

Sex-Related Allergic Rhinitis Prevalence Switch from Childhood to Adulthood: A Systematic Review and Meta-Analysis

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Keywords

Allergic rhinitis · Meta-analysis · Prevalence · Sex differences · Systematic review

Abstract

Background: A sex-related switch in the prevalence of asthma from childhood (male predominance) to adulthood (female predominance) has been described, but for allergic rhinitis this remains unclear. We aimed to examine sex- and age-group-specific differences in allergic rhinitis prevalence by systematically evaluating studies from across the globe. **Methods:** A systematic search of MEDLINE and Embase for population-based cross-sectional studies was performed regardless of the language of publication. The search was restricted to the present millennium (2000 to June 2014). Study quality was defined by the sampling method, response rate,

sample size, and data collection method. To assess sex differences in the prevalence of self- or parent-reported symptoms of rhinitis, calculated pooled estimates of the male-female ratio (MFR) were obtained using random-effects model meta-analyses due to heterogeneity. A meta-regression analysis was also performed. **Results:** Out of 6,539 publications identified, 67 cross-sectional population-based studies (291,726 males and 301,781 females) were included in our meta-analysis. In children (<11 years of age) significantly more boys than girls had rhinitis symptoms (MFR 1.21, 95% CI 1.17–1.25), whereas in adolescents (11 to <18 years of age) males were significantly less often affected than females (MFR 0.90, 95% CI 0.85–0.95). No sex-specific prevalence difference was observed in adults (MFR 0.96, 95% CI 0.83–1.17). These findings were consistent in all continents except in Asia, where the male predominance remained beyond childhood. **Conclusions:** The male predominance of rhinitis prevalence in child-

hood changed towards a female predominance in adolescence across the globe, except in Asia. Longitudinal studies are needed to confirm these cross-sectional data and examine possible determinants and underlying mechanisms.

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Introduction

The prevalence of asthma and rhinitis has increased over the past decades, reaching epidemic proportions in Western and developing countries [1]. Sex differences in the prevalence of asthma, eczema, and food allergy are observed in clinical and epidemiological studies [2]. In childhood, the asthma prevalence is higher in boys than in girls, whereas after puberty there is a female predominance of asthma persisting throughout adulthood [3, 4]. Conversely, allergic sensitization seems to remain more prevalent among male adults [5, 6]. However, little is known about the predominating sex in the prevalence of rhinitis in the pre- and postpubertal phases. During adolescence, by comparison to boys, the prevalence of rhinitis is higher in girls in Saudi Arabia and Brazil [7, 8] and lower in Iran [9] and Kuwait [10].

There are no systematic reviews on sex-specific differences in the prevalence of self- or parent-reported symptoms of rhinitis summarizing studies from childhood to adulthood. As with asthma, there may be a sex-related prevalence switch of rhinitis symptoms between boys and girls after puberty that persists throughout adulthood [3, 11].

The primary objective of this systematic review with meta-analyses of cross-sectional studies was to examine sex differences in the prevalence of self- or parent-reported rhinitis symptoms from childhood through adolescence into adulthood. Secondary objectives were to describe possible regional and temporal differences in the prevalence of rhinitis assessed in population-based cross-sectional studies.

Methods

Data Sources, Search Strategy, and Selection Criteria

This systematic review was reported in accordance with the recommendations set forth by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [12]. The protocol can be accessed at PROSPERO (www.crd.york.ac.uk/PROSPERO/, registration No. CRD42016036105). A systematic search was conducted using computerized bibliographic databases such as MEDLINE through the PubMed webpage and Embase, and the search was restricted to studies published in the first 14

years of the present millennium (2000–2014). Our search retrieved all relevant studies regardless of the language of publication. MeSH terms were chosen according to the database (minimal variations) and a selection of string terms to increase the capture of relevant papers (online suppl. search strategies; for all online suppl. material, see www.karger.com/doi/10.1159/000464324). The EndNote X7® (Thomson Reuters) bibliographic database was used to manage the results of our literature searches.

Inclusion and Exclusion Criteria

Study selection was based on an a priori set of inclusion and exclusion criteria. Broad inclusion criteria were used to take advantage of all available knowledge on the assessment of potential gender differences in the prevalence and/or incidence of rhinitis among the general population.

The inclusion criteria were the following: (1) studies that recruited participants of both sexes from the general population of all age groups, (2) reported prevalence and/or incidence of the disease stratified by sex and age if the population under study included children and adults, and/or that described risk factors explained by sex, (3) longitudinal or cross-sectional studies.

Studies that: (1) were not original (i.e., reviews, guidelines, etc.), (2) did not report prevalence and/or incidence estimates stratified by sex and age if the population under study included children and adults, (3) whose participants were selected by their occupation, (4) recruited only male or female participants, and (5) those studies that recruited patients from institutes such as allergy outpatient clinics, were excluded. The following study designs were excluded: ecological studies, case reports, case series, case-control studies, experimental studies, intervention studies, and clinical studies.

In the present systematic review, only the results of cross-sectional studies assessing the prevalence of self-reported or parent-reported symptoms of current rhinitis, defined as the presence of rhinitis symptoms in the last 12 months were reported.

Study Selection, Data Extraction and Quality Assessment

Study selection was performed following a 2-step process. First, 2 independent reviewers (M.P. and C.H.) conducted title scans in a parallel fashion. We rated each citation as: “include,” “exclude,” or “unclear.” Second, the same independent reviewers screened the abstracts of those records rated as “include” or “unclear.” Disagreements encountered in both steps were resolved through referral to a third reviewer (T.K. or M.F.).

Prior to data extraction, 2 reviewers (M.P. and M.F.) independently reviewed full texts of all selected publications rated as “include” or “unclear.” M.P. designed the data extraction form. The predesigned data extraction form with 5 studies selected from the pool of included studies was piloted and M.F., A.R., and T. Keller identified issues that served to improve the form. At least 2 reviewers (T. Keller, C.H., B.C., A.R., M.F., and M.P.) abstracted data from the selected full texts independently with disagreements through referral to a third reviewer (T.K.). We contacted the authors of several studies [13–17] by e-mail for further information regarding the measurements stratified by sex. Only the studies whose authors provided a response within 2 weeks were included in the meta-analyses.

Data were extracted on the following information using SoSci-Survey (<https://www.sosicisurvey.de/>): country, study design, description of the process of recruitment of participants, age of participants, sample size and residency, response rate, observation period, definition of disease and measurement, method of data

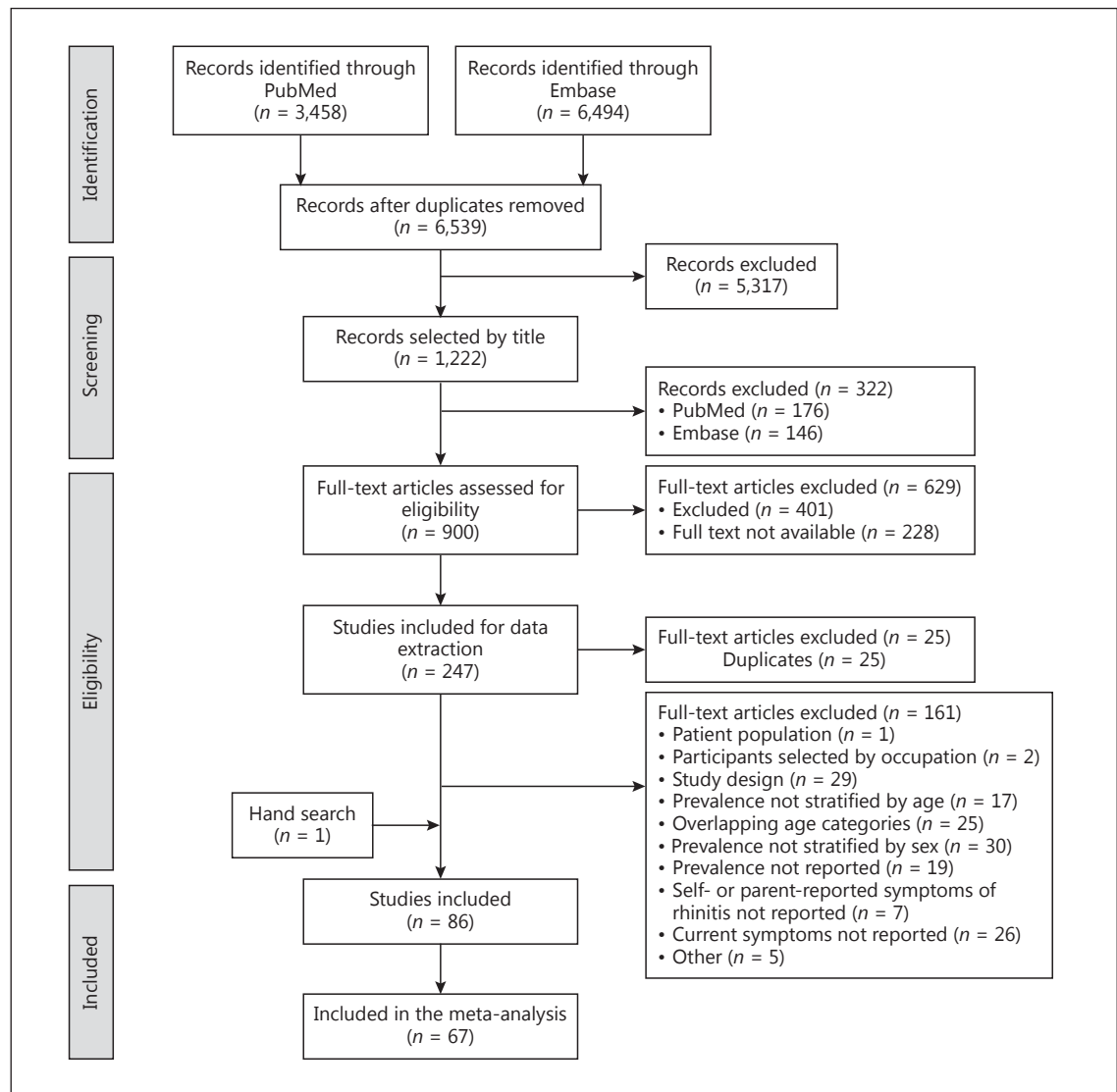


Fig. 1. PRISMA flow chart for the literature search.

collection, prevalence and incidence of rhinitis stratified by sex as well as sex-specific information on risk factors for rhinitis.

Study quality assessment was determined by 4 criteria: sampling method, response rate, sample size, and data collection method to investigate sources of heterogeneity between studies, if present. The maximum score was 5 points. Studies that scored 0–2 were labelled “low quality,” 3–4 were “moderate quality,” and a score of 5 indicated “high quality.”

Quantitative Data Synthesis

To assess sex differences in the prevalence of rhinitis before and after puberty we measured calculated pooled estimates of the male-female ratio (MFR), together with associated 95% confidence intervals (95% CI), using random-effects model meta-analyses with the inverse variance method due to the expected heterogeneity of the studies. I^2 was calculated to quantify inconsistency across stud-

ies. To investigate the source of potential heterogeneity we performed meta-regression analyses regarding the study period (conducted until 2000 vs. after 2000), region (continent), and residency (urban vs. mixed rural/urban background) as moderator variables. Statistical analyses were done using R and the STATA 12.0 software package (Stata Corporation, College Station, TX, USA).

Results

Characteristics of Included Studies

After the removal of duplicates, 6,539 hits were retrieved, of which 1,222 studies were identified after title screening. A total of 250 studies were eligible for data

extraction, of which 85 were included. One study suggested by the reviewer fit the inclusion criteria, giving a total of 86 cross-sectional studies (online suppl. references), of which 67 were included in the meta-analysis (Fig. 1). Studies were mainly of moderate to high quality. A detailed summary of the 86 studies and their quality rating score can be found in online supplementary Tables S1–S4.

The studies were conducted mainly in Asia (35) and Europe (28), followed by the Americas (16), Africa (5), and Oceania (2). The majority of the studies recruited children from an urban background. Fourteen studies assessed both children (aged around 6–7 years) and adolescents (aged around 13–14 years), and provided the prevalence stratified by age [9, 18–30].

The prevalence of rhinitis was questionnaire based, mainly using the International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire for children and adolescents ($n = 71$) [31], followed by the European Community Respiratory Health Survey (ECRHS) in adults ($n = 6$) [32]. A total of 46 studies examined sex differences in the prevalence of rhinitis in children aged <11 years, 43 in children aged 11–18 years, and 12 studies in adults (Table 1).

Pooled estimates were based on 88 MFRs from 67 studies that provided the necessary information to derive the MFR, including 291,726 males and 301,781 females (Fig. 2, 3).

Prevalence of Rhinitis Symptoms during Childhood

The meta-analysis for childhood included 35 studies with data from 133,885 males and 135,152 females (Fig. 2). The pooled estimates for the MFR of the prevalence of self- or parent-reported symptoms of rhinitis in children before puberty (<11 years) was 1.21 (95% CI 1.17–1.25).

None of the included studies reported a female predominance, although 12 studies did not report sex differences. The largest studies conducted in Korea [23, 33], Japan [22], and Spain [34] analyzed 57,358 males and 60,506 females and showed sex differences with an MFR similar to the pooled estimate.

Prevalence of Rhinitis Symptoms during and Shortly after Puberty

The meta-analysis for the age group of 11–17 years included 36 studies with data from 137,443 males and 142,939 females (Fig. 3). The pooled estimate for the MFR of the prevalence of rhinitis symptoms in adolescents aged 11–17 years was 0.90 (95% CI 0.85–0.95).

Table 1. Characteristics of studies included in the systematic review

Study characteristics	Cross-sectional studies, <i>n</i>
Total	86
Study period ¹	
1991–2000	23
2001–2014	61
Unknown	14
Region	
Africa	5
Asia	35
Europe	28
Americas	16
North/Central	8
South	8
Oceania	2
Sample size analyzed	
<1,000	10
1,001–5,000	34
5,001–10,000	23
10,001–100,000	18
>100,000	1
Age category ¹	
0–10 years	46
11–<18 years	43
18+ years	12
Urbanicity	
Urban	45
Rural/urban ²	30
Unclear/not reported	11
Method for assessing prevalence ¹	
ISAAC questionnaire	71
ECHRS questionnaire	6
Other questionnaire/s	9

ISAAC, International Study of Asthma and Allergies in Childhood; ECRHS, European Community Respiratory Health Survey.

¹ Total may exceed 86 as some studies reported the prevalence of rhinitis in several age categories.

² Subjects from 3 studies had a rural background only.

Three studies conducted in Korea [23], Iran [9], and Kuwait [10] showed a clear male predominance during and shortly after puberty, whereas 15 studies found a strong female predominance during and shortly after puberty. Three studies analyzed sex differences in the prevalence of rhinitis in 2 different time periods: New Zealand [28] (1993 and 2003), [35] (1995 and 2002), and Brazil [36] (2007 and 2010). They found a female predominance, which was similar in both study periods.

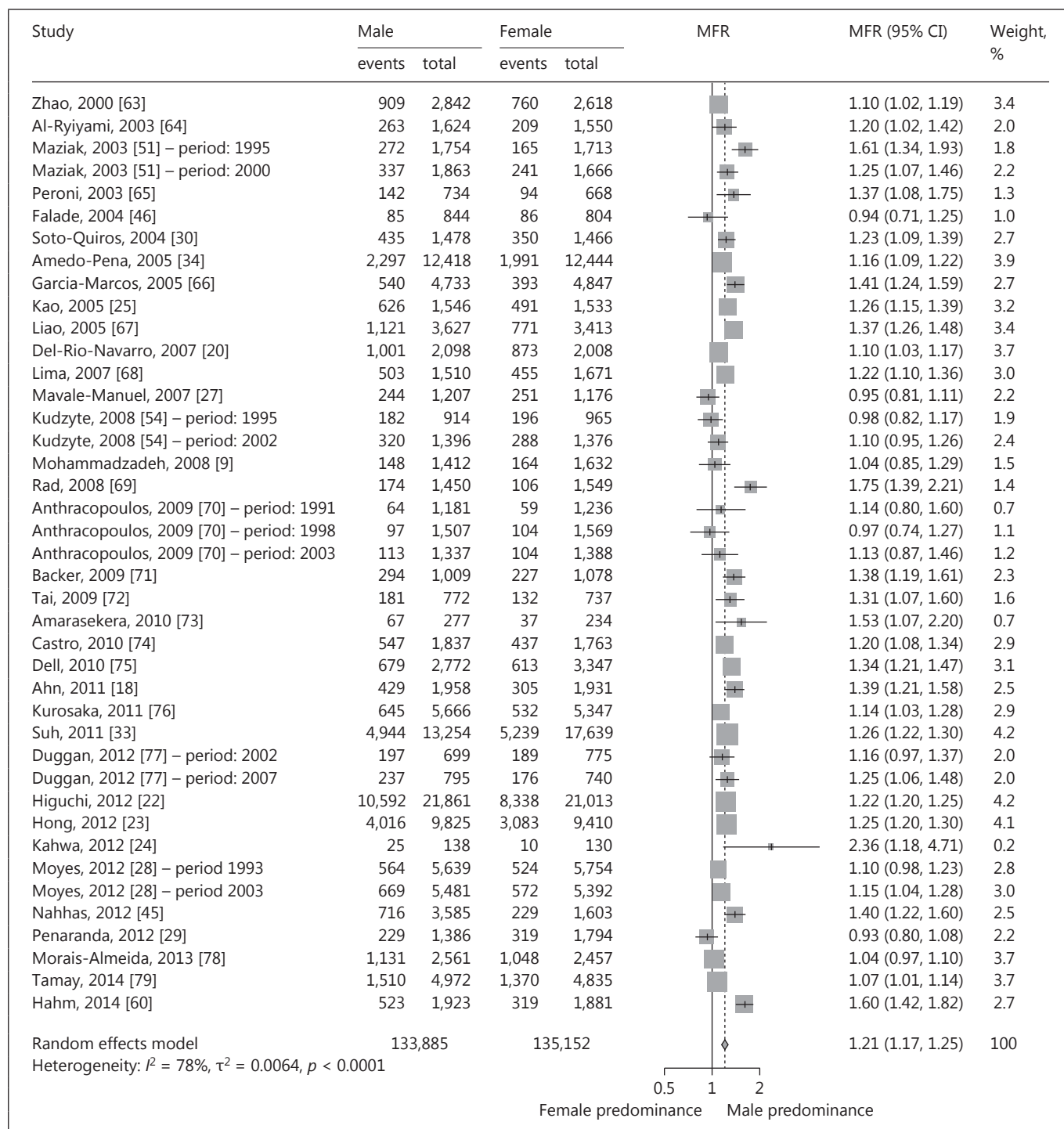


Fig. 2. Forest plot estimating the difference in prevalence of rhinitis between boys and girls aged <11 years (before puberty). The term “events” corresponds to the number of children with current rhinitis.

