych-Fata 2018 Nafsda difect model Nandom effects model Nafsda 2000 Morigomery 2001 Xu 2001 McKsever 2002 Bager 2003 Polster 2005 Palster 2005 Palster 2006 Mallen 2008 Park 2019 Comis 2020 Lu 2020 Hu 2021 Merza Lopez 2021 Kized effect model Random effects model Rando 2000 V	$\begin{array}{c} 0.23 & 0.1009 \\ 0.74 & 0.3229 \\ 0.49 & 0.2450 \\ 0.18 & 0.0687 \\ 0.24 & 0.0213 \\ \end{array} \\ \begin{array}{c} & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & $		1233 126 2100 1644 1200 799 1224 125 1202 121 128 120 121 128 120 121 128 120 121 128 120 121 128 120 121 128 120 121 128 120 121 128 120 129 129 129 129 129 129 129 129 129 129	[1.06; 1.43] [1.03; 1.54] [1.01; 2.67] [1.01; 2.67] [1.01; 2.67] [1.01; 1.43] [0.69; 2.08] [0.69; 2.08] [0.68; 1.24] [0.69; 2.24] [0.68; 1.24] [0.68; 1.24] [0.68; 1.24] [0.68; 1.24] [0.68; 1.24] [1.02; 3.17] [0.64; 1.74] [1.12; 1.40] [1.12; 1.40] [0.64; 1.74] [1.12; 1.40] [1.12; 1.40] [1.12	4 9% 4 9% 28% 0.3% 12.4% 0.4% 0.4% 0.4% 0.4% 0.4% 0.4% 0.4% 0.4% 0.3% 1.7% 1.2% 1.2% 1.2% 1.2% 0.3% 0.2%	5.11 4.14 0.8 12 2.0 0 2.0 0 2.0 0 2.0 0 2.0 0 2.0 0 2.0 0 2.0 0 2.0 0 2.0 0 2.0 0 2.0 0 2.0 0 2.0 0 2.0 0 2.0 0 2.0 0 2.0 2.
	g1 - Allergic disease Potsti 2005 Salam 2006 Pistiner 2008 Chu 2017 Krzych-Fata 2018 Kim 2019 Fixed effect model Random effects model Random effects model Nardsad 2000 Morigomery 2001 Xu 2001 McKsever 2002 Bager 2003 Poister 2005 Palar 2006 Malan 2006 Palar 2008 Patrone 2008 Random effects model Random effects model Randa 2000 Nu 2001 McKsever 2002 B	$\begin{array}{c} 0.23 & 0.1009 \\ 0.74 & 0.3229 \\ 0.49 & 0.2490 \\ 0.18 & 0.0887 \\ -0.24 & 0.0213 \\ \end{array} \\ \begin{array}{c} & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & $		1233 126 2100 1644 1200 799 1224 125 120 121 128 120 121 128 120 121 128 120 121 128 120 121 128 120 121 128 120 121 128 120 121 128 120 129 129 129 129 129 129 129 129 129 129	[1.06; 1.43] [1.03; 1.54] [1.01; 2.67] [1.01; 2.67] [1.01; 2.67] [1.01; 1.43] [0.69; 2.08] [0.69; 2.08] [0.69; 2.08] [0.68; 1.21] [0.90; 2.24] [0.80; 2.24] [0.80; 2.24] [0.80; 2.24] [0.80; 2.24] [0.80; 2.24] [0.80; 2.24] [1.02; 3.17] [0.90; 1.29] [0.10; 5.96] [1.12; 1.40] [0.65; 1.02] [1.12; 1.57] [1.12; 2.15] [1.12; 1.57] [1.12; 1.57] [1.12	4 9% 4 9% 2 8% 0 3% 12.4% 0 4% 0 4% 0 4% 0 4% 0 3% 0 3% 0 3% 12.4% 0 4% 0 3% 0 3% 0 3% 0 3% 0 3% 12.4% 0 3% 0 3% 0 3% 0 3	5.11 0.1 10.0 20.0 20.0 20.0 20.0 20.0 20
	91- Allergic disease Poktri 2005 Salam 2006 Pistiner 2008 Chu 2017 Krzych-Falta 2018 Krzych-Falta 2018 Krzych-Falta 2018 Krzych-Falta 2018 Anton effects model Random effects model Random effects model Random effects model Salar 2006 Pistiner 2008 Pistiner 2008	$\begin{array}{c} 0.23 & 0.1009 \\ 0.74 & 0.3229 \\ 0.49 & 0.2490 \\ 0.18 & 0.0887 \\ 0.24 & 0.0213 \\ \end{array}$		1233 126 2100 1844 1200 125 125 125 125 125 125 125 125 125 125	[1.06; 1.43] [1.03; 1.54] [1.01; 2.67] [1.01; 2.67] [1.02; 2.63] [1.02; 2.63] [1.02; 2.63] [1.02; 2.63] [1.02; 2.68] [0.68; 2.08] [0.68; 1.24] [0.68; 1.24] [0.68; 1.24] [1.15; 2.44] [0.68; 1.24] [1.16; 2.44] [1.16; 2.44] [1.16; 2.44] [1.16; 2.44] [1.16; 2.44] [1.16; 2.44] [1.16; 2.44] [1.17] [1.12; 1.34] [1.12; 1.34] [1.14] [1.16; 1.16] [1.16; 1.16] [1.16; 1.16] [1.16; 1.16] [1	4 9% 2 8% 0 3% 3 6% 3 6% 0 4% 3 6% 3 6% 3 6% 3 6% 3 6% 3 6% 3 6% 3 6	5.1'1 0.8' 120'20'20'20'20'20'20'20'20'20'20'20'20'2
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Supplementary Figure 2.



