

## Articles

# Worldwide variation in prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema: ISAAC

*The International Study of Asthma and Allergies in Childhood (ISAAC) Steering Committee\**

## Summary

**Background** Systematic international comparisons of the prevalences of asthma and other allergic disorders in children are needed for better understanding of their global epidemiology, to generate new hypotheses, and to assess existing hypotheses of possible causes. We investigated worldwide prevalence of asthma, allergic rhinoconjunctivitis, and atopic.

**Methods** We studied 463 801 children aged 13–14 years in 155 collaborating centres in 56 countries. Children self-reported, through one-page questionnaires, symptoms of these three atopic disorders. In 99 centres in 42 countries, a video asthma questionnaire was also used for 304 796 children.

**Findings** We found differences of between 20-fold and 60-fold between centres in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema, with four-fold to 12-fold variations between the 10th and 90th percentiles for the different disorders. For asthma symptoms, the highest 12-month prevalences were from centres in the UK, Australia, New Zealand, and Republic of Ireland, followed by most centres in North, Central, and South America; the lowest prevalences were from centres in several Eastern European countries, Indonesia, Greece, China, Taiwan, Uzbekistan, India, and Ethiopia. For allergic rhinoconjunctivitis, the centres with the highest prevalences were scattered across the world. The centres with the lowest prevalences were similar to those for asthma symptoms. For atopic eczema, the highest prevalences came from scattered centres, including some from Scandinavia and Africa that were not among centres with the highest asthma prevalences; the lowest prevalence rates of atopic eczema were similar in centres, as for asthma symptoms.

**Interpretation** The variation in the prevalences of asthma, allergic rhinoconjunctivitis, and atopic-eczema symptoms is striking between different centres throughout the world. These findings will form the basis of further studies to investigate factors that potentially lead to these international patterns.

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See Commentary page 1220

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## Introduction

There have been few studies of the population prevalence of allergic rhinitis and atopic eczema, and although hundreds of asthma-prevalence studies have been done in various parts of the world, they have seldom used standard approaches. An exception is the European Community Respiratory Health Survey (ECRHS),<sup>1–3</sup> which involved surveys of asthma and allergic-rhinitis prevalence in adults aged 20–44 years in 48 centres in 22 countries, although only nine centres in six countries were outside of western Europe. The ECRHS suggested that there were regional risk factors for asthma and allergic rhinitis in western Europe, but it did not comprehensively assess the global patterns. For children, the largest standard studies of the prevalences of asthma, allergic rhinitis, or atopic eczema have involved at most four countries.<sup>4–6</sup>

Thus, in some respects, the epidemiology of asthma and other allergic disorders is currently similar to that of cancer epidemiology in the 1950s and 1960s, when the international patterns of the incidence of cancer were studied.<sup>7</sup> These studies revealed striking international differences that gave rise to many new hypotheses, tested in further epidemiological studies that identified previously unknown risk factors for cancer. These risk factors may not have been in the hypotheses investigated if the initial international comparisons had been confined to few western countries. More specifically, Rose<sup>8,9</sup> has noted that whole populations may be exposed to risk factors for disease (eg, high exposure to house-dust-mite allergen) and the patterns may be apparent only when comparisons are made between, rather than within, populations.

Therefore, we carried out systematic, standardised, international comparisons of the prevalence of asthma and allergies to generate new hypotheses and to investigate existing hypotheses in the International Study of Asthma and Allergies in Childhood (ISAAC). The detailed findings for the prevalence and severity of the symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema in children aged 6–7 years and 13–14 years will be reported elsewhere. Here, we give an overview of the findings for children aged 13–14 years (the age-group that was studied by all participating centres), assess the relationship between the findings for the three disorders, and discuss the potential for future ecological and case-control studies.

## Methods

Phase one of the ISAAC programme<sup>10</sup> used a simple standard approach at minimum cost in as wide a range of centres and countries as possible, based on school populations to ensure

high response rates. We decided that phase-one studies would involve no invasive or expensive tests. We recruited collaborating centres through professional networks. Each centre agreed to adhere to the study protocol and to complete a registration document and obtain their own funding. Regional coordinators were responsible for the participation of centres within their regions.

The compulsory core sample of the study for all centres was children aged 13–14 years who completed simple one-page written questionnaires about symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema.<sup>10</sup> We report the answers to selected questions or combinations of selected questions: for asthma—“Have you had wheezing or whistling in the chest in the last 12 months?”; and for allergic rhinoconjunctivitis—“In the past 12 months, have you had a problem with sneezing, or a runny, or a blocked nose when you DID NOT have a cold or the flu? If yes: in the past 12 months, has this nose problem been accompanied by itchy-watery eyes?”; for atopic eczema—“Have you ever had an itchy rash which was coming and going for at least 6 months? If yes: Have you had this itchy rash at any time in the last 12 months? If yes: Has this itchy rash at any time affected any of the following places: the folds of the elbows, behind the knees, in front of the ankles, under the buttocks, or around the neck, ears, or eyes?”