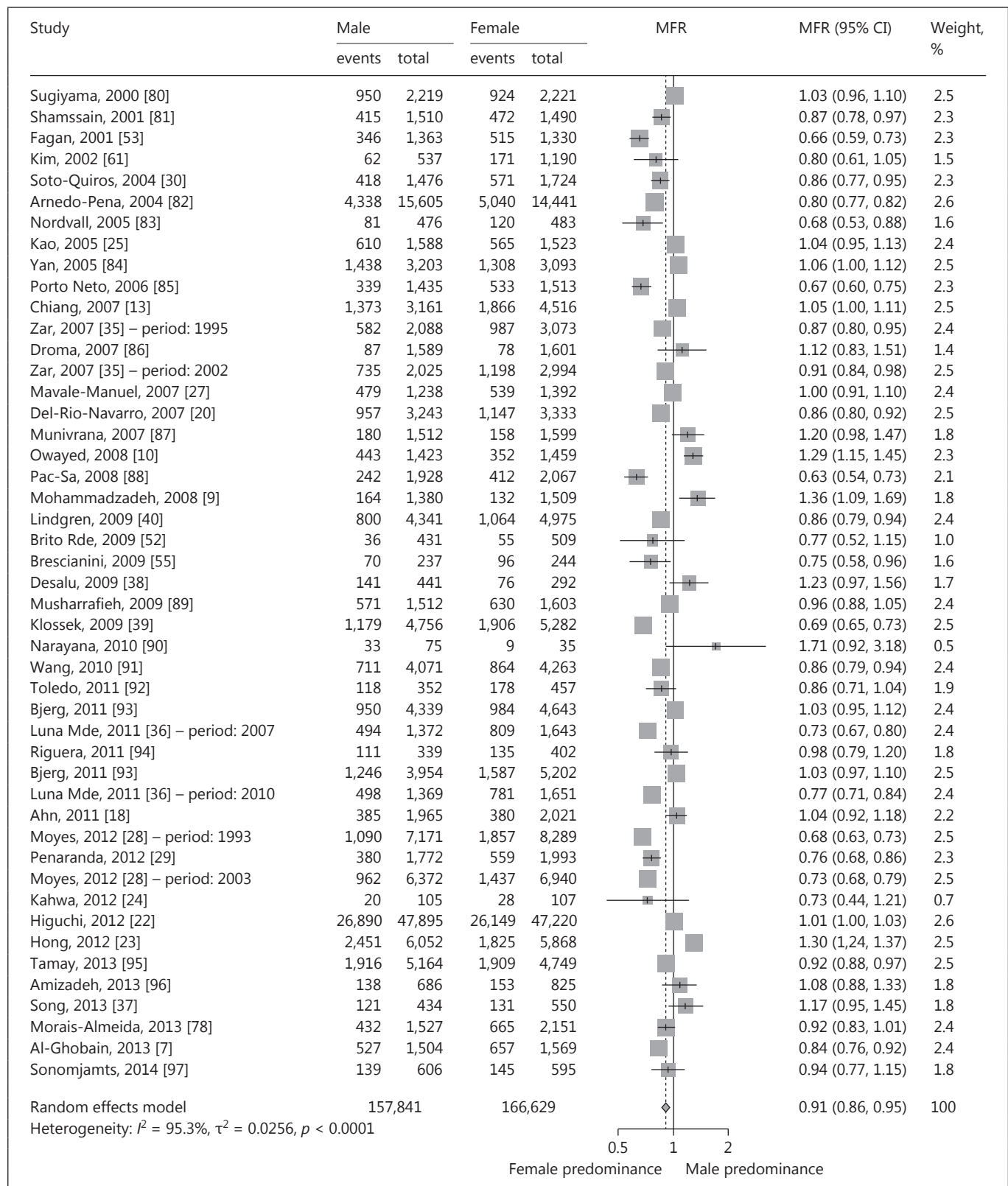


Fig. 3. Forest plot estimating the difference in prevalence of rhinitis between males and females during and after puberty (aged 11 to <18 years) and throughout adulthood (18+ years). The term “events” corresponds to the number of children with current rhinitis.

Prevalence of Rhinitis Symptoms throughout Adulthood

The meta-analysis for adulthood included 7 studies with data from 20,398 males and 23,690 females (Fig. 3). The pooled estimate for the MFR of the prevalence of symptoms of rhinitis in adults (aged 18 years and older) was 0.96 (95% CI 0.83–1.10). When the estimates including both pubertal and adult subjects were pooled, the MFR was 0.91 (95% CI 0.86–0.95), indicating a persistence in the female predominance.

None of the studies reported a male predominance in the prevalence of rhinitis during adulthood, although 2 studies conducted in Korea [37] (with 984 subjects aged ≥ 65 years) and Nigeria [38] (733 subjects aged 18–45 years) showed a borderline male predominance. In contrast, 2 European studies conducted in France [39] (10,038 subjects aged 18–65 years) and Sweden [40] (9,316 subjects aged 18–77 years) supported the persistence of a female predominance in the prevalence of rhinitis during adulthood. The 2 European studies were the only ones that also included middle-aged adults (aged 48–55 years). The other studies either included only elderly subjects, aged ≥ 65 years, or younger adults, aged 18–45 years.

Possible Influencing Factors for the Sex-Related Rhinitis Prevalence Switch

To explore the source of heterogeneity we performed meta-regression analyses with study period (until 2,000 vs. after 2,000), region (Asia vs. rest of the world), and residency (urban vs. rural/urban) as moderator variables. Only during puberty/adolescence and in adulthood, the region showed an effect as a moderator variable influencing the MFR ($p < 0.001$). Meta-regression analyses showed a sex-related rhinitis prevalence switch in studies conducted in non-Asian countries compared to those conducted in Asian countries. Only in the latter, a continuous male predominance from childhood to adulthood was observed.

Regional and Temporal Differences in the Prevalence of Rhinitis between Males and Females

As secondary outcomes, regional differences in the prevalence of rhinitis among males and females were explored (online suppl. Fig. S1, S2). Before puberty, all continents with the exception of the 2 African studies showed an MFR favoring a male predominance. During puberty and throughout adulthood, European, American, and studies conducted in Oceania supported a sex-related switch in rhinitis prevalence towards a female predominance. Studies conducted in Africa showed a borderline

female predominance, whereas Asian studies showed a borderline male predominance.

Temporal differences (before and after the year 2000) in the prevalence of rhinitis among males and females were also assessed (online suppl. Fig. S3, S4). Before puberty, both study periods supported the male predominance in the prevalence of rhinitis. Similarly, both study periods supported the sex-related switch towards a female predominance in the prevalence of rhinitis during puberty and throughout adulthood.

Discussion

Main Findings

This systematic review with meta-analyses confirmed the hypothesis that, as in asthma, there is a sex-switch in the prevalence of rhinitis, which occurs during puberty. We found a male predominance in childhood that shifted towards a slight female predominance at around puberty. However, this did not seem to persist into adulthood, where we saw a rather balanced prevalence between the sexes. We covered studies that recruited children 30 years apart (from 1990 to 2010), but when the pooled estimates were stratified by study period before and after the millennium, our findings did not change. When we stratified the results according to region, the sex-related prevalence switch during puberty was confirmed in studies conducted in Europe, the Americas, Oceania and, of borderline significance, in Africa, but not in the meta-analysis with only Asian studies. These also showed an overall male predominance of rhinitis prevalence in adults.

Strengths and Limitations

We used broad inclusion criteria to take advantage of the available knowledge on the assessment of potential sex differences in the prevalence of rhinitis among the general population. We searched the PubMed and Embase databases, which cover most of the available medical literature. Although we did not restrict our search to specific languages, we may have missed studies if they were published in journals not included in the 2 major databases.

We deliberately limited the search to the present millennium (from 2000 to 2014) since prevalence of allergic diseases and rhinitis may have changed during the last decades. Our pooled estimates relied heavily upon data from studies conducted mainly in Europe and Asia, suggesting that the generalizability of our findings may be affected by the study setting. Even studies conducted in

Asia do not cover the whole continent. Studies conducted in Africa and Oceania were underrepresented, accounting for only 8% of the studies.

We found considerable inconsistency in our main as well as in the subgroup analyses by age, region, and study period, as indicated by the Higgins' I^2 tests. Therefore, caution must be exercised when interpreting the summary measures of the meta-analyses. We explored potential sources of heterogeneity using meta-regression models including several covariates such as study period, region (continent), and residency, and found that "continent" explained some of the inconsistency across the studies. However, neither study period nor having an urban or rural background seemed to influence the sex-switch found during puberty. Furthermore, because the prevalence of allergens varies among Asian countries, such as Korea and Japan, caution must be exercised when interpreting the results from the Asian continent. However, no sex differences have been observed in the prevalence of allergic rhinitis among Korean and Japanese subjects (from childhood to adulthood; online suppl. Fig. S1, S2). AR can be classified as seasonal, perennial or occupational according to the exposed allergens. However, the difficulties in differentiating between seasonal and perennial symptoms have been acknowledged [41]. Cedar pollen is the most prevalent allergen in Japan, and subjects sensitized to cedar pollen are also sensitized to a myriad of other allergens, such as house dust mite, which is very common in all Asian countries. Bearing in mind the limitations of classifying rhinitis according to the type of allergens [41], the Allergic Rhinitis and Its Impact on Asthma (ARIA) initiative has proposed a new classification, "intermittent" or "persistent" rhinitis, based on the duration and severity of symptoms [41, 42]. This classification has been considered in guidelines by many countries, including Korea and Japan [41, 43], to make AR more comparable with Western countries.

In the present systematic review, we specifically included prevalence studies, i.e. cross-sectional investigations that do not allow a longitudinal assessment of a direct shift in the prevalence or incidence between boys and girls. Furthermore, we assessed the prevalence of self-reported and parent-reported symptoms of current rhinitis, defined as the presence of typical symptoms of rhinitis in the last 12 months. This is a widely used method in population studies since rhinitis definitions based on doctors' diagnoses would exclude some milder and moderate allergic rhinitis symptoms and is prone to sex-related bias since in many societies ill women are more likely to seek medical advice than men. The validation of question-

naire-based assessments of allergic rhinitis questions showed in a large Japanese study, for example, a very good diagnostic accuracy of simple questions regarding objective clinical measurements such as serum-specific IgE and tests for nasal eosinophilia [44]. However, we cannot rule out a possible overestimation in the prevalence of rhinitis when using validated questionnaires, such as the ISAAC [31] or ECRHS [32]. On the other hand, we are not aware of any indication that a possible overestimation of the prevalence differs between men and women, thus we assume that this would not affect the MFRs that we evaluated.

Response rates were not provided by sex, with the exception of 2 studies in which participation was similar between the sexes in 1 study (86 vs. 85%) [45], and slightly higher in males in the other (87 vs. 77%) [46]. In our meta-analysis by age group we focused on current rhinitis, defined as symptoms in the last 12 months to include possible seasonal rhinitis.

There was no differentiation between allergic and nonallergic rhinitis and it is possible that the sex switch differs between these diseases. In our review, very few studies examined sensitization to allergens to distinguish between allergic and nonallergic rhinitis by means of IgE or skin prick test. However, they were insufficient to statistically explore the effect of sensitization in males and females across the different age categories.

Comparison with Other Allergic Diseases

We have found several nonsystematic reviews on sex differences in asthma development [3, 5, 11] and other allergy-related diseases [47]. In the case of eczema, an insignificant sex difference or male predominance in preschool children was observed, whereas a female predominance was observed in adulthood [47]. In the case of asthma, a change in sex predominance favoring females has been observed with the transition from childhood to adulthood [3, 5]. Because asthma and rhinitis coexist more often than expected [48], we hypothesized that rhinitis may also undergo similar sex reversal during puberty [49]. Our results support this hypothesis, though they failed to show a female predominance in adulthood, likely due to the limited studies found in adults.

Possible Mechanisms Explaining Sex Differences

Cross-sectional population-based studies do not allow conclusions to be drawn on determinants (longitudinal studies needed) or mechanisms (e.g., experimental studies), but they may be used to generate hypotheses for possible explanations of the sex differences in the prevalence

of rhinitis. The potential determinants reported in the studies were related to anatomical differences, differences in the immune response profile [11, 50, 51], and physiological changes during puberty, such as endogenous [7, 18, 28, 52] or exogenous sexual hormones (birth control pills) [53]. Very few studies assessed the allergic sensitization status of children and adolescents with rhinitis. Other determinants reported were different patterns of vulnerability to lifestyle factors [51, 54] and in the perception of symptoms [55], as well as the use of cosmetics [7]. There is a genetic difference between boys and girls in the susceptibility to environmental exposures, such as gas cooking, smoking, ozone, pets, house dust mites or pollens [5]. Sex-specific differences in environmental exposures such as lifestyles and job patterns cannot be neglected [56]. Because of the complexity of allergy-related diseases, causes and associated factors explaining this phenomenon remain elusive. Although only few genetic studies have been stratified by sex, it seems that there are some asthma-related [3, 57] and allergic rhinitis-related [58] polymorphisms in females.

Implications for Research

Further research is needed to understand the sex-related switch occurring during puberty and fill the gaps in our knowledge. Longitudinal studies are required to confirm these cross-sectional results. Studies should also examine determinants and possible mechanisms for this sex-related rhinitis prevalence switch during puberty, considering allergic sensitization [50, 59–61]. Most of the studies have mainly investigated the prevalence of rhinitis in children, and limited literature has been found in adults likely due to the underestimation of its prevalence and medical significance [37]. Rhinitis in elderly adults is becoming common and studies should also consider this age group. In the present review, the number of studies in adults was scarce, mixing subjects aged between 18 and 65 years and beyond. Further studies in adults are required, particularly segregating premenopausal, menopausal, and post-menopausal females, given that hormonal changes occur during menopause. These should aim to elucidate the influence of sex hormones upon the prevalence of rhinitis using a standardized methodology and preferably also measuring sex hormones in the blood.

Our findings on regional differences are of great interest and may be due to ethnicity or environmental exposure. Research is needed assessing the diversity of rhinitis across the globe. Because rhinitis can have a perennial and a seasonal nature, differences between the northern and the southern hemisphere are expected. A review as-

sessing the prevalence of rhinitis in regions of the world suggested that the prevalence of rhinitis in Europe and the USA was more uniform compared to the greater diversity in the prevalence of rhinitis found in the rest of the world [62]. Our results contradict this study, as we found high heterogeneity both within and between European and American studies, although MFRs were similar.

Conclusions

Our global meta-analysis showed sex-related differences in rhinitis prevalence with a switch at around puberty from a male predominance to a female predominance. The male predominance from childhood seemed to persist in adolescence only in Asia. For the prevalence of rhinitis in adulthood, our systematic evaluation found no predominance in either males or females, although the number of studies was low. In the future, it will be mandatory to perform longitudinal studies differentiating between allergic and nonallergic rhinitis, in which the follow-up is continued into adulthood.

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Disclosure Statement

The authors have no conflicts of interest to declare.

Author Contributions

M.P. and T.K. conceived and designed the experiments. M.P., C.H., M.F., A.R., T. Keller, and B.C. performed the experiments. Data analysis and/or interpretation of the systematic review were conducted by M.P., M.F., A.R., and T. Keller. M.P., T. Keller, A.R., M.F., B.C., C.H., D.S.P., J.B., J.M.A., and T.K. contributed to the writing of the paper.