Supplementary Figure 3.

Study	TE seTE	Odds Ratio	OR	95%-CI	Weight (fixed)	Weight (random)
g1 = Allergic rhinitis		22				
Montgomery 2001	-0.03 0.1183	2	0.97	[0.77; 1.22]	5.6%	10.2%
Miyake 2007	-0.12 0.0659	1	0.89	[0.78; 1.01]	17.9%	12.5%
Ehlayel 2008	-0.58 0.1269	+3	0.56	[0.44; 0.72]	4.8%	9.8%
Valdivia 2010	-0.63 0.2109	-+-3	0.53	[0.35; 0.80]	1.7%	6.4%
Jelding-Dannemand 201	5 -1.20 0.7414		0.30	[0.07; 1.28]	0.1%	0.9%
Li 2015	-0.25 0.0525	B	0.78	[0.70; 0.86]	28.2%	13.0%
Bion 2016	0.00 0.1086	<u>11</u>	1.00	[0.81; 1.24]	6.6%	10.7%
Bion 2016	-1.02 0.3501	+	0.36	[0.18; 0.71]	0.6%	3.3%
Gorris 2020	-0.84 0.7116		0.43	[0.11; 1.73]	0.2%	1.0%
Fixed effect model		ŝ	0.81	[0.75; 0.86]	65.8%	
Random effects model		¢.	0.75	[0.63; 0.88]	**	67.9%
Heterogeneity: $l^2 = 73\%$, τ	² = 0.0348, <i>p</i> < 0.01	n new con na				
g1 = Asthma		222				
Miyake 2007	-0.04 0.0528		0.96	[0.87; 1.06]		13.0%
Ehlayel 2008	-0.68 0.1409	+ 3		[0.38; 0.67]		9.2%
Jelding-Dannemand 201				[0.47; 2.48]		2.49
Bion 2016	0.00 0.2094	20		[0.66; 1.51]		6.5%
Bion 2016	-1.61 0.9749 -	+ ***		[0.03; 1.35]		
Gorris 2020	-0.51 1.1019			[0.07; 5.20]		0.49
Fixed effect model		2.00		[0.81; 0.98]	34.2%	
Random effects model		0	0.77	[0.53; 1.13]		32.1%
Heterogeneity: $I^2 = 76\%$, τ^2	² = 0.1160, <i>p</i> < 0.01	700000				
Fixed effect model		17 2 6.		[0.79; 0.88]		
Random effects model		¢.	0.76	[0.66; 0.87]	-	100.0%
Heterogeneity: $l^2 = 74\%$, τ	² = 0.0382, p < 0.01	I ILL I				
Residual heterogeneity: 12	-740/ 0.04	0.1 0.5 1 2 10				