We also used a video asthma questionnaire, that showed clinical signs and symptoms of asthma followed by questions, which was strongly recommended for use in this age-group.<sup>11–13</sup> The European and international versions of the video showed five sequences of clinical asthma in different situations, of which two sequences were common to both versions. After each sequence, the children were asked to specify whether their breathing had been like the person in the video; the terms asthma or wheezing were not mentioned at any stage. We report answers to the first video sequence, which showed a person wheezing at rest. This video sequence was at least as sensitive and specific for predicting bronchial hyper-responsiveness as the written questionnaire, and more repeatable.<sup>11–13</sup> The video questionnaire was shown after the compulsory written questionnaire, to the same children, on the same occasion to keep any potential bias to a minimum, although the order has been shown not to affect the outcome.<sup>11</sup>

We calculated that a sample size of 3000 per age-group was needed to provide sufficient precision for estimates of symptom severity, but smaller sample sizes—minimum 1000—were sufficient to calculate rates.<sup>10</sup> We determined the sampling frame mainly by geographical areas and most centres (69%) chose schools within their study area by random selection. Standard guidelines for translation of the questionnaires from English were provided<sup>14</sup> in an attempt to decrease difficulties associated with the use of the questionnaires in many different languages.<sup>15</sup> These guidelines included the use of translators familiar with asthma terminology, consultation with the local community, back-translation into English by an independent translator, and pilot testing of the translation.

We present data received and verified by the ISAAC International Data Centre by June 30, 1996, which was checked by Nov 24, 1997 (table 1). For some collaborating centres, the data-collection and checking processes had not been completed by these deadlines; their findings will be included in future analyses.

For each of asthma, allergic-rhinoconjunctivitis, and atopic-eczema symptoms, we calculated 12-month prevalences by dividing the number of positive responses to each question by the number of completed questionnaires. Data are presented for each centre by country, with the results ordered by weighted mean rate of the country, from highest to lowest. We calculated variations in data by finding the difference between the highest and lowest centre rates, and between the highest and lowest rates from the 10th to 90th percentiles. We assessed the association between the rates of the different disorders by calculating Spearman's rank correlation coefficient. We compared the written and video asthma questionnaires by cross-tabulation of the results in tertiles. We calculated the