References

- ▶ 1 Eder W, Ege MJ, von Mutius E: The asthma epidemic. *N Engl J Med* 2006;355:2226–2235.
- ▶ 2 Kurukulaaratchy RJ, Karmaus W, Arshad SH: Sex and atopy influences on the natural history of rhinitis. *Curr Opin Allergy Clin Immunol* 2012;12:7–12.
- ▶ 3 Postma DS: Gender differences in asthma development and progression. *Gend Med* 2007;4(suppl B):S133–S146.
- ▶ 4 Vink NM, Postma DS, Schouten JP, Rosmalen JG, Boezen HM: Gender differences in asthma development and remission during transition through puberty: the Tracking Adolescents' Individual Lives Survey (TRAILS) study. *J Allergy Clin Immunol* 2010;126:498–504.e1–6.
- ▶ 5 Almqvist C, Worm M, Leynaert B: Impact of gender on asthma in childhood and adolescence: a GA²LEN review. *Allergy* 2008;63:47–57.
- ▶ 6 Goldhahn K, Bockelbrink A, Nocon M, Almqvist C, DunnGalvin A, Willich SN, Keil T: Sex-specific differences in allergic sensitization to house dust mites: a meta-analysis. *Ann Allergy Asthma Immunol* 2009;102:487–494.
- ▶ 7 Al-Ghobain MO, Al-Moamary MS, Al-Hajjaj MS, Al-Fayez AI, Basha SI: Prevalence of rhinitis symptoms among 16–18 years old adolescents in Saudi Arabia. *Indian J Chest Dis Allied Sci* 2013;55:11–14.
- ▶ 8 Luna Mde F, Fischer GB, Luna JR, Silva MG, Almeida PC, Chiesa D: Prevalences of asthma and rhinitis among adolescents in the city of Fortaleza, Brazil: temporal changes. *J Bras Pneumol* 2013;39:128–137.
- ▶ 9 Mohammadzadeh I, Ghafari J, Savadkoobi RB, Tamaddon A, Dooki MRE, Navaei RA: The prevalence of asthma, allergic rhinitis and eczema in north of Iran: the International Study of Asthma and Allergies in Childhood (ISAAC). *Iran J Pediatr* 2008;18:117–122.
- ▶ 10 Owayed A, Behbehani N, Al-Momen J: Changing prevalence of asthma and allergic diseases among Kuwaiti children: an ISAAC study (phase III). *Med Princ Pract* 2008;17:284–289.
- ▶ 11 Becklake MR, Kauffmann F: Gender differences in airway behaviour over the human life span. *Thorax* 1999;54:1119–1138.
- ▶ 12 Moher D, Liberati A, Tetzlaff J, Altman DG: Preferred reporting items for systematic reviews and meta-analyses: the Prisma Statement. *Int J Surg (London)* 2010;8:336–341.
- ▶ 13 Chiang LC, Chen YH, Hsueh KC, Huang JL: Prevalence and severity of symptoms of asthma, allergic rhinitis, and eczema in 10–15-year-old schoolchildren in central Taiwan. *Asian Pac J Allergy Immunol* 2007;25:1–5.
- ▶ 14 Dennis R, Caraballo L, Garcia E, Caballero A, Aristizabal G, Cordoba H, Rodriguez MN, Rojas MX, Orduz C, Cardona R, Blanco A, Egea E, Verbel C, Cala LL: Asthma and other allergic conditions in Colombia: a study in 6 cities. *Ann Allergy Asthma Immunol* 2004;93:568–574.
- ▶ 15 Li F, Zhou Y, Li S, Jiang F, Jin X, Yan C, Tian Y, Zhang Y, Tong S, Shen X: Prevalence and risk factors of childhood allergic diseases in eight metropolitan cities in China: a multicenter study. *BMC Public Health* 2011;11:437.
- ▶ 16 Olivieri M, Verlato G, Corsico A, Lo Cascio V, Bugiani M, Marinoni A, de Marco R: Prevalence and features of allergic rhinitis in Italy. *Allergy* 2002;57:600–606.
- ▶ 17 Selnes A, Nystad W, Bolle R, Lund E: Diverging prevalence trends of atopic disorders in Norwegian children: results from three cross-sectional studies. *Allergy* 2005;60:894–899.
- ▶ 18 Ahn K, Kim J, Kwon HJ, Chae Y, Hahm MI, Lee KJ, Park YM, Lee SY, Han M, Kim WK: The prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in Korean children: nationwide cross-sectional survey using complex sampling design (in Korean). *J Kor Med Assoc* 2011;54:769–778.
- ▶ 19 Al-Riyami BM, Al-Rawas OA, Al-Riyami AA, Jasim LG, Mohammed AJ: A relatively high prevalence and severity of asthma, allergic rhinitis and atopic eczema in schoolchildren in the Sultanate of Oman. *Respirology (Carlton)* 2003;8:69–76.
- ▶ 20 Del-Rio-Navarro BE, Luna-Pech JA, Berber A, Zepeda-Ortega B, Avila-Castañón L, Del-Rio-Chivardi JM, Baeza-Bacab M, Sienra-Monge JJ: Factors associated with allergic rhinitis in children from northern Mexico City. *J Investig Allergol Clin Immunol* 2007;17:77–84.
- ▶ 21 Futamura M, Ohya Y, Akashi M, Adachi Y, Odajima H, Akiyama K, Akasawa A: Age-related prevalence of allergic diseases in Tokyo schoolchildren. *Allergol Int* 2011;60:509–515.
- ▶ 22 Higuchi O, Adachi Y, Itazawa T, Ito Y, Yoshida K, Ohya Y, Odajima H, Akasawa A, Miyawaki T: Relationship between rhinitis and nocturnal cough in school children. *Pediatr Allergy Immunol* 2012;23:562–566.
- ▶ 23 Hong S, Son DK, Lim WR, Kim SH, Kim H, Yum HY, Kwon H: The prevalence of atopic dermatitis, asthma, and allergic rhinitis and the comorbidity of allergic diseases in children. *Environ Health Toxicol* 2012;27:e2012006.
- ▶ 24 Kahwa EK, Waldron NK, Younger NO, Edwards NC, Knight-Madden JM, Bailey KA, Wint YB, Lewis-Bell KN: Asthma and allergies in Jamaican children aged 2–17 years: a cross-sectional prevalence survey. *BMJ Open* 2012;2:e001132.
- ▶ 25 Kao CC, Huang JL, Ou LS, See LC: The prevalence, severity and seasonal variations of asthma, rhinitis and eczema in Taiwanese schoolchildren. *Pediatr Allergy Immunol* 2005;16:408–415.
- ▶ 26 Lévesque B, Rhainds M, Ernst P, Grenier AM, Kosatsky T, Audet N, Lajoie P: Asthma and allergic rhinitis in Quebec children. *Can Respir J* 2004;11:343–348.
- ▶ 27 Mavale-Manuel S, Joaquim O, Macome C, Almeida L, Nunes E, Daniel A, Malichocho J, Pedro A, Bandeira S, Eduardo E, Maciel L, Constance E, Marques S, Tembe A, de Blic J, Annesi-Maesano I: Asthma and allergies in schoolchildren of Maputo. *Allergy* 2007;62:265–271.
- ▶ 28 Moyes CD, Clayton T, Pearce N, Asher MI, Ellwood P, Mackay R, Mitchell E, Pattemore P, Stewart AW, Crane J: Time trends and risk factors for rhinoconjunctivitis in New Zealand children: an international study of asthma and allergies in childhood (ISAAC) survey. *J Paediatr Child Health* 2012;48:913–920.
- ▶ 29 Penaranda A, Aristizabal G, Garcia E, Vasquez C, Rodriguez-Martinez CE: Rhinoconjunctivitis prevalence and associated factors in school children aged 6–7 and 13–14 years old in Bogota, Colombia. *Int J Pediatr Otorhinolaryngol* 2012;76:530–535.
- ▶ 30 Soto-Quiros ME, Soto-Martinez M, Hanson LA: The high prevalence of rhinitis, rhinoconjunctivitis, and eczema in Costa Rican schoolchildren studied with the ISAAC protocol. *Pediatr Asthma Allergy Immunol* 2004;17:71–80.
- ▶ 31 Asher MI, Keil U, Anderson HR, Beasley R, Crane J, Martinez F, Mitchell EA, Pearce N, Sibbald B, Stewart AW, et al: International study of asthma and allergies in childhood (ISAAC): rationale and methods. *Eur Respir J* 1995;8:483–491.
- ▶ 32 Burney PG, Luczynska C, Chinn S, Jarvis D: The European Community Respiratory Health Survey. *Eur Respir J* 1994;7:954–960.
- ▶ 33 Suh M, Kim HH, Sohn MH, Kim KE, Kim C, Shin DC: Prevalence of allergic diseases among Korean school-age children: a nationwide cross-sectional questionnaire study. *J Kor Med Sci* 2011;26:332–338.
- ▶ 34 Arnedo-Pena A, Garcia-Marcos L, Garcia Hernandez G, Aguinagua Ontoso I, Gonzalez Diaz C, Morales Suarez-Varela M, Dominguez Aurrecochea B, Busquets Monge R, Blanco Quiros A, Batlles Garrido J, Miner Kanflanka I, Lopez-Silvarrey Varela A: Time trends and geographical variations in the prevalence of symptoms of allergic rhinitis in 6–7-year-old children from eight areas of Spain according to the ISAAC (in Spanish). *An Pediatr (Barc)* 2005;62:229–236.
- ▶ 35 Zar HJ, Ehrlich RI, Workman L, Weinberg EG: The changing prevalence of asthma, allergic rhinitis and atopic eczema in African adolescents from 1995 to 2002. *Pediatr Allergy Immunol* 2007;18:560–565.
- ▶ 36 Luna Mde F, Almeida PC, Silva MG: Asthma and rhinitis prevalence and co-morbidity in 13–14-year-old schoolchildren in the city of Fortaleza, Ceara State, Brazil (in Portuguese). *Cad Saude Publica* 2011;27:103–112.

- ▶ 37 Song WJ, Kim MY, Jo EJ, Kim MH, Kim TH, Kim SH, Kim KW, Cho SH, Min KU, Chang YS: Rhinitis in a community elderly population: relationships with age, atopy, and asthma. *Ann Allergy Asthma Immunol* 2013;111:347–351.
- ▶ 38 Desalu OO, Salami AK, Iseh KR, Oluboyo PO: Prevalence of self reported allergic rhinitis and its relationship with asthma among adult Nigerians. *J Investig Allergol Clin Immunol* 2009;19:474–480.
- ▶ 39 Klossek JM, Annesi-Maesano I, Pribil C, Didier A: INSTANT: national survey of allergic rhinitis in a French adult population-based sample (in French). *Presse Med (Paris)* 2009;38:1220–1229.
- ▶ 40 Lindgren A, Stroh E, Nihlén U, Montn  mery P, Axmon A, Jakobsson K: Traffic exposure associated with allergic asthma and allergic rhinitis in adults: a cross-sectional study in Southern Sweden. *Int J Health Geogr* 2009;8:25.
- ▶ 41 Lee CH, Jang JH, Lee HJ, Kim IT, Chu MJ, Kim CD, Won YS, Kim JW: Clinical characteristics of allergic rhinitis according to allergic rhinitis and its impact on asthma guidelines. *Clin Exp Otorhinolaryngol* 2008;1:196–200.
- ▶ 42 Bousquet J, van Cauwenberge P, Khaltaev N: Allergic rhinitis and its impact on asthma. *J Allergy Clin Immunol* 2001;108:S147–S334.
- ▶ 43 Okubo K, Kurono Y, Fujieda S, Ogino S, Uchio E, Odajima H, Takenaka H: Japanese guideline for allergic rhinitis 2014. *Allergol Int* 2014;63:357–375.
- ▶ 44 Okuda M: Epidemiology of Japanese cedar pollinosis throughout Japan. *Ann Allergy Asthma Immunol* 2003;91:288–296.
- ▶ 45 Nahhas M, Bhopal R, Anandan C, Elton R, Sheikh A: Prevalence of allergic disorders among primary school-aged children in Madinah, Saudi Arabia: two-stage cross-sectional survey. *PLoS One* 2012;7:e36848.
- ▶ 46 Falade AG, Olawuyi JF, Osinusi K, Onadeko BO: Prevalence and severity of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema in 6- to 7-year-old Nigerian primary school children: the International Study of Asthma and Allergies in Childhood. *Med Princ Pract* 2004;13:20–25.
- ▶ 47 Chen W, Mempel M, Schober W, Behrendt H, Ring J: Gender difference, sex hormones, and immediate type hypersensitivity reactions. *Allergy* 2008;63:1418–1427.
- ▶ 48 Pinart M, Benet M, Annesi-Maesano I, et al: Comorbidity of eczema, rhinitis, and asthma in IgE-sensitized and non-IgE-sensitized children in MeDALL: a population-based cohort study. *Lancet Respir Med* 2014;2:131–140.
- ▶ 49 Kurukulaarachy RJ, Karmaus W, Raza A, Matthews S, Roberts G, Arshad SH: The influence of gender and atopy on the natural history of rhinitis in the first 18 years of life. *Clin Exp Allergy* 2011;41:851–859.
- ▶ 50 Kong WJ, Chen JJ, Zheng ZY, Shi QM, Zhou Y: Prevalence of allergic rhinitis in 3–6-year-old children in Wuhan of China. *Clin Exp Allergy* 2009;39:869–874.
- ▶ 51 Maziak W, Behrens T, Brasky TM, Duhme H, Rzehak P, Weiland SK, Keil U: Are asthma and allergies in children and adolescents increasing? Results from ISAAC phase I and phase III surveys in Munster, Germany. *Allergy* 2003;58:572–579.
- ▶ 52 Brito Rde C, da Silva GA, Motta ME, Brito MC: The association of rhinoconjunctivitis and asthma symptoms in adolescents. *Rev Port Pneumol* 2009;15:613–628.
- ▶ 53 Fagan JK, Scheff PA, Hryhorczuk D, Ramakrishnan V, Ross M, Persky V: Prevalence of asthma and other allergic diseases in an adolescent population: association with gender and race. *Ann Allergy Asthma Immunol* 2001;86:177–184.
- ▶ 54 Kudzyte J, Griska E, Bojarskas J: Time trends in the prevalence of asthma and allergy among 6–7-year-old children: results from ISAAC phase I and III studies in Kaunas, Lithuania. *Medicina (Kaunas)* 2008;44:944–952.
- ▶ 55 Brescianini S, Brunetto B, Iacovacci P, D’Ippolito C, Alberti G, Schirru MA, Stazi MA, Pini C, Di Felice G, Barletta B: Prevalence of self-perceived allergic diseases and risk factors in Italian adolescents. *Pediatr Allergy Immunol* 2009;20:578–584.
- ▶ 56 Liebhart J, Dobek R, Malolepszy J, Wojtyniak B, Pisiewicz K, Plusa T, Gladysz U: The prevalence of allergic diseases in Poland – the results of the PMSEAD study in relation to gender differences. *Adv Clin Exp Med* 2014;23:757–762.
- ▶ 57 Schieck M, Schouten JP, Michel S, et al: Doublesex and mab-3 related transcription factor 1 (DMRT1) is a sex-specific genetic determinant of childhood-onset asthma and is expressed in testis and macrophages. *J Allergy Clin Immunol* 2016;138:421–431.
- ▶ 58 Fodor E, Garaczi E, Polyanka H, Koreck A, Kemeny L, Szell M: The rs3761548 polymorphism of FOXP3 is a protective genetic factor against allergic rhinitis in the Hungarian female population. *Hum Immunol* 2011;72:926–929.
- ▶ 59 Filipiak B, Heinrich J, Nowak D, Wichmann HE: The distribution in specific IgE and the prevalence of allergic symptoms in 25–64-years old inhabitants of an eastern and a western German city – results from Augsburg and Erfurt. *Eur J Epidemiol* 2001;17:77–84.
- ▶ 60 Hahm MI, Chae Y, Kwon HJ, Kim J, Ahn K, Kim WK, Lee SY, Park YM, Han MY, Lee KJ, Lee HY, Min I: Do newly built homes affect rhinitis in children? The ISAAC phase III study in Korea. *Allergy* 2014;69:479–487.
- ▶ 61 Kim SH, Kim YK, Lee MH, Hong SC, Bae JM, Min KU, Kim YY, Cho SH: Relationship between sensitization to citrus red mite (*Panonychus citri*) and the prevalence of atopic diseases in adolescents living near citrus orchards. *Clin Exp Allergy* 2002;32:1054–1058.
- ▶ 62 Katelaris CH, Lee BW, Potter PC, Maspero JF, Cingi C, Lopatin A, Saffer M, Xu G, Walters RD: Prevalence and diversity of allergic rhinitis in regions of the world beyond Europe and North America. *Clin Exp Allergy* 2012;42:186–207.
- ▶ 63 Zhao TB, Wang HJ, Chen YZ, Xiao ML, Duo LK, Liu G, Lau YL, Karlberg J: Prevalence of childhood asthma, allergic rhinitis and eczema in Urumqi and Beijing. *J Paediatr Child Health* 2000;36:128–133.
- ▶ 64 Al-Riyami BM, Al-Rawas OA, Al-Riyami AA, Jasim LG, Mohammed AJ: A relatively high prevalence and severity of asthma, allergic rhinitis and atopic eczema in schoolchildren in the sultanate of Oman. *Respirology (Carlton)* 2003;8:69–76.
- ▶ 65 Peroni DG, Piacentini GL, Alfonsi L, Zerman L, Di Blasi P, Visona G, Nottogar F, Boner AL: Rhinitis in pre-school children: prevalence, association with allergic diseases and risk factors. *Clin Exp Allergy* 2003;33:1349–1354.
- ▶ 66 Garcia-Marcos L, Morales Suarez-Varela M, Miner Canflanca I, Batlles Garrido J, Blanco Quiros A, Lopez-Silvarrey Varela A, Garcia Hernandez G, Guillen-Grima F, Gonzalez Diaz C, Huerta Gonzalez I, Arnedo Pena A, Busquets Monge R: BCG immunization at birth and atopic diseases in a homogeneous population of Spanish schoolchildren. *Int Arch Allergy Immunol* 2005;137:303–309.
- ▶ 67 Liao MF, Huang JL, Chiang LC, Wang FY, Chen CY: Prevalence of asthma, rhinitis, and eczema from ISAAC survey of schoolchildren in central Taiwan. *J Asthma* 2005;42:833–837.
- ▶ 68 Lima RG, Pastorino AC, Casagrande RR, Sole D, Leone C, Jacob CM: Prevalence of asthma, rhinitis and eczema in 6–7 years old students from the western districts of Sao Paulo City, using the standardized questionnaire of the “International Study of Asthma and Allergies in Childhood” (ISAAC)-phase IIIB. *Clinics (Sao Paulo)* 2007;62:225–234.
- ▶ 69 Rad MH, Hamzezhadeh A: Allergic disease in 6–7-year-old schoolchildren in Urmia, Islamic Republic of Iran. *East Mediterr Health J* 2008;14:1044–1053.
- ▶ 70 Anthracopoulos MB, Antonogeorgos G, Lioios E, Triga M, Panagiotopoulou E, Priftis KN: Increase in chronic or recurrent rhinitis, rhinoconjunctivitis and eczema among schoolchildren in Greece: three surveys during 1991–2003. *Pediatr Allergy Immunol* 2009;20:180–186.
- ▶ 71 Backer C, Barraza-Villarrea A, Moreno-Macfas H, Escamilla-Nunez C, Romieru EI: The effects of a rural environment on the prevalence of allergic rhinitis among schoolchildren in Mexicali, Baja California, Mexico (in Spanish). *Rev Panam Salud Publica* 2009;25:431–437.
- ▶ 72 Tai A, Volkmer R, Burton A: Prevalence of asthma symptoms and atopic disorders in preschool children and the trend over a decade. *J Asthma* 2009;46:343–346.
- ▶ 73 Amarasekera ND, Gunawardena NK, de Silva NR, Weerasinghe A: Prevalence of childhood atopic diseases in the western province of Sri Lanka. *Ceylon Med J* 2010;55:5–8.