Study	TE seTE	Odds Ratio	OR	95%-CI	Weight (fixed)	Weight (random)
		πĨ				
g1 = Allergic disease	0.45 0.0007		0.00	10.04.0.041	1 70/	10 50
Polster 2005	-0.15 0.0297	t.		[0.81; 0.91]	4.7%	13.5%
Krzych-Falta 2018	-0.14 0.0407	Ť.		[0.80; 0.94]		11.7%
Krzych-Falta 2018	-0.21 0.0932	1		[0.67; 0.97]		5.4%
Fixed effect model		0		[0.82; 0.90]	7.6%	
Random effects mode		Ŷ	0.86	[0.82; 0.90]	**	30.5%
Heterogeneity: $I^2 = 0\%$, τ^2	⁺ = 0, <i>p</i> = 0.78					
g1 = Allergic rhinitis						
Nafstad 2000	-0.22 0.2233		0.80	[0.52; 1.24]	0.1%	1.3%
Nafstad 2000	-0.36 0.3741 -		0.70	[0.34; 1.46]	0.0%	0.5%
Montgomery 2001	-0.19 0.0858		0.83	[0.70; 0.98]	0.6%	6.0%
Montgomery 2001	-0.20 0.0996		0.82	[0.67; 1.00]	0.4%	4.9%
Polster 2005	-0.26 0.0363	4	0.77	[0.72; 0.83]	3.1%	12.4%
Westergaard 2007	-0.26 0.0429	-i	0.77	[0.71; 0.84]	2.2%	11.4%
Westergaard 2007	-0.39 0.0636	+	0.68	[0.60; 0.77]	1.0%	8.3%
Lu 2020	-0.53 0.1281		0.59	[0.46; 0.76]	0.3%	3.4%
Lu 2020	-0.89 0.2241			[0.26; 0.64]		1.3%
Fixed effect model		¢.	0.75	[0.72; 0.79]	7.8%	
Random effects mode				[0.68: 0.80]		49.4%
Heterogeneity: $I^2 = 51\%$,	$t^2 = 0.0060, p = 0.04$					
g1 = Asthma						
Nafstad 2000	0.10 0.1944	÷	1 10	[0.75; 1.61]	0.1%	1.6%
Nafstad 2000	-0.69 0.3071			[0.27; 0.91]		0.7%
Krzych-Falta 2018	-0.17 0.0070	in in		[0.83; 0.85]		16.1%
Krzych-Falta 2018	-0.27 0.1911	<u></u>		[0.52; 1.11]		1.7%
Fixed effect model	0.21 0.1011	ě.		[0.83; 0.85]		1.1.1
Random effects mode		ä		[0.69; 1.00]	0.110.10	20.1%
Heterogeneity: $l^2 = 41\%$,			0.00	[0.00] 1.00]		20117
Fixed effect model			0.83	[0.82; 0.84]	100.0%	
Random effects mode	d	6		[0.75; 0.83]	100.0 /0	100.0%
Heterogeneity: $l^2 = 66\%$			0.15	[0.10, 0.00]	-	100.07

Random effects model		\$		0.7
Heterogeneity: $l^2 = 66\%$, $\tau^2 = 0.0043$, $p < 0.01$		÷.		
Residual heterogeneity: /2 = 41%, p = 0.06	0.5	1	2	