| Centre                              | Collaborator    | Video | Response rate (%) | Number of children |
|-------------------------------------|-----------------|-------|-------------------|--------------------|
| <b>Albania</b> (Tiranë [Alb])       | A Priftanji     | Y     | 96.8              | 2957               |
| <b>Algeria</b> (Algiers [Arab]) *   | A Bezzaoucha    | N     | 97.8              | 1173               |
| <b>Argentina</b>                    |                 |       |                   |                    |
| Buenos Aires (Sp)                   | N Salmun        | Y     | 87.7              | 2996               |
| Rosario (Sp)                        | N Salmun        | Y     | 91.2              | 3008               |
| <b>Australia</b>                    |                 |       |                   |                    |
| Adelaide (Eng)                      | D Kennedy       | Y     | 95.1              | 3030               |
| Melbourne (Eng)                     | C Robertson     | Y     | 97.3              | 2759               |
| Perth (Eng)†                        | L Landau        | Y     | 93.0              | 3650               |
| Sydney (Eng)                        | A Bouman        | Y     | 90.1              | 2839               |
| <b>Austria</b>                      |                 |       |                   |                    |
| Saltzburg (Ger)                     | J Reidler       | Y     | 85.1              | 3371               |
| Urfahr-Umgebung (Ger)               | G Haidinger     | Y     | 92.6              | 1515               |
| <b>Belgium</b> (Antwerp [Dut])      | P A Vermeire    | N     | 97.4              | 1515               |
| <b>Brazil</b>                       |                 |       |                   |                    |
| Curitiba (Port)                     | N Rosário       | N     | 93.9              | 3004               |
| Porto Alegre (Port)                 | R Stein         | N     | 96.8              | 3195               |
| Recife (Port)                       | P Gd M Bezerra  | N     | 97.6              | 3086               |
| Salvador (Port)*                    | L S dF Souza    | N     | 93.4              | 3162               |
| São Paulo (Port)*                   | D Solé          | N     | 94.0              | 3007               |
| <b>Canada</b>                       |                 |       |                   |                    |
| Hamilton (Eng)‡                     | M Sears         | Y     | 67.4              | 3051               |
| Saskatoon (Eng)‡                    | B Taylor        | Y     | 70.5              | 1901               |
| <b>Chile</b>                        |                 |       |                   |                    |
| Central Santiago (Sp)§              | I Sanchez       | N     | 99.7              | 2944               |
| Punta Arenas (Sp)                   | L Amarales      | Y     | 93.1              | 3482               |
| South Santiago (Sp)                 | E Cortez        | Y     | 96.5              | 3051               |
| Valdivia (Sp)                       | M Calvo-Gil     | N     | 81.6              | 3231               |
| <b>China</b>                        |                 |       |                   |                    |
| Beijing (Ch)                        | Y Chen          | Y     | 99.0              | 4167               |
| Chongqing (Ch)                      | K-H Chen        | Y     | 99.2              | 4296               |
| Guangzhou (Ch)                      | N S Zhong       | Y     | 99.7              | 3855               |
| Hong Kong (Ch)                      | C Lai           | Y     | 95.6              | 4666               |
| Shanghai (Ch)                       | M Bao-Shan      | Y     | 99.3              | 3483               |
| Wulumuqi (Ch)                       | M-L Xiao        | Y     | 97.7              | 3207               |
| <b>Costa Rica</b> (Costa Rica [Sp]) | M E Soto-Quirós | N     | 91.4              | 3200               |
| <b>Estonia</b>                      |                 |       |                   |                    |
| Narva (Rus)                         | M-A Riikjarv    | N     | 86.4              | 1424               |
| Tallinn (Est)                       | M-A Riikjarv    | Y     | 85.3              | 3560               |
| <b>Ethiopia</b>                     |                 |       |                   |                    |
| Addis Ababa (Amh)                   | K Melaku        | N     | 98.6              | 2951               |
| Jima (Amh) *                        | B Seyoum        | N     | 98.9              | 3027               |
| <b>Finland</b>                      |                 |       |                   |                    |
| Helsinki (Fin)                      | M Kajosaari     | Y     | 94.6              | 2855               |
| Kuopio County (Fin)                 | J Pekkanen      | Y     | 96.5              | 2878               |
| Lapland Area (Fin)                  | L Soiniinen     | Y     | 97.3              | 3077               |
| Turku and Pori County (Fin)         | T A Koivikko    | Y     | 96.9              | 3085               |
| <b>France</b>                       |                 |       |                   |                    |
| Marseilles (Fr)                     | D Charpin       | Y     | 83.5              | 3494               |
| Montpellier (Fr)                    | P Godard        | N     | 92.6              | 3384               |
| Pessac (Fr)¶                        | A Taytard       | N     | 73.9              | 3302               |
| Strasbourg (Fr)                     | E Quoix         | Y     | 79.8              | 5403               |
| West Marne (Fr)                     | I Annesi        | N     | 85.6              | 2961               |
| <b>Georgia</b>                      |                 |       |                   |                    |
| Kutaisi (Geo)                       | N Khetsuriani   | N     | 89.6              | 3297               |
| Tbilisi (Geo)                       | A Gamkrelidze   | N     | 90.8              | 3449               |
| <b>Germany</b>                      |                 |       |                   |                    |
| Greifswald (Ger)                    | A Kramer        | Y     | 87.5              | 3169               |
| Münster (Ger)                       | U Keil          | Y     | 94.0              | 4003               |
| <b>Greece</b> (Athens [Grk])        | C Gratziau      | N     | 87.0              | 2561               |
| <b>India</b>                        |                 |       |                   |                    |
| Akola (Hin/Mar/Eng)                 | R Maheshwari    | N     | 86.2              | 2138               |
| Bombay (Hin/Mar/Eng)                | M K Joshi       | Y     | 90.9              | 4225               |
| Bombay (Hin/Mar/Eng)                | U Pai           | N     | 88.4              | 2226               |
| Bombay (Mar/Eng)                    | K Raghavan      | Y     | 99.4              | 3178               |
| Borivali (Hin/Mar/Eng)              | V A Khatar      | Y     | 100.0             | 3878               |
| Chandigarh (Hin/Eng)                | L Kumar         | Y     | 97.4              | 3129               |
| Jodhpur (Hin)                       | K C Jain        | Y     | 84.5              | 1094               |
| Kottayam (Maly)                     | T U Sukumaram   | N     | 90.7              | 2047               |
| Madras* (Tam/Eng)                   | S Rajajee       | Y     | 90.0              | 1903               |
| Madras (Tam/Eng)                    | N Somu          | Y     | 96.2              | 3086               |
| New Delhi (Hin/Eng)                 | G R Sethi       | Y     | 100.0             | 3026               |
| Neyveli (Tam/Eng)                   | G Jayaraj       | Y     | 99.9              | 3281               |
| Orissa (Hin/Eng)                    | P K Kar         | Y     | 100.0             | 1248               |
| Pune (Hin/Eng)                      | N M Hanumante   | Y     | 99.8              | 2702               |