- 74 Castro LK, Cerci Neto A, Ferreira Filho OF: Prevalence of symptoms of asthma, rhinitis and atopic eczema among students between 6 and 7 years of age in the city of Londrina, Brazil. *J Bras Pneumol* 2010;36:286–292.
- 75 Dell SD, Foty RG, Gilbert NL, Jerrett M, To T, Walter SD, Stieb DM: Asthma and allergic disease prevalence in a diverse sample of Toronto school children: results from the Toronto Child Health Evaluation Questionnaire (T-CHEQ) study. *Can Respir J* 2010;17:e1–e6.
- 76 Kurosaka F, Terada T, Tanaka A, Nakatani Y, Yamada K, Nishikawa J, Oka K, Takahashi H, Mogami A, Yamada T, Nakano T, Shima M, Nishio H: Risk factors for wheezing, eczema and rhinoconjunctivitis in the previous 12 months among six-year-old children in Himeji City, Japan: food allergy, older siblings, day-care attendance and parental allergy history. *Allergol Int* 2011;60:317–330.
- 77 Duggan EM, Sturley J, Fitzgerald AP, Perry IJ, Hourihane JO: The 2002–2007 trends of prevalence of asthma, allergic rhinitis and eczema in Irish schoolchildren. *Pediatr Allergy Immunol* 2012;23:464–471.
- 78 Morais-Almeida M, Santos N, Pereira AM, Branco-Ferreira M, Nunes C, Bousquet J, Fonseca JA: Prevalence and classification of rhinitis in preschool children in Portugal: a nationwide study. *Allergy* 2013;68:1278–1288.
- 79 Tamay Z, Akcay A, Ergin A, Guler N: Prevalence of allergic rhinitis and risk factors in 6- to 7-year-old children in Istanbul, Turkey. *Turk J Pediatr* 2014;56:31–40.
- 80 Sugiyama K, Sugiyama T, Toda M, Yukawa T, Makino S, Fukuda T: Prevalence of asthma, rhinitis and eczema among 13–14-year-old schoolchildren in Tochigi, Japan. *Allergol Int* 2000;49:205–211.
- 81 Shamssain MH, Shamsian N: Prevalence and severity of asthma, rhinitis, and atopic eczema in 13- to 14-year-old schoolchildren from the northeast of England. *Ann Allergy Asthma Immunol* 2001;86:428–432.
- 82 Arnedo-Pena A, Garcia-Marcos L, Blanco-Queros A, Gimeno AM, Ontoso IA, Diaz CG, Vazquez CD, Busquets-Monge R, Suarez-Varela MM, Garrido JB, Varela ALS, De Andoin NG: Time trends in prevalence of symptoms of allergic rhinitis in 13–14 year-old schoolchildren in 8 areas of Spain between 1993–1994 and 2001–2002 according to the international study of asthma and allergies in childhood (ISAAC) (in Spanish). *Med Clin (Barc)* 2004;123:490–495.
- 83 Nordvall SL, Janson C, Kalm-Stephens P, Foucard T, Torén K, Alving K: Exhaled nitric oxide in a population-based study of asthma and allergy in schoolchildren. *Allergy* 2005;60:469–475.
- 84 Yan DC, Ou LS, Tsai TL, Wu WF, Huang JL: Prevalence and severity of symptoms of asthma, rhinitis, and eczema in 13- to 14-year-old children in Taipei, Taiwan. *Ann Allergy Asthma Immunol* 2005;95:579–585.
- 85 Porto Neto AC, D'Agostini Annes R, Wolff NMM, Klein AP, Dos Santos FC, Dullius JL, Gressler M, Muller LS, Angonese CF, Menna-Barreto S: Prevalence and severity of asthma, rhinitis, and atopic eczema in 13- to 14-year-old schoolchildren from southern Brazil. *Allergy Asthma Clin Immunol* 2006;2:3–10.
- 86 Droma Y, Kunii O, Yangzom Y, Shan M, Pingzo L, Song P: Prevalence and severity of asthma and allergies in schoolchildren in Lhasa, Tibet. *Clin Exp Allergy* 2007;37:1326–1333.
- 87 Munivrana H, Vorko-Jovic A, Munivrana S, Kursar M, Medlobi-Gluhak M, Vlahek P: The prevalence of allergic diseases among croatian school children according to the ISAAC phase one questionnaire. *Med Sci Monit* 2007;13:CR505–CR509.
- 88 Pac-Sa MR, Museros-Recatala L, Arnedo-Pena A, Bellido-Blasco JB, Puig-Barbera J, Artero-Sivera A, Campos-Cruanes JB, Aguinaga-Ontoso I: Risk factors for symptoms of allergic rhinitis in adolescents in Castellon, Spain (in Spanish). *Rev Panam Salud Publica* 2008;23:333–340.
- 89 Musharrafieh U, Al-Sahab B, Zaitoun F, El-Hajj MA, Ramadan F, Tamim H: Prevalence of asthma, allergic rhinitis and eczema among Lebanese adolescents. *J Asthma* 2009;46:382–387.
- 90 Narayana PP, Prasanna MP, Narahari SR, Guruprasad AM: Prevalence of asthma in school children in rural India. *Ann Thorac Med* 2010;5:118–119.
- 91 Wang HY, Pizzichini MM, Becker AB, Duncan JM, Ferguson AC, Greene JM, Rennie DC, Senthilselvan A, Taylor BW, Sears MR: Disparate geographic prevalences of asthma, allergic rhinoconjunctivitis and atopic eczema among adolescents in five Canadian cities. *Pediatr Allergy Immunol* 2010;21:867–877.
- 92 Toledo MF, Rozov T, Leone C: Prevalence of asthma and allergies in 13- to 14-year-old adolescents and the frequency of risk factors in carriers of current asthma in Taubate, Sao Paulo, Brazil. *Allergol Immunopathol* 2011;39:284–290.
- 93 Bjerg A, Ekerljung L, Middelvelld R, Dahlén SE, Forsberg B, Franklin K, Larsson K, Lötvall J, Olafsdóttir IS, Torén K, Lundbäck B, Janson C: Increased prevalence of symptoms of rhinitis but not of asthma between 1990 and 2008 in Swedish adults: comparisons of the ECRHS and GA²LEN surveys. *PLoS One* 2011;6:e16082.
- 94 Riguera D, Andre PA, Zanetta DM: Sugar cane burning pollution and respiratory symptoms in schoolchildren in Monte Aprazivel, Southeastern Brazil. *Rev Saude Publica* 2011;45:878–886.
- 95 Tamay Z, Akcay A, Ergin A, Guler N: Effects of dietary habits and risk factors on allergic rhinitis prevalence among Turkish adolescents. *Int J Pediatr Otorhinolaryngol* 2013;77:1416–1423.
- 96 Amizadeh M, Safizadeh H, Bazargan N, Farrokhdost Z: Survey on the prevalence of allergic rhinitis and its effect on the quality of high school students' life. *Iran J Otorhinolaryngol* 2013;25:79–84.
- 97 Sonomjams M, Dashdemberel S, Logii N, Nakae K, Chigusa Y, Ohhira S, Ito C, Sagara H, Makino S: Prevalence of asthma and allergic rhinitis among adult population in Ulaanbaatar, Mongolia. *Asia Pac Allergy* 2014;4:25–31.

LEGENDS IN THE SUPPLEMENT

Search strategies. Search terms and equations used for this review in PubMed and Embase databases

Table S1. Characteristics of the included studies assessing prevalence of rhinitis before puberty (<11y)

Table S2. Characteristics of the included studies assessing prevalence of rhinitis during and shortly after puberty (11-<18y)

Table S3. Characteristics of the included studies assessing prevalence of rhinitis in adults

Table S4. Study quality assessment of the included studies

Figure S1. Forest plot estimating sex differences in the prevalence of rhinitis before puberty stratified by continent. The term “Events” corresponds to the number of children with current rhinitis.

Figure S2. Forest plot estimating sex difference in prevalence of rhinitis between males and females during and after puberty (aged 11-<18 years) and throughout adulthood (18+ years) stratified by continent. The term “Events” corresponds to the number of children with current rhinitis.

Figure S3. Forest plot estimating the difference in prevalence of rhinitis between boys and girls aged up to the age of 10 years (before puberty) stratified by study period (before the year 2000). The term “Events” corresponds to the number of children with current rhinitis.

Figure S4. Forest plot estimating the difference in prevalence of rhinitis between males and females during and after puberty (aged 11-<18 years) and throughout adulthood (18+ years) stratified by study period (after the year 2000). The term “Events” corresponds to the number of children with current rhinitis.

S-References. References of the 85 included studies.

Supplementary References

- S1 Ahn K, Kim J, Kwon HJ, Chae Y, Hahm MI, Lee KJ, Park YM, Lee SY, Han M, Kim WK: The prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in korean children: Nationwide cross-sectional survey using complex sampling design. [korean]. Journal of the Korean Medical Association 2011;54:769-778.
- S2 Al-Riyami BM, Al-Rawas OA, Al-Riyami AA, Jasim LG, Mohammed AJ: A relatively high prevalence and severity of asthma, allergic rhinitis and atopic eczema in schoolchildren in the sultanate of oman. Respirology (Carlton, Vic) 2003;8:69-76.
- S3 Amarasekera ND, Gunawardena NK, de Silva NR, Weerasinghe A: Prevalence of childhood atopic diseases in the western province of sri lanka. The Ceylon medical journal 2010;55:5-8.
- S4 Annesi-Maesano I, Hulin M, Lavaud F, Raherison C, Kopferschmitt C, de Blay F, Charpin DA, Denis C: Poor air quality in classrooms related to asthma and rhinitis in primary schoolchildren of the french 6 cities study. Thorax 2012;67:682-688.
- S5 Anthracopoulos MB, Antonogeorgos G, Liolios E, Triga M, Panagiotopoulou E, Priftis KN: Increase in chronic or recurrent rhinitis, rhinoconjunctivitis and eczema among schoolchildren in greece: Three surveys during 1991-2003. Pediatric allergy and immunology: official publication of the European Society of Pediatric Allergy and Immunology 2009;20:180-186.
- S6 Arnedo-Pena A, Garcia-Marcos L, Garcia Hernandez G, Aguinagua Ontoso I, Gonzalez Diaz C, Morales Suarez-Varela M, Dominguez Aurrecoechea B, Busquets Monge R, Blanco Quiros A, Batlles Garrido J, Miner Kanflanka I, Lopez-Silvarrey Varela A: Time trends and geographical variations in the prevalence of symptoms of allergic rhinitis in 6-7-year-old children from eight areas of spain according to the isaac. [spanish] tendencia

temporal y variaciones geograficas de la prevalencia de sintomas de rinitis alergica en escolares de 6-7 anos de ocho areas espanolas, segun el isaac. *Anales de Pediatría* 2005;62:229-236.

S7 Backer C, Barraza-Villarrea A, Moreno-Macfas H, Escamilla-Nunez C, Romieru EI: The effects of a rural environment on the prevalence of allergic rhinitis among schoolchildren in mexicali, baja california, mexico. [spanish] efecto del ambiente rural sobre la prevalencia de rinitis alergica en escolares de mexicali, baja california, mexico. *Revista Panamericana de Salud Publica/Pan American Journal of Public Health* 2009;25:431-437.

S8 Castro LK, Cerci Neto A, Ferreira Filho OF: Prevalence of symptoms of asthma, rhinitis and atopic eczema among students between 6 and 7 years of age in the city of londrina, brazil. *Jornal brasileiro de pneumologia: publicacao oficial da Sociedade Brasileira de Pneumologia e Tisiologia* 2010;36:286-292.

S9 Dell SD, Foty RG, Gilbert NL, Jerrett M, To T, Walter SD, Stieb DM: Asthma and allergic disease prevalence in a diverse sample of toronto school children: Results from the toronto child health evaluation questionnaire (t-cheq) study. *Canadian Respiratory Journal* 2010;17:e1-e6.

S10 Del-Rio-Navarro BE, Luna-Pech JA, Berber A, Zepeda-Ortega B, Avila-Castanon L, Del-Rio-Chivardi JM, Baeza-Bacab M, Sienra-Monge JJ: Factors associated with allergic rhinitis in children from northern mexico city. *Journal of investigational allergology & clinical immunology* 2007;17:77-84.

S11 Duggan EM, Sturley J, Fitzgerald AP, Perry IJ, Hourihane JO: The 2002-2007 trends of prevalence of asthma, allergic rhinitis and eczema in irish schoolchildren. *Pediatric allergy and immunology: official publication of the European Society of Pediatric Allergy and Immunology* 2012;23:464-471.

S12 Falade AG, Olawuyi JF, Osinusi K, Onadeko BO: Prevalence and severity of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema in 6- to 7-year-old nigerian primary school children: The international study of asthma and allergies in childhood. Medical principles and practice : international journal of the Kuwait University, Health Science Centre 2004;13:20-25.

S13 Futamura M, Ohya Y, Akashi M, Adachi Y, Odajima H, Akiyama K, Akasawa A: Age-related prevalence of allergic diseases in tokyo schoolchildren. Allergology international : official journal of the Japanese Society of Allergology 2011;60:509-515.

S14 Garcia-Marcos L, Morales Suarez-Varela M, Miner Canflanca I, Batlles Garrido J, Blanco Quiros A, Lopez-Silvarrey Varela A, Garcia Hernandez G, Guillen-Grima F, Gonzalez Diaz C, Huerta Gonzalez I, Arnedo Pena A, Busquets Monge R: Bcg immunization at birth and atopic diseases in a homogeneous population of spanish schoolchildren. International archives of allergy and immunology 2005;137:303-309.

S15 Hahm MI, Chae Y, Kwon HJ, Kim J, Ahn K, Kim WK, Lee SY, Park YM, Han MY, Lee KJ, Lee HY, Min I: Do newly built homes affect rhinitis in children? The isaac phase iii study in korea. Allergy 2014;69:479-487.

S16 Higuchi O, Adachi Y, Itazawa T, Ito Y, Yoshida K, Ohya Y, Odajima H, Akasawa A, Miyawaki T: Relationship between rhinitis and nocturnal cough in school children. Pediatric allergy and immunology : official publication of the European Society of Pediatric Allergy and Immunology 2012;23:562-566.

S17 Hong S, Son DK, Lim WR, Kim SH, Kim H, Yum HY, Kwon H: The prevalence of atopic dermatitis, asthma, and allergic rhinitis and the comorbidity of allergic diseases in children. Environmental health and toxicology 2012;27:e2012006.

S18 Kahwa EK, Waldron NK, Younger NO, Edwards NC, Knight-Madden JM, Bailey KA, Wint YB, Lewis-Bell KN: Asthma and allergies in jamaican children aged 2-17 years: A cross-sectional prevalence survey. *BMJ open* 2012;2

S19 Kao CC, Huang JL, Ou LS, See LC: The prevalence, severity and seasonal variations of asthma, rhinitis and eczema in taiwanese schoolchildren. *Pediatric allergy and immunology : official publication of the European Society of Pediatric Allergy and Immunology* 2005;16:408-415.