С

D	Study	TE s	seTE	Odds Ratio	OR	95%-CI	Weight (fixed)	Weight (random)
	g1 = Allergic disease			1				
	Polster 2005	-0.15 0.0				[0.81; 0.91]		
	Krzych-Falta 2018 Fixed effect model	-0.21 0.0	0932	10		[0.67; 0.97] [0.81; 0.90]	3.8% 41.3%	7.6%
	Random effects mode	E				[0.81; 0.90]	41.370	21.3%
	Heterogeneity: $l^2 = 0\%$, τ^2		.54		0.00	[0.01, 0.30]		21.070
	g1 = Allergic rhinitis							
	Nafstad 2000	-0.36 0.3				[0.34; 1.46]		
	Montgomery 2001	-0.20 0.0				[0.67; 1.00]		7.1%
	Bager 2003	-0.26 0.1				[0.61; 0.98]		5.6%
	Bager 2003	-0.37 0.1				[0.52; 0.91]		
	Polster 2005	-0.26 0.0				[0.72; 0.83]		
	Westergaard 2007	-0.39 0.0		1		[0.60; 0.77]	8.2%	10.3%
	Westergaard 2007	-0.20 0.0		1		[0.72; 0.94]		9.9%
	Westergaard 2007 Han 2019	-0.36 0.0				[0.59; 0.83]		8.1% 1.7%
	Han 2019 Han 2019	-0.12 0.1				[0.54; 1.48] [0.70; 1.83]		
	Lu 2020	-0.89 0.1				[0.70, 1.63]		
	Fixed effect model	-0.05 0.4	2241	j.		[0.20, 0.04]		2.2/0
	Random effects mode	1		3		[0.69: 0.81]		65.4%
	Heterogeneity: $I^2 = 41\%$, 1		8, p = 0.08	4	0.10	[0.00, 0.01]		00.470
	g1 = Asthma							
	Nafstad 2000	-0.69 0.3				[0.27; 0.91]		
	Bager 2003	-0.03 0.1				[0.74; 1.27]		4.8%
	Bager 2003	0.05 0.1				[0.79; 1.40]		4.3%
	Krzych-Falta 2018	-0.27 0.1	1911	1		[0.52; 1.11]		2.9%
	Fixed effect model Random effects mode			M		[0.76; 1.07]		13.3%
	Heterogeneity: $I^2 = 49\%$, a		n = 0.12	T	0.80	[0.67; 1.10]		10.070
	· · · ·	- 0.0286	o, p = 0.12					
	Fixed effect model Random effects mode	1		è		[0.77; 0.83] [0.73; 0.84]		 100.0%
	Heterogeneity: 12 = 56%, 1	r ² = 0.0086	6, p < 0.01					
	Residual heterogeneity: 12	= 39%, p =	= 0.06	0.5 1 2				

B	Study	TE s	eTE	Odds Ratio	OR	95%-CI	Weight (fixed)	Weight (random)
	g1 = Allergic rhinitis	0.00 0.	400	IJ	0.07	10 77 4 001	2.40	0.10
	Montgomery 2001	-0.03 0.1				[0.77; 1.22]		6.4%
	Miyake 2007	-0.04 0.0				[0.84; 1.09]	10.7%	9.9%
	Bion 2016 FAIR cohort			U		[0.75; 1.20]		6.3%
	Bion 2016 IoW cohort	-0.11 0.1				[0.74; 1.10]		7.5%
	Han 2019	-0.62 0.1				[0.40; 0.73]		4.8%
	Tong 2020	-0.22 0.0			0.80	[0.70; 0.91]	10.7%	9.9%
	Hu 2021	-0.26 0.0				[0.70; 0.85]	19.3%	11.1%
	Wang 2022	-0.15 0.1				[0.68; 1.08]	3.5%	6.6%
	Tong 2022 Fixed effect model	-0.27 0.0	050				11.9% 69.5%	10.2%
	Random effects mode	t.		1		[0.78; 0.87] [0.76; 0.91]	03.0%	72.7%
	Heterogeneity: $I^2 = 61\%$, 1		p < 0.01		0.00	[0.10, 0.01]		12.170
	g1 = Asthma							
	Miyake 2007	0.05 0.0				[0.94; 1.17]	15.2%	10.7%
	Bion 2016 FAIR cohort	-0.12 0.2		- +		[0.56; 1.41]		2.6%
	Bion 2016 IoW cohort	-0.05 0.		++		[0.66; 1.36]		3.7%
	Hu 2021	-0.17 0.0	0603	*		[0.75; 0.95]		10.4%
	Fixed effect model					[0.88; 1.02]	30.5%	
	Random effects mode Heterogeneity: $I^2 = 60\%$,		ρ = 0.06		0.94	[0.80; 1.09]		27.3%
	Fixed effect model			ķ		[0.82; 0.90]		
	Random effects mode Heterogeneity: 1 ² = 67%, 1 Residual heterogeneity: 1 ²	² = 0.0133			0.86 7 2	[0.79; 0.93]	-	100.0%