| Centre                                                 | Collaborator       | Video | Response rate (%) | Number of children |
|--------------------------------------------------------|--------------------|-------|-------------------|--------------------|
| <b>Indonesia</b> (Bandung [Indo])†                     | B Karnen           | Y     | 95·7              | 2249               |
| <b>Iran</b>                                            |                    |       |                   |                    |
| Rasht (Pers)                                           | M-R Masjedi        | Y     | 99·0              | 3182               |
| Tehran (Pers)                                          | M-R Masjedi        | N     | 86·4              | 2691               |
| <b>Italy</b>                                           |                    |       |                   |                    |
| Ascoli Piceno (Ital)                                   | S Bonini           | Y     | 99·2              | 1130               |
| Cosenza (Ital)                                         | E Bonci            | N     | 89·4              | 1068               |
| Cremona (Ital)                                         | F Rusconi          | Y     | 99·3              | 1201               |
| Emilia-Romagna (Ital)                                  | M Blocca           | Y     | 97·7              | 3961               |
| Empoli (Ital)                                          | L Chetoni          | Y     | 97·7              | 1046               |
| Firenze (Ital)                                         | E Chellini         | Y     | 96·7              | 1171               |
| Frosinone (Ital)†                                      | R Ronchetti        | N     | 96·3              | 1147               |
| Milano (Ital)                                          | L Bisanti          | Y     | 96·8              | 3373               |
| Roma (Ital)                                            | F Forastiere       | Y     | 94·2              | 3323               |
| Siena (Ital)                                           | E Renzoni          | N     | 97·4              | 1181               |
| Torino (Ital)                                          | G Ciccone          | Y     | 97·5              | 1242               |
| Trento (Ital)¶                                         | S Piffer           | N     | 94·4              | 4426               |
| Verona (Ital)                                          | A Boner            | Y     | 98·1              | 2208               |
| <b>Japan</b> (Fukuoka [Jap])                           | S Nishima          | Y     | 94·2              | 2831               |
| <b>Kenya</b>                                           |                    |       |                   |                    |
| Eldoret (Eng)                                          | F O Esamai         | Y     | 100·0             | 3024               |
| Nairobi (Eng)                                          | J A Odhiambo       | Y     | 99·0              | 3243               |
| <b>Kuwait</b> (Kuwait [Arab])*‡                        | J A Al-Momen       | Y     | 70·4              | 1056               |
| <b>Latvia</b>                                          |                    |       |                   |                    |
| Riga (Lat/Rus)                                         | M Leja             | Y     | 95·3              | 3004               |
| Rural Latvia (Lat/Rus)                                 | M Leja             | Y     | 91·9              | 3145               |
| <b>Lebanon</b> (Beirut [Arab])*                        | F M Ramadam        | Y     | 100·0             | 2993               |
| <b>Malaysia</b>                                        |                    |       |                   |                    |
| Alor Setarl (Mal)                                      | K H Teh            | Y     | 91·0              | 3298               |
| Ipoh (Mal)*†                                           | W Y Lim            | Y     | 97·0              | 3313               |
| Klang Valley (Mal)                                     | J de Bruyne        | Y     | 91·4              | 6079               |
| Kota Bharu (Mal/Ch)                                    | B S Quah           | Y     | 95·9              | 3113               |
| Muar (Mal/Ch)*                                         | K W Chum           | N     | 90·5              | 2833               |
| <b>Malta</b> (Malta [Malt/Eng])                        | S Montefort        | Y     | 88·7              | 4184               |
| <b>Mexico</b> (Cuernavaca [Sp])                        | I Romieu           | N     | 92·3              | 3102               |
| <b>Morocco</b>                                         |                    |       |                   |                    |
| Casablanca (M Arab)                                    | Z Boueyad          | Y     | 98·4              | 3183               |
| Marrakech (M Arab)                                     | Z Boueyad          | Y     | 89·7              | 2900               |
| Rabat (Arab/Fr)                                        | A Bennis           | Y     | 96·7              | 3276               |
| <b>New Zealand</b>                                     |                    |       |                   |                    |
| Auckland (Eng)                                         | I Asher            | Y     | 94·6              | 3206               |
| Bay of Plenty (Eng)                                    | C Moyes            | Y     | 88·5              | 2813               |
| Christchurch (Eng)                                     | P Pattemore        | Y     | 95·5              | 3191               |
| Hawke's Bay (Eng)                                      | D Barry            | Y     | 96·7              | 3550               |
| Nelson (Eng)                                           | R Mackay           | Y     | 92·4              | 1839               |
| Wellington (Eng)                                       | J Crane            | Y     | 88·9              | 4424               |
| <b>Nigeria</b> (Ibadan [Eng])                          | B O Onadeko        | N     | 76·4              | 3057               |
| <b>Oman</b> (Al-Khod [Arab])                           | B M S Al Riyami    | N     | 94·0              | 3174               |
| <b>Pakistan</b> (Karachi [Urdu/Eng])                   | Z A Bhutta         | Y     | 100·0             | 1829               |
| <b>Panama</b> (David-Panamá [Sp])*                     | G Cukier           | N     | 96·2              | 2885               |
| <b>Paraguay</b> (Asunción [Sp/Gur])                    | J A Guggiari-Chase | Y     | 93·2              | 2966               |
| <b>Peru</b> (Lima [Sp])                                | P Chiarella        | Y     | 96·6              | 3158               |
| <b>Philippines</b> (Metro Manila [Filo/Eng])           | F Cua-Lim          | Y     | 95·5              | 3207               |
| <b>Poland</b>                                          |                    |       |                   |                    |
| Krakow (Pol, 1993)                                     | G Lis              | N     | 92·5              | 3750               |
| Krakow (Pol, 1995)                                     | G Lis              | N     | 92·5              | 2786               |
| Poznan (Pol)                                           | A Breborowicz      | Y     | 89·2              | 3631               |
| <b>Portugal</b>                                        |                    |       |                   |                    |
| Funchal (Port)                                         | F D Borges         | Y     | 96·5              | 3532               |
| Lisbon (Port)                                          | J E Rosado Pinto   | N     | 93·1              | 3030               |
| Portmao (Port)†                                        | C Nunes            | N     | 99·6              | 1058               |
| Porto (Port)                                           | J L dos Santos     | N     | 81·9              | 3131               |
| <b>Republic of Ireland</b> (Republic of Ireland [Eng]) | L Clancy           | N     | 92·1              | 3147               |
| <b>Romania</b> (Cluj [Rom])                            | D Dumitrascu       | N     | 99·0              | 3396               |
| <b>Russia</b> (Moscow [Rus])                           | R Khaitov          | Y     | 85·3              | 3411               |
| <b>Singapore</b> (Singapore [Eng])                     | B-W Lee            | Y     | 91·4              | 4206               |
| <b>South Africa</b> (Cape Town Afr/Xh)                 | H Nelson           | Y     | 82·8              | 5173               |