S20 Kong WJ, Chen JJ, Zheng ZY, Shi QM, Zhou Y: Prevalence of allergic rhinitis in 3-6-year-old children in wuhan of china. *Clinical and experimental allergy : journal of the British Society for Allergy and Clinical Immunology* 2009;39:869-874.

S21 Kudzyte J, Griska E, Bojarskas J: Time trends in the prevalence of asthma and allergy among 6-7-year-old children. Results from isaac phase i and iii studies in kaunas, lithuania. *Medicina (Kaunas, Lithuania)* 2008;44:944-952.

S22 Kurosaka F, Terada T, Tanaka A, Nakatani Y, Yamada K, Nishikawa J, Oka K, Takahashi H, Mogami A, Yamada T, Nakano T, Shima M, Nishio H: Risk factors for wheezing, eczema and rhinoconjunctivitis in the previous 12 months among six-year-old children in himeji city, japan: Food allergy, older siblings, day-care attendance and parental allergy history. *Allergology international : official journal of the Japanese Society of Allergology* 2011;60:317-330.

S23 Levesque B, Rhains M, Ernst P, Grenier AM, Kosatsky T, Audet N, Lajoie P: Asthma and allergic rhinitis in quebec children. *Canadian respiratory journal : journal of the Canadian Thoracic Society* 2004;11:343-348.

S24 Liao MF, Huang JL, Chiang LC, Wang FY, Chen CY: Prevalence of asthma, rhinitis, and eczema from isaac survey of schoolchildren in central taiwan. The Journal of asthma : official journal of the Association for the Care of Asthma 2005;42:833-837.

S25 Lima RG, Pastorino AC, Casagrande RR, Sole D, Leone C, Jacob CM: Prevalence of asthma, rhinitis and eczema in 6 - 7 years old students from the western districts of sao paulo city, using the standardized questionnaire of the "international study of asthma and allergies in childhood" (isaac)-phase iiib. Clinics (Sao Paulo, Brazil) 2007;62:225-234.

S26 Mavale-Manuel S, Joaquim O, Macome C, Almeida L, Nunes E, Daniel A, Malichocho J, Pedro A, Bandeira S, Eduardo E, Maciel L, Constance E, Marques S, Tembe A, de Blic J, Annesi-Maesano I: Asthma and allergies in schoolchildren of maputo. Allergy 2007;62:265-271.

S27 Maziak W, Behrens T, Brasky TM, Duhme H, Rzehak P, Weiland SK, Keil U: Are asthma and allergies in children and adolescents increasing? Results from isaac phase i and phase iii surveys in munster, germany. Allergy 2003;58:572-579.

S28 Mohammadzadeh I, Ghafari J, Savadkoobi RB, Tamaddon A, Dooki MRE, Navaei RA: The prevalence of asthma, allergic rhinitis and eczema in north of iran: The international study of asthma and allergies in childhood (isaac). Iranian Journal of Pediatrics 2008;18:117-122.

S29 Montefort S, Muscat HA, Caruana S, Lenicker H: Allergic conditions in 5-8-year-old maltese schoolchildren: Prevalence, severity, and associated risk factors [isaac]. Pediatric allergy and immunology : official publication of the European Society of Pediatric Allergy and Immunology 2002;13:98-104.

S30 Morais-Almeida M, Santos N, Pereira AM, Branco-Ferreira M, Nunes C, Bousquet J, Fonseca JA: Prevalence and classification of rhinitis in preschool children in portugal: A nationwide study. *Allergy* 2013;68:1278-1288.

S31 Moyes CD, Clayton T, Pearce N, Asher MI, Ellwood P, Mackay R, Mitchell E, Pattemore P, Stewart AW, Crane J: Time trends and risk factors for rhinoconjunctivitis in new zealand children: An international study of asthma and allergies in childhood (isaac) survey. *Journal of paediatrics and child health* 2012;48:913-920.

S32 Nahhas M, Bhopal R, Anandan C, Elton R, Sheikh A: Prevalence of allergic disorders among primary school-aged children in madinah, saudi arabia: Two-stage cross-sectional survey. *PloS one* 2012;7:e36848.

S33 Okuda M: Epidemiology of japanese cedar pollinosis throughout japan. *Annals of allergy, asthma & immunology: official publication of the American College of Allergy, Asthma, & Immunology* 2003;91:288-296.

S34 Penaranda A, Aristizabal G, Garcia E, Vasquez C, Rodriguez-Martinez CE: Rhinoconjunctivitis prevalence and associated factors in school children aged 6-7 and 13-14 years old in bogota, colombia. *International journal of pediatric otorhinolaryngology* 2012;76:530-535.

S35 Peroni DG, Piacentini GL, Alfonsi L, Zerman L, Di Blasi P, Visona G, Nottegar F, Boner AL: Rhinitis in pre-school children: Prevalence, association with allergic diseases and risk factors. *Clinical and experimental allergy : journal of the British Society for Allergy and Clinical Immunology* 2003;33:1349-1354.

S36 Rad MH, Hamzezadeh A: Allergic disease in 6--7-year-old schoolchildren in urmia, islamic republic of iran. *Eastern Mediterranean health journal = La revue de sante de la Mediterranee orientale = al-Majallah al-sihhiyah li-sharq al-mutawassit* 2008;14:1044-1053.

- S37 Sanchez-Lerma B, Morales-Chirivella FJ, Penuelas I, Blanco Guerra C, Mesa Lugo F, Aguinaga-Ontoso I, Guillen-Grima F: High prevalence of asthma and allergic diseases in children aged 6 to [corrected] 7 years from the canary islands. [corrected]. *Journal of investigational allergology & clinical immunology* 2009;19:383-390.
- S38 Selnes A, Nystad W, Bolle R, Lund E: Diverging prevalence trends of atopic disorders in norwegian children. Results from three cross-sectional studies. *Allergy* 2005;60:894-899.
- S39 Simoni M, Annesi-Maesano I, Sigsgaard T, Norback D, Wieslander G, Nystad W, Canciani M, Sestini P, Vieggi G: School air quality related to dry cough, rhinitis and nasal patency in children. *The European respiratory journal* 2010;35:742-749.
- S40 Soto-Quiros ME, Soto-Martinez M, Hanson LA: The high prevalence of rhinitis, rhinoconjunctivitis, and eczema in costa rican schoolchildren studied with the isaac protocol. *Pediatric Asthma, Allergy and Immunology* 2004;17:71-80.
- S41 Suh M, Kim HH, Sohn MH, Kim KE, Kim C, Shin DC: Prevalence of allergic diseases among korean school-age children: A nationwide cross-sectional questionnaire study. *Journal of Korean medical science* 2011;26:332-338.
- S42 Tai A, Volkmer R, Burton A: Prevalence of asthma symptoms and atopic disorders in preschool children and the trend over a decade. *The Journal of asthma : official journal of the Association for the Care of Asthma* 2009;46:343-346.
- S43 Tamay Z, Akcay A, Ergin A, Guler N: Prevalence of allergic rhinitis and risk factors in 6- to 7-yearold children in istanbul, turkey. *The Turkish journal of pediatrics* 2014;56:31-40.

- S44 Wang J, Li B, Yu W, Yang Q, Wang H, Huang D, Sundell J, Norback D: Rhinitis symptoms and asthma among parents of preschool children in relation to the home environment in chongqing, china. *PloS one* 2014;9:e94731.
- S45 Wu WF, Wan KS, Wang SJ, Yang W, Liu WL: Prevalence, severity, and time trends of allergic conditions in 6-to-7-year-old schoolchildren in taipei. *Journal of investigational allergology & clinical immunology* 2011;21:556-562.
- S46 Zhao TB, Wang HJ, Chen YZ, Xiao ML, Duo LK, Liu G, Lau YL, Karlberg J: Prevalence of childhood asthma, allergic rhinitis and eczema in urumqi and beijing. *Journal of paediatrics and child health* 2000;36:128-133.
- S47 Al-Ghobain MO, Al-Moamary MS, Al-Hajjaj MS, Al-Fayez AI, Basha SI: Prevalence of rhinitis symptoms among 16 to 18 years old adolescents in saudi arabia. *The Indian journal of chest diseases & allied sciences* 2013;55:11-14.
- S48 Amizadeh M, Safizadeh H, Bazargan N, Farrokhdoost Z: Survey on the prevalence of allergic rhinitis and its effect on the quality of high school students' life. *Iranian journal of otorhinolaryngology* 2013;25:79-84.
- S49 Arnedo-Pena A, Garcia-Marcos L, Blanco-Quiros A, Gimeno AM, Ontoso IA, Diaz CG, Vazquez CD, Busquets-Monge R, Suarez-Varela MM, Garrido JB, Varela ALS, De Andoin NG: Time trends in prevalence of symptoms of allergic rhinitis in 13-14 year-old schoolchildren in 8 areas of spain between 1993-1994 and 2001-2002 according to the international study of asthma and allergies in childhood (isaac). [spanish] evolucion temporal de la prevalencia de sintomas de rinitis alergica en escolares de 13-14 anos de 8 areas espanolas entre 1993-1994 y 2001-2002 segun el estudio internacional sobre asma y alergias en la infancia (isaac). *Medicina clinica* 2004;123:490-495.

S50 Awadh Behbehani N, Abal A, Syabbalo NC, Abd Azeem A, Shareef E, Al-Momen J: Prevalence of asthma, allergic rhinitis, and eczema in 13- to 14-year-old children in kuwait: An isaac study. *Annals of Allergy, Asthma and Immunology* 2000;85:58-63.

S51 Brescianini S, Brunetto B, Iacovacci P, D'Ippolito C, Alberti G, Schirru MA, Stazi MA, Pini C, Di Felice G, Barletta B: Prevalence of self-perceived allergic diseases and risk factors in italian adolescents. *Pediatric allergy and immunology: official publication of the European Society of Pediatric Allergy and Immunology* 2009;20:578-584.

S52 Chiang LC, Chen YH, Hsueh KC, Huang JL: Prevalence and severity of symptoms of asthma, allergic rhinitis, and eczema in 10- to 15-year-old schoolchildren in central taiwan. *Asian Pacific journal of allergy and immunology / launched by the Allergy and Immunology Society of Thailand* 2007;25:1-5.

S53 Brito Rde C, da Silva GA, Motta ME, Brito MC: The association of rhinoconjunctivitis and asthma symptoms in adolescents. *Revista portuguesa de pneumologia* 2009;15:613-628.

S54 Droma Y, Kunii O, Yangzom Y, Shan M, Pingzo L, Song P: Prevalence and severity of asthma and allergies in schoolchildren in lhasa, tibet. *Clinical and experimental allergy : journal of the British Society for Allergy and Clinical Immunology* 2007;37:1326-1333.

S55 Fagan JK, Scheff PA, Hryhorczuk D, Ramakrishnan V, Ross M, Persky V: Prevalence of asthma and other allergic diseases in an adolescent population: Association with gender and race. *Annals of allergy, asthma & immunology: official publication of the American College of Allergy, Asthma, & Immunology* 2001;86:177-184.

S56 Graif Y, Garty BZ, Livne I, Green MS, Shohat T: Prevalence and risk factors for allergic rhinitis and atopic eczema among schoolchildren in israel: Results from a national

study. *Annals of allergy, asthma & immunology: official publication of the American College of Allergy, Asthma, & Immunology* 2004;92:245-249.

S57 Kim SH, Kim YK, Lee MH, Hong SC, Bae JM, Min KU, Kim YY, Cho SH: Relationship between sensitization to citrus red mite (*panonychus citri*) and the prevalence of atopic diseases in adolescents living near citrus orchards. *Clinical and experimental allergy : journal of the British Society for Allergy and Clinical Immunology* 2002;32:1054-1058.

S58 Koffi N, Aka J, Nigue L, Kouassi B, Ngom A, Amon-Dick F, Nibaud A, Fadiga A, Aka-Danguy E: Prevalence of allergic diseases in childhood: Ivory coast isaac study, phase i. [french] prevalence des maladies allergiques de l'enfant: Resultats de l'enquete isaac - cote d'ivoire phase i. *Revue Francaise d'Allergologie et d'Immunologie Clinique* 2000;40:539-547.

S59 Luna Mde F, Almeida PC, Silva MG: [asthma and rhinitis prevalence and co-morbidity in 13-14-year-old schoolchildren in the city of fortaleza, ceara state, brazil]. *Cadernos de saude publica* 2011;27:103-112.

S60 Mercer MJ, Joubert G, Ehrlich RI, Nelson H, Poyser MA, Puterman A, Weinberg EG: Socioeconomic status and prevalence of allergic rhinitis and atopic eczema symptoms in young adolescents. *Pediatric Allergy and Immunology* 2004;15:234-241.

S61 Munivrana H, Vorko-Jovic A, Munivrana S, Kursar M, Medlobi-Gluhak M, Vlahek P: The prevalence of allergic diseases among croatian school children according to the isaac phase one questionnaire. *Medical science monitor : international medical journal of experimental and clinical research* 2007;13:Cr505-509.

S62 Musharrafieh U, Al-Sahab B, Zaitoun F, El-Hajj MA, Ramadan F, Tamim H: Prevalence of asthma, allergic rhinitis and eczema among lebanese adolescents. *The Journal of asthma : official journal of the Association for the Care of Asthma* 2009;46:382-387.

S63 Narayana PP, Prasanna MP, Narahari SR, Guruprasad AM: Prevalence of asthma in school children in rural india. *Annals of Thoracic Medicine* 2010;5:118-119.

S64 Nordvall SL, Janson C, Kalm-Stephens P, Foucard T, Toren K, Alving K: Exhaled nitric oxide in a population-based study of asthma and allergy in schoolchildren. *Allergy* 2005;60:469-475.

S65 Owayed A, Behbehani N, Al-Momen J: Changing prevalence of asthma and allergic diseases among kuwaiti children. An isaac study (phase iii). *Medical principles and practice : international journal of the Kuwait University, Health Science Centre* 2008;17:284-289.

S66 Pac-Sa MR, Museros-Recatala L, Arnedo-Pena A, Bellido-Blasco JB, Puig-Barbera J, Artero-Sivera A, Campos-Cruanes JB, Aguinaga-Ontoso I: Risk factors for symptoms of allergic rhinitis in adolescents in castellon, spain. [spanish] factores de riesgo de sintomas de rinitis alergica en adolescentes de castellon, espana. *Revista Panamericana de Salud Publica/Pan American Journal of Public Health* 2008;23:333-340.

S67 Porto Neto AC, D'Agostini Annes R, Wolff NMM, Klein AP, Dos Santos FC, Dullius JL, Gressler M, Muller LS, Angonese CF, Menna-Barreto S: Prevalence and severity of asthma, rhinitis, and atopic eczema in 13- to 14-year-old schoolchildren from southern brazil. *Allergy, Asthma and Clinical Immunology* 2006;2:3-10.

S68 Riguera D, Andre PA, Zanetta DM: Sugar cane burning pollution and respiratory symptoms in schoolchildren in monte aprazivel, southeastern brazil. *Revista de saude publica* 2011;45:878-886.

S69 Shamssain MH, Shamsian N: Prevalence and severity of asthma, rhinitis, and atopic eczema in 13- to 14-year-old schoolchildren from the northeast of england. *Annals of allergy, asthma & immunology : official publication of the American College of Allergy, Asthma, & Immunology* 2001;86:428-432.

S70 Sugiyama K, Sugiyama T, Toda M, Yukawa T, Makino S, Fukuda T: Prevalence of asthma, rhinitis and eczema among 13-14-year-old schoolchildren in tochigi, japan. *Allergology International* 2000;49:205-211.

S71 Tamay Z, Akcay A, Ergin A, Guler N: Effects of dietary habits and risk factors on allergic rhinitis prevalence among turkish adolescents. *International journal of pediatric otorhinolaryngology* 2013;77:1416-1423.

S72 Toledo MF, Rozov T, Leone C: Prevalence of asthma and allergies in 13- to 14-year-old adolescents and the frequency of risk factors in carriers of current asthma in taubate, sao paulo, brazil. *Allergologia et immunopathologia* 2011;39:284-290.

S73 Wang HY, Pizzichini MM, Becker AB, Duncan JM, Ferguson AC, Greene JM, Rennie DC, Senthilselvan A, Taylor BW, Sears MR: Disparate geographic prevalences of asthma, allergic rhinoconjunctivitis and atopic eczema among adolescents in five canadian cities. *Pediatric allergy and immunology : official publication of the European Society of Pediatric Allergy and Immunology* 2010;21:867-877.

S74 Yan DC, Ou LS, Tsai TL, Wu WF, Huang JL: Prevalence and severity of symptoms of asthma, rhinitis, and eczema in 13- to 14-year-old children in taipei, taiwan. *Annals of allergy, asthma & immunology : official publication of the American College of Allergy, Asthma, & Immunology* 2005;95:579-585.

S75 Zar HJ, Ehrlich RI, Workman L, Weinberg EG: The changing prevalence of asthma, allergic rhinitis and atopic eczema in african adolescents from 1995 to 2002. *Pediatric allergy and immunology : official publication of the European Society of Pediatric Allergy and Immunology* 2007;18:560-565.