| Centre                            | Collaborator        | Video | Response rate (%) | Number of children |
|-----------------------------------|---------------------|-------|-------------------|--------------------|
| <b>South Korea</b>                |                     |       |                   |                    |
| Provincial Korea (Kor)¶**         | S-I Lee             | Y     | 98·3              | 6990               |
| Seoul (Kor)¶**                    | S-I Lee             | Y     | 95·6              | 2993               |
| <b>Spain</b>                      |                     |       |                   |                    |
| Barcelona (Sp)                    | R M Busquets        | Y     | 91·2              | 3031               |
| Bilbao (Sp)                       | A D Rubio           | Y     | 89·8              | 3212               |
| Cádiz (Sp)                        | A R Asensio         | Y     | 96·0              | 3270               |
| Cartagena (Sp)                    | L García-Marcos     | Y     | 95·1              | 3017               |
| Castellón (Sp)                    | A Arnedo-Pena       | Y     | 93·6              | 3094               |
| Pamplona (Sp/Basq)                | F Guillén Grima     | Y     | 94·0              | 3040               |
| Valencia (Sp)                     | M M M Suárez-Varela | Y     | 99·9              | 3179               |
| Valladolid (Sp)*                  | A Blanco Quirós     | Y     | 99·8              | 3178               |
| <b>Sweden</b>                     |                     |       |                   |                    |
| Linköping (Swed)                  | N-I Kjellman        | Y     | 95·7              | 3377               |
| Stockholm/Uppsala (Swed)‡‡        | T Foucard           | Y     | 91·2              | 3075               |
| <b>Taiwan</b> (Taipei [Ch])¶¶     | K-H Hsieh           | Y     | 93·3              | 11 400             |
| <b>Thailand</b>                   |                     |       |                   |                    |
| Bangkok (Thai)‡                   | P Vichyanond        | Y     | 74·8              | 3713               |
| Chiang Mai (Thai)                 | M Trakultivakorn    | Y     | 94·7              | 3927               |
| <b>UK</b>                         |                     |       |                   |                    |
| Anglia and Oxford (Eng)†          | H R Anderson        | N     | 88·1              | 2324               |
| Guernsey (Eng)                    | D Jeff              | N     | 91·2              | 1170               |
| Isle of Man (Eng)                 | P V Powell          | N     | 91·1              | 1467               |
| Jersey (Eng)                      | C R Grainger        | N     | 89·7              | 1135               |
| North East and Yorkshire (Eng)    | H R Anderson        | N     | 83·1              | 3709               |
| North Thames (Eng)†               | H R Anderson        | N     | 85·4              | 2220               |
| North West (Eng)                  | H R Anderson        | N     | 83·2              | 3029               |
| Scotland (Eng)                    | H R Anderson        | N     | 84·6              | 4444               |
| South Thames (Eng)†               | H R Anderson        | N     | 86·9              | 2297               |
| South and West (Eng)†             | H R Anderson        | N     | 90·5              | 2707               |
| Sunderland (Eng)                  | M H Shamssain       | N     | 89·9              | 2092               |
| Surrey/Sussex (Eng)               | D Strachan          | N     | 91·0              | 2114               |
| Trent (Eng)†                      | H R Anderson        | N     | 89·0              | 2207               |
| Wales (Eng)†                      | H R Anderson        | N     | 86·1              | 2351               |
| West Midlands (Eng)†              | H R Anderson        | N     | 85·4              | 2219               |
| <b>Uruguay</b> (Montevideo [Sp])* | D Hotgado de Cuesta | Y     | 93·1              | 3072               |
| <b>USA</b>                        |                     |       |                   |                    |
| Chicago (Eng)†¶‡‡                 | V Persky            | N     | 89·9              | 1422               |
| Chicago (Sp/Eng)‡‡                | V Persky            | N     | 93·5              | 3756               |
| Seattle (Eng)†¶                   | G Redding           | Y     | 80·3              | 2330               |
| <b>Uzbekistan</b>                 |                     |       |                   |                    |
| Samarkand (Rus)*                  | T Aripova           | Y     | 87·9              | 1758               |
| Tashkent (Rus)*                   | T Aripova           | Y     | 96·8              | 2904               |