S76 Bjerg A, Ekerljung L, Middelveld R, Dahlen SE, Forsberg B, Franklin K, Larsson K, Lotvall J, Olafsdottir IS, Toren K, Lundback B, Janson C: Increased prevalence of symptoms

of rhinitis but not of asthma between 1990 and 2008 in swedish adults: Comparisons of the ecchs and ga(2)len surveys. PloS one 2011;6:e16082.

S77 Desalu OO, Salami AK, Iseh KR, Oluboyo PO: Prevalence of self reported allergic rhinitis and its relationship with asthma among adult nigerians. Journal of investigational allergology & clinical immunology 2009;19:474-480.

S78 Filipiak B, Heinrich J, Nowak D, Wichmann HE: The distribution in specific ige and the prevalence of allergic symptoms in 25-64-years old inhabitants of an eastern and a western german city--results from augsburg and erfurt. European journal of epidemiology 2001;17:77-84.

S79 Hannaford PC, Simpson JA, Bisset AF, Davis A, McKerrow W, Mills R: The prevalence of ear, nose and throat problems in the community: Results from a national cross-sectional postal survey in scotland. Family practice 2005;22:227-233.

S80 Klossek JM, Annesi-Maesano I, Pribil C, Didier A: [instant: National survey of allergic rhinitis in a french adult population based-sample]. Presse medicale (Paris, France : 1983) 2009;38:1220-1229.

S81 Konno S, Hizawa N, Fukutomi Y, Taniguchi M, Kawagishi Y, Okada C, Tanimoto Y, Takahashi K, Akasawa A, Akiyama K, Nishimura M: The prevalence of rhinitis and its association with smoking and obesity in a nationwide survey of japanese adults. Allergy 2012;67:653-660.

S82 Kurt E, Metintas S, Basyigit I, Bulut I, Coskun E, Dabak S, Deveci F, Fidan F, Kaynar H, Kunt Uzaslan E, Onbasi K, Ozkurt S, Pasaoglu Karakis G, Sahan S, Sahin U, Oguzulgen K, Yildiz F, Mungan D, Yorgancioglu A, Gemicioglu B, Fuat Kalyoncu A: Prevalence and risk factors of allergies in turkey (parfait): Results of a multicentre cross-sectional study in adults. The European respiratory journal 2009;33:724-733.

- S83 Lindgren A, Stroh E, Nihlen U, Montnemery P, Axmon A, Jakobsson K: Traffic exposure associated with allergic asthma and allergic rhinitis in adults. A cross-sectional study in southern sweden. *International journal of health geographics* 2009;8:25.
- S84 Morais-Almeida M, Pite H, Pereira AM, Todo-Bom A, Nunes C, Bousquet J, Fonseca J: Prevalence and classification of rhinitis in the elderly: A nationwide survey in portugal. *Allergy: European Journal of Allergy and Clinical Immunology* 2013;68:1150-1157.
- S85 Song WJ, Kim MY, Jo EJ, Kim MH, Kim TH, Kim SH, Kim KW, Cho SH, Min KU, Chang YS: Rhinitis in a community elderly population: Relationships with age, atopy, and asthma. *Annals of allergy, asthma & immunology : official publication of the American College of Allergy, Asthma, & Immunology* 2013;111:347-351.
- S86 Sonomjamts M, Dashdemberel S, Logii N, Nakae K, Chigusa Y, Ohhira S, Ito C, Sagara H, Makino S: Prevalence of asthma and allergic rhinitis among adult population in ulaanbaatar, mongolia. *Asia Pacific allergy* 2014;4:25-31.

Table S1. Characteristics of the included studies assessing prevalence of rhinitis before puberty (<11y)

Study Ref (N=46)	Country	Sampling method	Residency	Method for assessing PR	Sample analysed	Study period	Rhinitis	
							M (%)	F (%)
Ahn et al ^{S1}	Korea	Children from 1st year of elementary (6292 schools) and middle school (3137 schools) were chosen from a random sample of 45 primary and 40 middle schools across the nation (7 metropolitan regions and 9 provinces).	Rural/Urban	ISAAC Q	8115	2010	6-7y 429/1958 (21.9)	6-7y 305/1931 (15.8)
Al-Riyami et al ^{S2}	Oman	A nationwide sample of public schools were chosen for conducting the stratified multistage sampling method, using the 10 health regions of Oman as a strata. The first stage of sampling consisted of randomly selecting schools as primary sample units from each health region. In the second stage, one class was chosen randomly from each school as the secondary sample unit with participation of all children in the selected class. The total national target sample was distributed among the 10 regions of the country using the proportion allocation method.	U/NR	ISAAC Q	3893	-	6-7y 263/1624 (16.2)	6-7y 209/1550 (13.5)
Amarasekera et al ^{S3}	Sri Lanka	Children in the fifth grade of school, attending 17 state schools in the 3 districts of the Western Province of Sri Lanka. Participating schools were selected by multi-stage stratified randomisation. In the first stage, stratification was done by type of schools recognised by the Ministry of Education. In the second stage, schools of each type were randomly selected from rural and urban areas, in proportion to the size of the urban and rural populations of the province. In the third stage, in each selected school, one class in Grade 5 was randomly selected as the study population.	Rural/Urban	ISAAC Q	511	2006	10y 67/277 (24.2)	10y 37/234 (15.8)
Annesi-Maesano et al ^{S4}	France	Recruited schoolchildren (9-10 years) from unclear sample "including 6 cities", "401 randomly chosen classrooms in 108 primary schools attended by 6590 children"	Urban	ISAAC Q	6590	-	9-10y (13.1)	9-10y (10.7)

Anthracopoulos et al ^{S5}	Greece	3 separate cross-sectional surveys of 8-10 year old children. Identical methodology in the targeting, distribution and collection of the parental questionnaire.	Urban	Other Q “Current” refers to “in the last 2 years”.	2417	1991	8-10y 64/1181 (5.4)	8-10y 59/1236 (4.8)
					3076	1998	8-10y 97/1507 (6.4)	8-10y 104/1569 (6.6)
					2725	2003	8-10y 113/1337 (8.5)	8-10y 104/1388 (7.5)
Arnedo-Pena et al ^{S6}	Spain	Phase III (2001-2002) included schoolchildren from 8 centres (Asturias, Barcelona, Bilbao, Pamplona, Madrid, Castellon, Valencia, Cartagena) and results were compared with phase I (1993-1994). In 3 centres schools were selected by simple randomisation, and the rest of the centres included all the schools in the area.	Rural/Urban	ISAAC Q	24862	2002	6-7 y 2297/12418 (18.5)	6-7 y 1991/12444 (16.1)
Backer et al ^{S7}	Mexico	A population-based cross-sectional study was performed by applying a standardized questionnaire to a random sample of 2087 school children 6-7 years old living in the city of Mexicali, capital of Baja California, north of Mexico. 55 schools were randomly selected among all elementary schools of Mexicali.	Rural/Urban	ISAAC Q	2087	2004	6-7 y 294/1009 (29.1)	6-7 y 227/1078 (21.1)
Castro et al ^{S8}	Brazil	The study target population consisted of public school students aged from 6 to 7 years living in the city of Londrina, Brazil. They selected 38 schools, distributed proportionally among the five regions of the city: northern; southern; eastern; western; and downtown. All children in the established age range enrolled in these schools were invited to participate in the study.	Urban	ISAAC Q	3600	2008	6-7y 547/1837 (29.8)	6-7y 437/1763 (24.8)
Dell et al ^{S9}	Canada	Schools were selected by use of a random number generator from a pool of 556 eligible schools within the two publicly funded school boards in Toronto (Toronto District School Board and the Toronto Catholic District School Board).	Urban	ISAAC Q	5619	2006	Mean 6.7y 679/2772 (24.5)	Mean 6.7y 613/3347 (18.3)

Del-Rio-Navarro et al ^{S10}	Mexico	A total of 50 elementary and 27 high schools were sampled which were randomly selected in the four participating city precincts (Miguel Hidalgo, Azcapotzalco, Gustavo A Madero, and Venustiano Carranza).	Urban	ISAAC Q	4016	2005	6-7y 1001/2098 (47.7)	6-7y 873/2008 (43.5)
Duggan et al ^{S11}	Ireland	Two cross-sectional studies were performed 5 yr apart (2002 and 2007), in the same 24 randomly selected state primary schools in Cork (city and suburbs). Both cross-sectional studies were carried out in the same season and used identical methodology.	Urban	ISAAC Q	1474	2002	6-9y 197/699 (28.2)	6-9y 189/775 (24.4)
					1535	2007	6-9y 237/795 (29.8)	6-9y 176/740 (23.8)
					1648	1995	6-7y 85/844 (10.1)	6-7y 86/804 (10.7)
Falade et al ^{S12}	Nigeria	31 primary schools were randomly selected from a total of 272 primary schools in Ibadan (one of the most densely populated cities in Africa), and 2,325 children aged 6–7 years were selected from grades 1 and 2.	Urban					
Futamura et al ^{S13}	Japan	Setagaya is located in the center of Tokyo. The study covered all 9 grades from 64 public elementary schools and 31 public junior high schools, with approximately 80% of the children attending these public schools.	Urban	ISAAC Q	27 917	2005	6y: 21.2 7y: 23.1 8y: 26.3 9y: 27.1 10y: 35.6	6y: 17.7 7y: 22.3 8y: 23.9 9y: 25.4 10y: 34.5
Garcia-Marcos et al ^{S14}	Spain	The cities of Bilbao, San Sebastian and La Coruña included all schools within the city district. Asturias (a province) included a random sample of schools.	Rural/Urban	ISAAC Q	9590	2002	6-7y 540/4733 (11.4)	6-7y 393/4847 (8.1)
Hahm et al ^{S15}	Korea	The sampling method was a stratified two-stage cluster sampling design, based on a comprehensive national list of schools at the time. First, schools were stratified by geographical region and school location (metropolitan, urban, rural). For each stratum, sample schools were selected using a systematic ‘probability proportional to size’ (PPS) sampling procedure. In the second stage, three classes were selected randomly from the first grade of each sample school, and all students were asked to participate.	Rural/Urban	ISAAC Q and SPT	3804	2010	6-7y AR: 523/1923 (27.2) NAR: 927/1923 (48.2)	6-7y AR: 319/1881 (17.0) NAR: 723/1881 (38.5)

Higuchi et al ^{S16}	Japan	To ensure nationwide representation, schools were randomly selected from all prefectures. The total number of children recruited was 179,218, approximately 2% of the pediatric population, according to data from the National Institute of Population and Social Security Research.	Rural/Urban	ISAAC Q	139 506	2008	6-7y 10592/21861 (48.5)	6-7y 8338/21013 (39.7)
Hong et al ^{S17}	Korea	This study enrolled 38,201 children between 0 and 13 years of age from 34 elementary schools and 136 children's daycare centers to participate in the 'Seoul Atopy Friendly School'.	Urban	ISAAC Q	31 201	2010	0-9y 4016/9825 (40.9)	0-9y 3083/9410 (32.8)
Kahwa et al ^{S18}	Jamaica	Stratified, multistage cluster sampling design using enumeration districts (EDs) as primary sampling units. Briefly, in stage 1, a random sample of EDs was selected proportional to parish size and independently from both urban and rural EDs. Stage 2 involved the selection of households using systematic probability sampling. The Kish selection table ⁷ was used to select one eligible child per household in stage 3 yielding a sample size of 2017.	Rural/Urban	ISAAC Q	2017	2007	6-7y 25/138 (18.1)	6-7y 10/130 (7.7)
Kao et al ^{S19}	Taiwan	The area studied was Taoyuan County, northern Taiwan. First-grade children (aged 6–8) or eighth-grade (aged 13–15) children were recruited. One-stage stratified cluster random sampling was used in this study.	U/NR	ISAAC Q	6190	2002	6-8y 626/1546 (40.5)	6-8y 491/1533 (32.0)
Kong et al ^{S20}	China	Sixteen kindergartens located in the urban area of Wuhan were randomly selected from the complete sampling frame of all kindergartens in the area. In each kindergarten, three classes were randomly selected from the three grades (top, middle and bottom grade).	Urban	Authors designed a Q that was checked by experts of rhinology and epidemiology.	1211	2005	3-6y Rhinitis 28.4 (24.9-31.8) Rhinitis + SPT 13.0 (10.4-15.6)	3-6y Rhinitis 25.6 (22.0-29.2) Rhinitis + SPT 7.7 (5.5-9.9)

				Based on ISAAC Q and SPT.				
Kudzyte et al ^{S21}	Lithuania	Repeated cross-sectional epidemiological study was performed in 1994–1995 and 2001–2002 following the ISAAC protocol. Both surveys were conducted in the same population of children, randomly selected from the same primary schools in Kaunas.	Urban	ISAAC Q	1879	1994-1995	6-7y 182/914 (19.9)	6-7y 196/965 (20.3)
					2772	2001-2002	6-7y 320/1396 (22.9)	6-7y 288/1376 (20.9)
Kurosaka et al ^{S22}	Japan	We studied the epidemiology of allergic symptoms in six-year-old children attending primary schools throughout Himeji City, Japan, during a two-year period from 2005 to 2006. Himeji City, situated close to the Seto Inland Sea, has a population of about 530,000. The southern area of the city is industrial, with steel manufacture predominating, the central area is urban with a large population, and the northern area is rural with farmlands.	Rural/Urban	ISAAC Q	11 013	2006	6y 645/5666 (11.4)	6y 532/5347 (10.0)
Levesque et al ^{S23}	Canada	The Health and Social Survey of Quebec Children and Youth (HSSCY) recruited 189 schools to make up 3 separate samples of approx 1500 children aged 9, 13 and 16 years. The 3 samples were weighted to make them representative of all Quebec children of the same age.	Rural/Urban	ISAAC Q	3613	1999	9y (19.2)	9y (14.4)
Liao et al ^{S24}	Taiwan	A stratified random sampling method was used (47 schools were sampled randomly from the list of all elementary schools in Changhwa County by 16 districts, areas, and school size). In addition 4 areas in Changhwa county were classified for the comparison of the prevalence, including (1) the “TaiHao Petroleum Company area” with a lot of air-pollution due to a petrochemical company located in the northern part of the county; (2) the “XiZhou area” nearby a huge incinerator located in the southern part of the county; (3) the area of the coastal region; and	U/NR	ISAAC Q	7040	2002	6-8y 1121/3627 (30.9)	6-8y 771/3413 (22.6)

		(4) the rest of Changhwa County.						
Lima et al ^{S25}	Brazil	The districts included in this study correspond to 5.4% of the total population of São Paulo and present high demographic densities, including favelas, with predominantly low incomes ¹⁵⁻¹⁷ . Thirty-five exclusively municipal public schools distributed throughout this district whose population presents precarious living conditions were chosen.	Urban	ISAAC Q	3312	2002	6-7y 503/1510 (33.3)	6-7y 455/1671 (27.2)
Mavale-Manuel et al ^{S26}	Mozambique	From a total of 126 schools registered in Maputo, 21 primary schools and six secondary schools were randomly selected by stratifying for geographic (urban, suburban and semi-rural) location and inhabitant's density so as to be representative of the distribution of the population in Maputo.	Rural/Urban	ISAAC Q	5013	2004	6-7y 244/1207 (20.2)	6-7y 251/1176 (21.3)
Maziak et al ^{S27}	Germany	This study uses the information collected on two occasions 5 years apart (Phase I 1994/1995, Phase III 1999/2000). A random sample of all schools in the city of Münster was selected, and all pupils in the two grades with the highest proportion of 6–7 and 13–14 year olds were approached.	Urban	ISAAC Q	14 569	1994-1995	6-7y 272/1754 (15.5)	6-7y 165/1713 (9.6)
						1999-2000	6-7y 337/1863 (18.1)	6-7y 241/1666 (14.5)
Mohammadzadeh et al ^{S28}	Iran	Our sample study had 2 groups: the first group consisted of children aged 6-7 years and in the second group were 12-14 year-old children. The exclusion criteria in this study were mentally retarded children and those visiting rural schools. Each school was a cluster. 59 elementary schools and 62 guidance schools were randomly selected.	Urban	ISAAC Q	5933	2003	6-7y 148/1412 (10.5)	6-7y 164/1632 (10.1)
Montefort et al ^{S29}	The Maltese Islands	Twenty-four state primary schools from Malta and Gozo were randomly chosen. The schools were scattered all over the two islands, and the total number of children within the two school was 4,465. This constituted 59.1% of children within this age group attending state schools in the Maltese Islands.	Rural/Urban	ISAAC Q	3506	-	5-8y (21.4)	5-8y (19.9)
Morais-Almeida et al ^{S30}	Portugal	A multistep selection strategy was used to obtain a representative sample of the target population.	Rural/Urban	ISAAC Q and ARIA	5018	2007	3-5y	3-5y

		First, the number of participants needed from each Portuguese region was defined based on the data from the 2001 Census on 3- to 5-year-old children. Second, Portuguese municipalities were randomly selected until reaching a prespecified number of children, considering that each municipality would provide between 50 and 70 individuals. Finally, kindergartens and parish centers within the selected municipalities were chosen for data collection based on children's distribution, comfort, privacy, and low interference with the usual activities of the participants.					1131/2561 (44.2)	1048/2457 (42.7)
Moyes et al ^{S31}	New Zealand	In each participating centre, schools were selected by sequential random sampling or by using all schools in the sampling frame so that 3000 6- to 7-year-olds and 3000 13- to 14-year-olds were surveyed.	Rural/Urban	ISAAC Q	24 185	1993	6-7y 564/5639 (10.0)	6-7y 524/5754 (9.1)
Nahhas et al ^{S32}	Saudi Arabia	A list of all government and private primary schools (aged 6-12y) in Madinah was obtained from the General Directorate of Education in the Madinah region. Schools were then stratified (according to the geographical area and sex) and a random sample of 38 schools (9 schools for girls and 29 for boys) was approached.	Urban	ISAAC Q	5188	2008	6-8y 716/3585 (20.0)	6-8y 229/1603 (14.3)
Okuda ^{S33}	Japan	Two-step stratified random samplings were performed in individual zones. First, 390 of 3,370 places from cities, towns, and villages in Japan were randomly selected by the probability proportional sampling method in proportion to the overall population with respect to age (3 to 79 years) and sex on the basis of the National Census Report in 1995. As the second step, 2 subjects in each of the 7 age and sex groups (14 subjects in total for each factor) were sampled randomly from the resident registration lists of the aforementioned 390 places.	Rural/Urban	Other Q	10 866 (in total)	2001	3-9y 12.8% (9.3-16.2)	3-9y 9.7% (6.6-12.7)

Penaranda et al ^{S34}	Colombia	Among the 4535 registered educational institutions in Bogota schools were selected within neighbourhoods SES 3 and 4 (42% of the overall) for local security reasons. They randomly selected 74 of these schools for the 6–7 year age-group, and 48 for the 13–14 year age-group.	Urban	ISAAC Q	7085	2002	6-7y 229/1386 (16.5)	6-7y 319/1794 (17.8)
Peroni et al ^{S35}	Italy	Eighteen nursery schools located in the urban area of Verona (North-East part of Italy) were randomly selected from the complete sampling frame of all schools of the area.	Urban	ISAAC Q and SPT	1402	2001	3-5y 142/734 (19.4)	3-5y 94/668 (14.1)
Rad et al ^{S36}	Iran	They divided Urmia city into 11 homogenous clusters and selected 4 clusters by random sampling. A total of 25 schools were selected by systematic random sampling in each selected cluster.	Urban	ISAAC Q	2999	2003	6-7y 174/1450 (12.0)	6-7y 106/1549 (6.9)
Sanchez-Lerma et al ^{S37}	Spain	Research team sent a letter to all school principals explaining the objectives of the study and inviting them to participate. Personal interviews with interested principals were held.	Urban	ISAAC Q	1871	-	6-7y 42.9 (39.8-46.1)	6-7y 37.4 (34.2-40.5)
Selnes et al ^{S38}	Norway	1985: The schools were randomly selected within the three northernmost counties of Norway, Nordland, Troms and Finnmark. The 1995 study was designed as a 10-year follow-up to the study conducted in 1985. The 2000 study was part of an ISAAC-II Europe study. All 9–11 years old children in the counties of Troms and Finnmark were invited to participate.	U/NR	Other Q	1794	1985	9-11y (18.5)	9-11y (14.5)
					1432	1995	9-11y (27.2)	9-11y (22.1)
				ISAAC Q	3853	2000	9-11y (32.2)	9-11y (27.0)
Simoni et al ^{S39}	Italy; France; Norway; Sweden; Denmark	The cross-sectional HESE study involved six operational units in five European countries (Siena and Udine, Italy; Reims, France; Oslo, Norway; Uppsala, Sweden; and Aarhus, Denmark). 21 schools (46 classrooms) with heterogeneous characteristics were selected, including a broad age range of buildings and a variety of location characteristics (about half in environmentally more advantaged areas and half	U/NR	ISAAC Q, Acoustic rhinometry, nasal secretions	654	2004-2005	Mean 10y (33)	Mean 10y (31)

		in less advantaged areas).						
Soto-Quiros et al ^{S40}	Costa Rica	From a total of 5000 educational centers registered in Costa Rica in 1995, 75 centers representative of the country were selected by random stratification on the basis of geographical location, rural and urban regions, and size.	Rural/Urban	ISAAC Q	6144	1995	6-7y 435/1478 (29.4)	6-7y 350/1466 (23.9)
Suh et al ^{S41}	Korea	The clustered random sampling method was used to obtain a representative population of elementary school students in each type of residential area. Residential areas were divided into four groups: metropolitan, provincial, rural, and industrial areas. An industrial area was defined as an industrial complex harboring an elementary school (the study included 17 out of a total of 40 industrial complexes in Korea in the industrial area group). Among 87 elementary schools in industrial area, 25 elementary schools (29%) were randomly selected. In each group except the industrial area, 10% of the elementary schools, of which the number of class was over 3, were randomly selected. Then, one class of each grade (among grades 3 through 5; 8-11 yr old) of each elementary school was randomly selected.	Rural/Urban	ISAAC Q	30 893	2006	8-11y 4944/13254 (37.3)	8-11y 5239/17639 (29.7)
Tai et al ^{S42}	Australia	The Children, Youth and Women's Health Service (CYWHS)(Child and Youth Health Campus) has a state-based community health service that routinely conducts a school entry health check for all preschool (4- to 5-year-old) children in South Australia.	U/NR	ISAAC Q	1509	2006	4-5y 181/772 (23.4)	4-5y 132/737 (17.9)
Tamay et al ^{S43}	Turkey	The number of primary school children attending Grade 1 in İstanbul was 211,446. Of those children, 5% from each district were planned to be included in the survey. The number of schools and children were calculated according to the number of children attending Grade 1 in each district.	Urban	ISAAC Q	9875	2004-2005	6-7y 1510/4972 (30.4)	6-7y 1370/4835 (28.3)
Wang et al ^{S44}	China	The questionnaires were distributed to children's	Rural/Urban	Other Q	4530	2010-	1-8y	1-8y

		parents through teachers in kindergartens in three districts (Shapingba, Jiulongpo, Yubei) that were randomly selected from 9 districts of Chongqing city. From the 54 randomly selected kindergartens (15 from Shapingba, 21 from Jiulongpo and 18 from Yubei), 7117 subjects (one parent per child aged from 1–8 years old) were selected.				2011	Weekly (2.9) Less common (43.0)	Weekly (3.2) Less common (44.5)
Wu et al ^{S45}	Taiwan	In total, 26418 students from 153 elementary schools in Taipei's 12 administrative districts were investigated.	Rural/Urban	ISAAC Q	24 999	2007	6-7y (47.7)	6-7y (37.8)
Zhao et al ^{S46}	China	All primary schools in the Xuanwu District, Beijing and the Tianshan District, Urumqi were identified. Schools in the two districts were randomly recruited using the random number table until a sample size of around 3500 students in each city was obtained.	Urban	ISAAC Q	5818 (2978 (Beijing) + 2840 (Urumqi))	1996	6-7y 909/2842 (32.0)	6-7y 760/2618 (29.0)

PR; Prevalence of rhinitis; ISAAC: International Study of Asthma and Allergies in Childhood; Q: questionnaire; SPT: Skin prick test; M: male; F: female; U/NR: unclear/not reported

Table S2. Characteristics of the included studies assessing prevalence of rhinitis during and shortly after puberty (11-<18y)

Study Ref (N=43)	Country	Sampling method	Residency	Method for assessing PR	Sample analysed	Study period	Rhinitis	
							M (%)	F (%)
Ahn et al ^{S1}	Korea	Described in Table S1	Rural/Urban	ISAAC Q	8115	2010	13-14y 385/1965 (19.6)	13-14y 380/2021 (18.8)
Al-Ghobain et al ^{S47}	Saudi Arabia	Schools and students were selected using a two-stage cluster sample. In the first stage, a random selection method was used to select 46 secondary schools from a list of 405 schools. To conduct the sampling, we divided Riyadh into four districts (northern, eastern, southern, and western) based on proximity to two major highways. Fifteen percent of the boys schools and 10% of the girls schools were selected from each district based on proportional probability. During the second stage, 3 classes (one per grade level) were selected from each school. Thus, 138 classes were identified. Each class was considered to be a cluster, and all the students in the selected classes constituted the target group.	Urban	ISAAC Q	3073	2010	16-18y 527/1504 (35.0)	16-18y 657/1569 (41.9)
Al-Riyami et al ^{S2}	Oman	Described in Table S1	U/NR	ISAAC Q	3174	-	13-14y (25.5)	13-14y (22.1)
Amizadeh et al ^{S48}	Iran	High school children in the city of Kerman, 1840 students (15-18 years old) selected through cluster sampling.	Urban	SFAR	1511	2002	15-18y 138/686 (20.1)	15-18y 153/825 (18.6)
Arnedo-Pena et al ^{S49}	Spain	Cross-sectional study including schoolchildren aged 13-14y from 9 centres of which 7 had urban population (Barcelona, Bilbao, Cartagena, Castellon, Madrid, Pamplona and Valencia) and 2 the population was mixed (Asturias and Valladolid). Three centers (Asturias, Valencia y Valladolid) conducted a random sampling to select the schools.	Rural/Urban	ISAAC Q	30 046	2002	13-14y 4338/15605 (27.8)	13-14y 5040/14441 (34.9)

Awadh Behbehani et al ^{S50}	Kuwait	Public schools chosen randomly from 5 governorates, 8 schools per govern., 4 and 5th grades (13-14 years)	U/NR	ISAAC Q	3110	-	13-14y 31.4 (29-33.8)	13-14y 30 (27.8-32.2)
Brescianini et al ^{S51}	Italy	A cross-sectional study was carried out in two small semi-urban towns in the south-east of Rome (central Italy), Ciampino and Marino. The study population included 481 students aged 11–15 yr old attending three different secondary schools, located in Ciampino (n= 99) and Marino (n= 382).	Rural/Urban	ISAAC Q	481	2004	11-15y 70/237 (29.5)	11-15y 96/244 (39.3)
Chiang et al ^{S52}	Taiwan	Data was collected through cluster sampling from a total of nine elementary schools and five junior high schools in central Taiwan.	U/NR	ISAAC Q	11 874	-	13-15y 1373/3161 (43.4)	13-15y 1866/4516 (41.3)
De Brito et al ^{S53}	Brazil	A cross-sectional study, with two components: a study in prevalence and an inter-case study (rhinitis symptoms) with a comparison group (no rhinitis symptoms), based on information from questionnaires applied in phase 3 of ISAAC in Recife.	Urban	ISAAC Q	940	2002	13-14y 36/431 (8.4)	13-14y 55/509 (10.8)
Del-Rio-Navarro et al ^{S10}	Mexico	Described in Table S1	Urban	ISAAC Q	6576	2005	13-14y 957/3243 (29.5)	13-14y 1147/3333 (34.4)
Droma et al ^{S54}	China	All eight public junior high schools accessible in the urban area of Lhasa were recruited for this study and all 3196 students, ranging in age from 13 to 14 years, were invited to participate.	Urban	ISAAC Q	3190	2001	13-14y 87/1589 (5.5)	13-14y 78/1601 (4.9)
Fagan et al ^{S55}	USA	Seventh through twelfth grade, students attending school in a Mississippi River community in Illinois were targeted for the survey. All schools in East Moline, Illinois (one high school, five public junior high schools, and two parochial elementary schools) were approached to participate.	Urban	ISAAC Q	2693	1994	13-18y 346/1363 (25.4)	13-18y 515/1330 (38.7)
Futamura et al ^{S13}	Japan	Described in Table S1	Urban	ISAAC Q	27 917	2005	11y: 33.0 12y: 35.2 13y: 29.3 14y: 27.0	11y:31.9 12y:32.3 13y:27.1 14y: 30.1

Graif et al ^{S56}	Israel	To obtain a representative sample of 13- to 14-year-old schoolchildren, 141 schools were chosen at random from a Ministry of Education list of schools by district. For each school sampled, all eighth grade children were included in the study.	Rural/Urban	ISAAC Q	10 057	-	13-14y (8.7)	13-14y (10.2)
Higuchi et al ^{S16}	Japan	Described in Table S1	Rural/Urban	ISAAC Q	139 506	2008	13-14y 26890/47895 (56.1)	13-14y 26149/47220 (55.4)
Hong et al ^{S17}	Korea	Described in Table S1	Urban	ISAAC Q	31 201	2010	10-13y 2451/6052 (40.5)	10-13y 1825/5868 (31.1)
Kahwa et al ^{S18}	Jamaica	Described in Table S1	Rural/Urban	ISAAC Q	2017	2007	13-14y 20/105 (19.0)	13-14y 28/107 (26.2)
Kao et al ^{S19}	Taiwan	Described in Table S1	U/NR	ISAAC Q	6190	2002	13-15y 610/1588 (38.4)	13-15y 565/1523 (37.1)
Kim et al ^{S57}	Korea	A total of 2005 adolescents (aged 11-16 y) were enrolled in this study. All subjects were recruited from 4 high schools in rural areas with citrus orchards and had been living in these areas since infancy.	Rural only	ISAAC Q and SPT	1727	-	16-18y 62/537 (11.6)	16-18y 171/1190 (14.4)
Koffi et al ^{S58}	Ivory Coast	The secondary schools were chosen by simple random sampling of 11 centres of 3 towns: Man (5 schools), Korhogo (3 schools), Abidjan (3 schools).	Urban	ISAAC Q	3045	-	13-14y Abidjan: 17.9 Man: 20.2 Korhogo: 13.8	13-14y Abidjan: 13.8 Man: 10.7 Korhogo: 5.6
Levesque et al ^{S23}	Canada	Described in Table S1	Rural/Urban	ISAAC Q	3613	1999	13y (26.6)	13y (21.3)
							16y (29.6)	16y (26.5)
Luna et al ^{S59}	Brazil	In 2006, among the schools who had in their records a number ≤50 adolescents in the age range of the study, 29 were randomly selected,	Urban	ISAAC Q	3015	2006-2007	13-14y 494/1372 (36.0)	13-14y 809/1643 (49.2)

		distributed among the six regional administrations, respecting the proportion of students aged 13-14y from every region and thus ensuring the sample is representative of a heterogeneous population.			3020	2010	13-14y 498/1369 (36.4)	13-14y 539/1392 (38.7)
Mavale-Manuel et al ^{S26}	Mozambique	Described in Table S1	Rural/Urban	ISAAC Q	5013	2004	13-14y 479/1238 (38.7)	13-14y 539/1392 (38.7)
Mercer et al ^{S60}	South Africa	Thirty-three schools were selected by stratified random sampling from three socio-politically defined strata to represent the demographic make-up of the greater Cape Town metropolis.	Urban	ISAAC Q	4336-4663	1995	13-14y (30.2)	13-14y (30.5)
Mohammadzadeh et al ^{S28}	Iran	Described in Table S1	Urban	ISAAC Q	5933	2003	12-14y 164/1380 (11.9)	12-14y 132/1509 (8.7)
Moyes et al ^{S31}	New Zealand	Described in Table S1	Rural/Urban	ISAAC Q	24 185	1993	13-14y 1090/7171 (15.2)	13-14y 1857/8289 (22.4)
						2003	13-14y 962/6372 (15.1)	13-14y 1437/6940 (20.7)
Munivvana et al ^{S61}	Croatia	The target population was children aged 12 years 0 months to 14 years 11 months (6th–8th grades of school) from 27 elementary schools. Method of sample randomisation was not described.	Rural/Urban	ISAAC Q	3111	2005	12-14y 180/1512 (11.9)	12-14y 158/1599 (9.9)
Musharrafieh et al ^{S62}	Lebanon	A random sample of fifty-five private and public schools from different regions in Lebanon were contacted. Lebanon was witnessing security and political turmoil that followed the assassination of the Prime Minister. Due to these unstable circumstances many schools denied participation in the study. Thus, a convenient sample of 13 schools (3 public and 10 private) from 5 Lebanese provinces accepted to take part in the study.	Urban	ISAAC Q	3115	2005	13-14y 571/1512 (37.8)	13-14y 630/1603 (39.3)
Narayana et al ^{S63}	India	Carried out in three schools of Subramanya, a rural area in Dakshina Kannada District of Karnataka state in India.	Rural only	ISAAC Q	573	-	13-15y 33/75 (44)	13-15y 9/35 (25.7)