Afr=Afrikaans; Alb=Albanian; Amh=Amharic; Arab=Arabic; Basq=Basque; Ch=Chinese; Dut=Dutch; Eng=English; Est=Estonian; Fil=Filipino; Fin=Finnish; Fr=French; Geo=Georgian; Ger=German; Grk=Greek; Gug=Gugurati; Gur=Guarani; Hind=Hindu; Indo=Indonesian; Ital=Italian; Jap=Japanese; Kor=Korean; Lat=Latvian; Mal=Malay; Malt=Maltese; Maly=Malyalam; M Arab=Moroccan Arabic; Mar=Marathi; Per=Persian; Pol=Polish; Port=Portuguese; Rom=Romanian; Rus=Russian; Sp=Spanish; Swed=Swedish; Tam=Tamil; Thai=Thai; Urdu=Urdu; Xh=Xhosa. \*Single data entry. †Less than ten schools. ‡Response rate <80%. §No date of interview or date of birth on questionnaire. ¶Data recoded to eliminate inconsistent responses. ||No age or date of birth on questionnaire. \*\*No age on questionnaire. ††No sex information provided. ‡‡No eczema questionnaire.

Table 1: Language and video questionnaire used, response rates, and sample sizes by centre

proportion of children who reported symptoms of asthma, allergic rhinoconjunctivitis, or atopic eczema, or combinations of these symptoms. We also calculated the overall 12-month prevalence rates of symptoms of at least two of the three disorders and categorised them in ranges of 2·9% or less, 3·0–5·9%, 6·0–8·9%, and 9% or more.

## Results

463 801 children aged 13–14 years participated in 155 collaborating centres in 56 countries (table). The video questionnaire was used as well as the written questionnaire in 99 (64%) of these centres in 42 countries, for 304 796 children. Response rates were more than 80% in 149 (96%) centres. Written questionnaires were translated into 39 languages, including English (50 centres [32·2%]), Spanish (21 centres [13·5%]), Italian (13 centres [8·4%]), Chinese (nine centres [5·8%]), and Portuguese (nine centres [5·8%]).

|                              | Video questionnaire |        |       | Total |
|------------------------------|---------------------|--------|-------|-------|
|                              | Lower               | Middle | Upper |       |
| <b>Written questionnaire</b> |                     |        |       |       |
| Lower                        | 24                  | 8      | 1     | 33    |
| Middle                       | 8                   | 16     | 9     | 33    |
| Upper                        | 1                   | 9      | 23    | 33    |
| Total                        | 33                  | 33     | 33    | 99    |

Table 2: **Distribution of centres by tertiles, based on written and video asthma questionnaires**