Nordvall et al ^{S64}	Sweden	The schools were randomized prior to the investigation. For practical reasons, the investigation was started in one school located adjacent to the Children's hospital. A random order of inclusion was followed for the remainder of the schools, to include approximately 1000 schoolchildren in the study. Nine schools were finally included in the study.	Urban	ISAAC Q	959	1999	13-14y 81/476 (17.0)	13-14y 120/483 (24.8)
Owayed et al ^{S65}	Kuwait	A list of intermediate level schools from each of the five governorates in Kuwait was obtained from the Department of Education. Eight schools, four for boys and four for girls, from each governorate were selected using random table.	U/NR	ISAAC Q	2882	2002	13-14y 443/1423 (31.1)	13-14y 352/1459 (24.1)
Pac-Sa et al ^{S66}	Spain	The study population were schoolchildren from first and second grade of compulsory secondary education, that is, adolescents aged 13 and 14 years age of all schools and colleges, both public and private or semi-private, from Castellon and surrounding locations.	U/NR	ISAAC Q	3995	2002	12-17y 242/1928 (12.6)	12-17y 412/2067 (19.9)
Penaranda et al ^{S34}	Colombia	Described in Table S1	Urban	ISAAC Q	7085	2002	13-14y 380/1772 (21.4)	13-14y 559/1993 (28.1)
Porto Neto et al ^{S67}	Brazil	The students were selected from children who attended the public and private schools of Passo Fundo. Information regarding the number of schools and students was obtained from the records at the Secretariat of Education. A total of 46 schools were identified. From these, 26 schools were chosen by systematic randomized sampling	Urban	ISAAC Q	2948	2002	13-14y 339/1435 (23.6)	13-14y 533/1513 (35.2)
Riguera et al ^{S68}	Brazil	In the city, there were 1,214 children in the age group of interest, of whom 1,076 were enrolled between the fifth and eighth grades in three schools (14.6% at a private school, 78.3% at a municipal school and 7.1% at a state school).	Urban	ISAAC Q	772	2007	13-14y 111/339 (32.8)	13-14y 135/402 (33.6)
Shamssain et al ^{S69}	United Kingdom	They prepared sampling frames of mixed-sex state schools with more than 100 pupils in each schoolyear. One school was randomly selected from each sampling frame, to produce 33 schools for study.	U/NR	ISAAC Q	3000	-	13-14y 415/1510 (27.5)	13-14y 472/1490 (31.7)

Soto-Quiros et al ^{S40}	Costa Rica	Described in Table S1	Rural/Urban	ISAAC Q	6144	1995	13-14y 418/1476 (23.8)	13-14y 571/1724 (33.1)
Sugiyama et al ^{S70}	Japan	According to the ISAAC protocol, all second-grade junior high school students (13–14 years of age) in Utsunomiya City and Tochigi City, including Mibu town, were study targets. The ISAAC questionnaires were distributed in 16 of 22 schools in Utsunomiya City and in eight of nine schools in Tochigi City via the educational committee.	Urban	ISAAC Q	4466	1996	13-14y 950/2219 (42.8)	13-14y 924/2221 (41.6)
Tamay et al ^{S71}	Turkey	The number of schools and children were calculated according to the number of children attending Grade 8 in each district. Of those children, 5% from each district were planned. 10,894 children aged 13–14 year in randomly selected 61 primary schools of 32 districts without selection by urban or suburban residence or variations in socioeconomic status were surveyed by the ISAAC questionnaire.	Urban	ISAAC Q	9991	-	13-14y 1916/5164 (37.1)	13-14y 1909/4749 (40.2)
Toledo et al ^{S72}	Brazil	A cross-sectional study of a random sample probability sample by conglomerates was used in which the prevalence of asthma was evaluated in the city of Taubate, São Paulo State, in Brazil.	Urban	ISAAC Q	809	-	13-14y 118/352 (33.5)	13-14y 178/457 (39.0)
Wang et al ^{S73}	Canada	We analysed Canadian data from cross-sectional Phase 3 studies within ISAAC, conducted in two Phase 3A centres (Hamilton, Saskatoon) and three Phase 3B centres (Vancouver, Winnipeg and Halifax). In each centre, the investigators recruited participants using randomly selected schools as sampling units except in Saskatoon where all schools were contacted.	Urban	Other Q.	8334	2003	13-14y 711/4071 (17.5)	13-14y 864/4263 (20.3)
Yan et al ^{S74}	Taiwan	Two junior high schools in each of the 12 school districts in Taipei were randomly chosen to enter the study.	Urban	ISAAC Q	6303	2002	13-14y 1438/3203 (44.9)	13-14y 1308/3093 (42.3)

Zar et al ^{S75}	South Africa	Schools within the Cape Town metropolitan area were selected by stratified random sampling in both surveys to achieve a representative spread of pupils across the area. The three strata comprised schools with predominantly black (Xhosa speaking) pupils, mixed-race (majority Afrikaans speaking) pupils and white pupils (now integrated to varying degrees).	Urban	ISAAC Q	5178	1995	13-14y 582/2088 (27.9)	13-14y 987/3073 (32.1)
					5037	2002	13-14y 735/2025 (36.3)	13-14y 1198/2994 (40.0)

PR; Prevalence of rhinitis; ISAAC: International Study of Asthma and Allergies in Childhood; Q: questionnaire; SFAR: score for allergic rhinitis; SPT: Skin prick test; M: male; F: female.

Table S3. Characteristics of the included studies assessing prevalence of rhinitis in adults.

Study Ref (N=12)	Country	Sampling method	Residency	Method for assessing PR	Sample analysed	Study period	Rhinitis	
							M (%)	F (%)
Bjerg et al ^{S76}	Sweden	2 cross-sectional surveys, EXHRS in 1990, Ga2len-Survey in 2008 selected for this analysis were those participants from both surveys that were in the same age range (20-44) and from the same centres using a random sample technique.	Rural only	ECRHS and GA ² LEN Q	8982	1990	20-44y 950/4339 (21.9)	20-44y 984/4643 (21.2)
					9156	2008	20-44y 1246/3954 (31.5)	20-44y 1587/5202 (30.5)
Desalu et al ^{S77}	Nigeria	The study area has 12 electoral wards, obtained from the state electoral commission. To select the participants, a multi-stage cluster sampling approach was used based on cluster equality and homogeneity. The electoral wards were defined as clusters and a sample frame containing the list of 12 clusters was constructed. Of these, 9 were selected by simple random sampling. A list of households was drawn up for each cluster and these were also randomly selected.	Urban	ECRHS Q	733	2005-2006	18-45y 141/441 (32.0)	18-45y 76/292 (26.0)
Filipiak et al ^{S78}	Germany	The city of Erfurt (former GDR) is located in the centre of Germany and Augsburg in the south. The total population of the two cities are similar. In the city of Augsburg (MONICA study) a total of 311 subjects was selected in each sex and 10-year age group from the population register of the city. In the city of Erfurt (Stage II ECRHS study) subjects were randomly selected.	Urban	ECRHS Q and IgE/SPT	3222	1991-1992 Erfurt	25-64y (9.5)	25-64y (9.3)
						1994-1995 Augsburg	25-64y (15.0)	25-64y (18.9)
Hannaford et al ^{S79}	United Kingdom	A postal questionnaire was sent to a random sample of 1000 residents in each of the 12 mainland Health Boards of Scotland (with Orkney and Shetland residents included in the Grampian sample) and 100 residents in the Western Isles.	Rural/Urban	Other Q	15 788	1998	30-44: 20.2 45-59: 12.2 60-74: 8.8 75+: 8.9	30-44: 24.3 45-59: 15.1 60-74: 9.5 75+: 6.8
Klossek et al ^{S80}	France	This cross-sectional survey was carried out in 2006 in a French population-based sample. The data were collected by a polling organization in 3 waves using	Urban	SFAR and ARIA	10 038	2006	18-65y 1179/4756	18-65y 1906/5282

		face-to-face interviews at home.					(24.8)	(36.1)
Konno et al ^{S81}	Japan	A population-based, cross-sectional study was conducted with Japanese subjects 20–79 years of age, living in ten different areas of Japan. Detailed methods for selecting areas, participants were not described but a reference was provided.	Urban	ECRHS Q	22 819	2006-2007	20-29y: 48.2 (45.7-50.7) 30-39y: 45.2 (42.9-47.4) 40-49y: 40.9 (38.6-43.2) 50-59y: 32.9 (31.0-34.9) 60-69y: 25.2 (23.4-27.1) 70-79y: 18.0 (16.1-19.9)	20-29y: 47.8 (45.2-50.4) 30-39y: 49.7 (47.5-51.9) 40-49y: 50.0 (47.8-52.2) 50-59y: 38.7 (36.8-40.6) 60-69y: 29.6 (27.7-31.4) 70-79y: 20.1 (18.2-22.0)
Kurt et al ^{S82}	Turkey	14 cities were selected from different geographical regions of the country. Schools were selected randomly from rural and urban areas of each city.	Rural/Urban	Other Q	25 843	2000	Mean 40y Rural: 17.5 (16.7–18.2) Urban: 11.7 (11.4–12.0)	Mean 35y Rural: 21.2 (20.4–22.0) Urban: 17.0 (16.4–17.6)
Lindgren et al ^{S83}	Sweden	In 2000, a questionnaire was sent to a total of 11933 randomly selected individuals aged 18–77 and 9319 (78%) answered. The study population originated from two different study populations, 5039 individuals (response rate 71%) from a new random selection, and 4280 individuals (response rate 87%) constituting a follow-up group from an earlier selection.	Rural/Urban	Other Q	9319	2000	18-77y AR: 800/4341 (18.4) NAR: 266/4341 (6.1)	18-77y AR: 1064/4975 (21.4) NAR: 339/4975 (8.0)
Morais-Almeida et al ^{S84}	Portugal	A stratified (by gender, age, and region), multistep defined sample was used. In a first phase, the number of needed participants from each Portuguese region was defined based on the data from the 2001 Portuguese Census. In a second phase, municipalities were selected within each of the five Portuguese regions until reaching a prespecified number of elder	Rural/Urban	ECRHS Q. VAS scale and ARIA	3678	2008	65+y 432/1527 (28.3)	65+y 665/2151 (30.9)

		subjects in proportion to the sample size. The final selection was made using a random-route methodology, where households and nursing homes were included, in each location.						
Okuda ^{S33}	Japan	Described in Table S1	Rural/Urban	Other Q	10 866 (in total)	2001	20-29y: 22.1 (10.4-27.7) 30-39y: 22.1 (17.3-26.8) 40-49y: 24.8 (20.2-29.4) 50-59y: 14.7 (10.7-18.6) 60-79y: 10.6 (7.5-13.7)	20-29y: 21.9 (16.9-26.8) 30-39y: 25.8 (21.5-30.1) 40-49y: 26.1 (21.8-30.3) 50-59y: 24.1 (19.8-28.4) 60-79y: 10.6 (7.6-13.6)
Song et al ^{S85}	Korea	Possible subjects were recruited using a stratified random sampling method and were invited by postal mail and then by telephone to participate.	Urban	Other Q and SPT	984	2006	≥65y 121/434 (27.9)	≥65y 131/550 (23.8)
Sonomjamts et al ^{S86}	Mongolia	Ten family clinics out of 52 were selected randomly which were estimated to cover approx 20000 population at large. 5 family clinics are located in the centre of the city and other 5 clinics are selected peripheral area of the city. Total of approx 1200 adults aged 20 years and over were planned to be randomly selected. The household registration was continued until the desired sample size of qualified respondents was reached.	Urban	ECRHS Q, WHO Protocol for Assessment of P of Major RD and GINA	1021	-	≥20y 139/606 (22.9)	≥20y 145/595 (24.4)

PR; Prevalence of rhinitis; RD: respiratory diseases; ECRHS: European Community Respiratory Health Survey; Q: questionnaire; SFAR: score for allergic rhinitis; GINA: Global Initiative for Asthma; ARIA: Allergic Rhinitis and its Impact on Asthma; VAS analogue scale: Visual analogue Scale for Rhinitis; SPT: Skin prick test; M: male; F: female.

Table S4. Study quality assessment of the included studies

Study Ref	Representativity			Reliability	Quality rating score Max= 5
	Sampling method Probability sampling (including: simple random, systematic, stratified g, cluster, two-stage and multi-stage sampling)=1 Non-probability sampling (including: purposive, quota , convenience and snowball sampling)=0	Sample size Calculated=1 Not calculated= 0	Response rate Reported=1 Not reported or if RR<60% =0	Data collection method ISAAC/ECHRS=2 Non-ISAAC/ECHRS but validated questionnaires=1 Non- validated questionnaires or Not clearly defined=0	
Ahn et al ^{S1}	1	0*	1	2	4
Al-Ghobain et al ^{S47}	1	1	1	2	5
Al-Riyami et al ^{S2}	1	0*	1	2	4
Amarasekera et al ^{S3}	1	0	1	2	4
Amizadeh et al ^{E48}	1	0	1	1	3
Annesi-Maesano et al ^{S4}	1	1	0	2	4
Anthracopoulos et al ^{S5}	1	1	1	0	3
Arnedo-Pena et al ^{S49}	1	0*	1	2	4
Arnedo-Pena et al ^{S6}	1	1	1	2	5
Awadh Behbehani et al ^{S50}	1	0*	0	2	3
Backer et al ^{S7}	1	0*	1	2	4
Bjerg et al ^{S76}	1	1	1	1	4
Brescianini et al ^{S51}	0	0*	0	2	2
Castro et al ^{S8}	0	0	1	2	3
Chiang et al ^{S52}	1	1	1	2	5
De Brito et al ^{S53}	1	1	0	2	4
Dell et al ^{S9}	1	1	1	2	5
Del-Rio-Navarro et al ^{S10}	1	0*	1	2	4
Desalu et al ^{S77}	1	1	1	1	4
Droma et al ^{S54}	1	0*	1	2	4
Duggan et al ^{S11}	1	1	1	2	5
Fagan et al ^{S55}	0	0	1	2	3
Falade et al ^{S12}	1	1	1 RR given for boys (87%) and girls (77%)	2	5
Filipiak et al ^{S78}	1	1	1	1	4
Futamura et al ^{S13}	1	1	1	2	5
Garcia-Marcos et	1	1	1	2	5

al ^{S14}					
Graif et al ^{S56}	1	1	1	2	5
Hahm et al ^{S15}	1	1	1	2	5
Hannaford et al ^{S79}	1	0	1	2	4
Higuchi et al ^{S16}	1	1	1	2	5
Hong et al ^{S17}	1	1	0	2	4
Kahwa et al ^{S18}	1	1	1	2	5
Kao et al ^{S19}	1	0	1	2	4
Kim et al ^{S57}	1	0	1	2	4
Klossek et al ^{S80}	1	0	1	1	3
Koffi et al ^{S58}	1	1	1	1	4
Kong et al ^{S20}	1	0	1	2	4
Konno et al ^{S81}	1	0	1	1	3
Kudzyte et al ^{S21}	1	0	1	2	4
Kurosaka et al ^{S22}	1	0	1	2	4
Kurt et al ^{S82}	1	0	1	1	3
Levesque et al ^{S23}	0	1	1	2	4
Liao et al ^{S24}	1	0	1	2	4
Lima et al ^{S25}	0	0	1	2	3
Lindgren et al ^{S83}	1	0	1	0	2
Luna et al ^{S59}	1	0	1	2	4
Mavale-Manuel et al ^{S26}	1	0	1	2	4
Maziak et al ^{S27}	1	0	1	2	4
Mercer et al ^{S60}	1	0	1	2	4
Mohammadzadeh et al ^{E28}	1	0*	1	2	4
Montefort et al ^{E29}	1	0	1	2	4
Morais-Almeida et al ^{S30}	1	1	1	2	5
Morais-Almeida et al ^{S84}	1	1	1	2	5
Moyes et al ^{S31}	1	0	1 (one center had a RR< 60% and was excluded from the analysis)	2	4
Munivvana et al ^{S61}	0	0	1	2	3
Musharrafieh et al ^{S62}	0 (random sampling originally planned but due to war issues, a convenient sample was used)	0	0	2	2
Nahhas et al ^{S32}	1	0	1 (RR given for boys (86.2%) and girls 84.6%)	2	4

Narayana et al ^{S63}	0	0	0	2	2
Nordvall et al ^{S64}	0 (schools were randomized except for one which was chosen by convenience)	0	1	2	3
Okuda ^{S33}	1	0	0 (RR= 53.7%)	1	2
Owayed et al ^{S65}	1	0	1	2	4
Pac-Sa et al ^{S66}	0	0	1	2	3
Penaranda et al ^{S34}	1	0	1	2	4
Peroni et al ^{S35}	1	0	1	2	4
Porto Neto et al ^{S67}	1	1	1	2	5
Rad et al ^{S36}	1	0*	1	2	4
Riguera et al ^{S68}	0	0	1	2	3
Sanchez-Lerma et al ^{S37}	0	1	1 (RR= 60.6%)	2	4
Selnes et al ^{S38}	1	0	1	0 (1985 and 1995) and 2 (2000)	2 (1985; 1995) and 4 (2000)
Shamssain et al ^{S69}	1	1	1	2	5
Simoni et al ^{S39}	0	0	1	2	3
Song et al ^{S85}	1	0	1	1	4
Sonomjamts et al ^{S86}	1	0 (desired but not calculated)	0	2	3
Soto-Quiros et al ^{S40}	1	0	1	2	4
Sugiyama et al ^{S70}	0	0	0	2	2
Suh et al ^{S41}	1	0	1 (RR= 61.8%)	2	4
Tai et al ^{E42}	0	0	1 (RR= 65%)	2	3
Tamay et al ^{S43}	1	1	1	2	5
Tamay et al ^{S71}	1	1	1	2	5
Toledo et al ^{E72}	1	1	1	2	5
Wang et al ^{S44}	1	0	1	1	3
Wang et al ^{S73}	1	0*	0 (only in one center RR>60%. Acknowledged in limitations)	2	3
Wu et al ^{S45}	1 (all schools in Taipei)	0	1	2	4
Yan et al ^{S74}	1	0	1	2	4
Zar et al ^{S75}	1	0	1	2	4
Zhao et al ^{S46}	1	0 (approx. size given but rationale not provided)	1	2	4

*In accordance with the ISAAC committee recommendation, a sample size of 3000 schoolchildren was used.