12-month prevalences of asthma from the written questionnaires for each centre by country are shown in figure 1. The highest prevalence was about 20 times higher than in the centre with the lowest prevalence (range 1·6–36·8%), with an eight-fold variation seen between the 10th and 90th percentiles (3·9–30·6%). 12-month prevalences of asthma symptoms from the first video sequence are shown in figure 2. Worldwide patterns were similar to those from the written questionnaire; results were concordant in 63 (64%) of 99 centres for distribution of centres by tertiles (table 2). The rank correlation coefficient between centre prevalences for written and video questionnaires was 0·76 ( $p<0\cdot0001$ ). The prevalence of asthma symptoms reported on the video questionnaire was generally lower than that reported on the written questionnaire, probably because the video questionnaire asked for information on more severe asthma symptoms (wheezing at rest) than the written questionnaire (any wheezing).

12-month prevalences of symptoms of allergic rhinoconjunctivitis for each centre by country are shown in figure 3. We found about a 30-fold variation in the

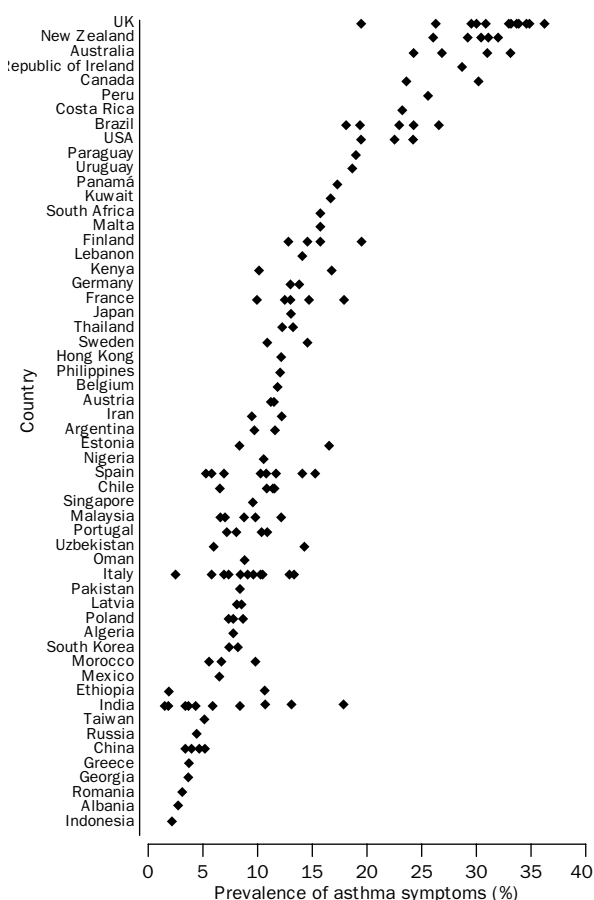


Figure 1: **12-month prevalences of self-reported asthma symptoms from written questionnaires**

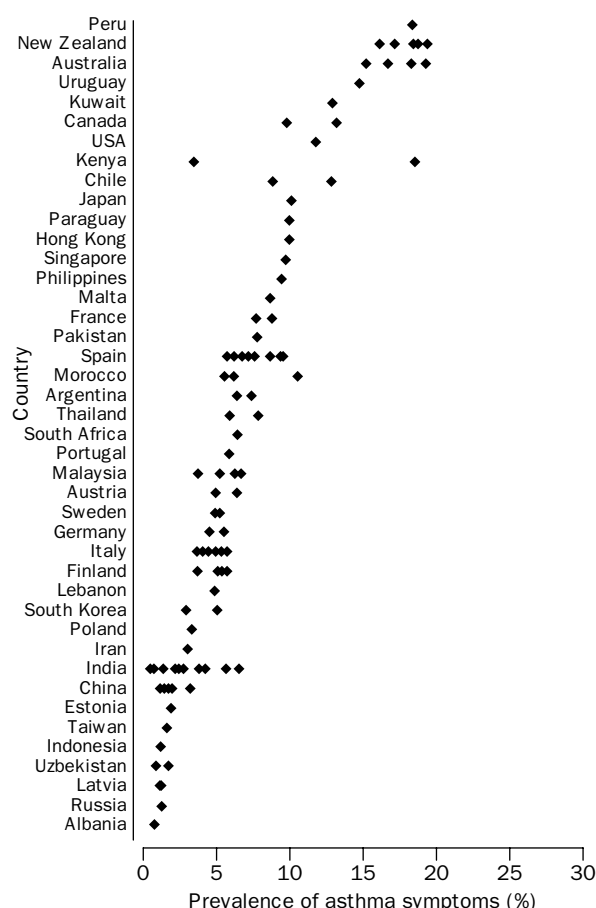


Figure 2: **12-month prevalences of asthma symptoms from video questionnaires**

rate of allergic-rhinoconjunctivitis symptoms between centres (range 1·4–39·7%), with a four-fold variation seen between the 10th and 90th percentiles (4·9–21·0%). The grouping of centres with a high prevalence of allergic-rhinoconjunctivitis symptoms into specific regions was less well defined than for asthma; by contrast, the centres with the lowest symptom prevalences for allergic rhinoconjunctivitis were similar to those for asthma symptoms (figures 1–3).

12-month prevalences of symptoms of atopic eczema for each centre by country are shown in figure 4. There was more than a 60-fold variation in prevalences of atopic-eczema symptoms between centres (0·3–20·5%), with an eight-fold variation between the 10th and 90th percentiles (2·0–15·6%). The international patterns for the prevalences of atopic-eczema symptoms differed in some ways from those for asthma and allergic rhinoconjunctivitis (figure 5). Nevertheless, significant correlations were seen between the prevalences of the different disorders.

The prevalence of symptoms of at least two of the three disorders varied from 0·3% to 18·5%, with an 11-fold variation between the 10th and 90th percentiles (1·4–15·6%; figure 6). Among symptomatic children, 72·9% had had symptoms of only one of the three disorders in the previous 12 months (figure 6).

## Discussion

The ISAAC programme has allowed a worldwide assessment of the prevalence of self-reported symptoms of asthma, allergic rhinoconjunctivitis, and atopic

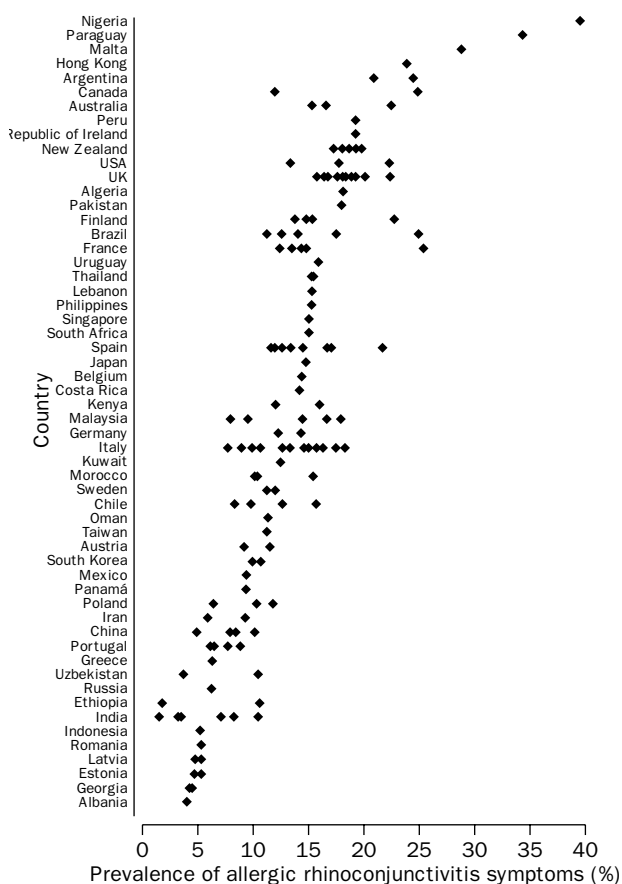


Figure 3: **12-month prevalences of allergic rhinoconjunctivitis symptoms**

eczema in children by standard methods. For many collaborating centres, the measurements were the first in their country of symptoms of these disorders, and for many countries, the participation of more than one centre enabled comparisons within countries. The worldwide variations in rates, and partly the variations seen within some countries, suggest that environmental factors (in their broadest sense) may be critical to the development of these disorders in childhood.

Despite the use of standard simple questionnaires, validated study protocols, including those for the use and translation of questionnaires, and stringent quality-control measures, difficulties in the comparability of information will unavoidably influence the results to some degree. For example, the questionnaires were translated into 39 languages, some of which had no colloquial terms for symptoms such as wheezing. Another difficulty is the sensitivity and specificity of the listed symptoms to identify children with the specific disorders. Although the questionnaires had been validated before the study,<sup>11-13,16-18</sup> our findings may not be applicable to countries in which infectious disorders with similar symptoms may be prevalent.

Our method of population sampling may also have been a potential source of bias, with school-based samples not being representative of children aged 13-14 years in some communities. However, the proportion of children who did not attend school would have been small for most centres. Response bias could have occurred if there were great variations in response rates and if participation was related to symptoms. However, a similar study in adults<sup>19</sup> that had lower response rates

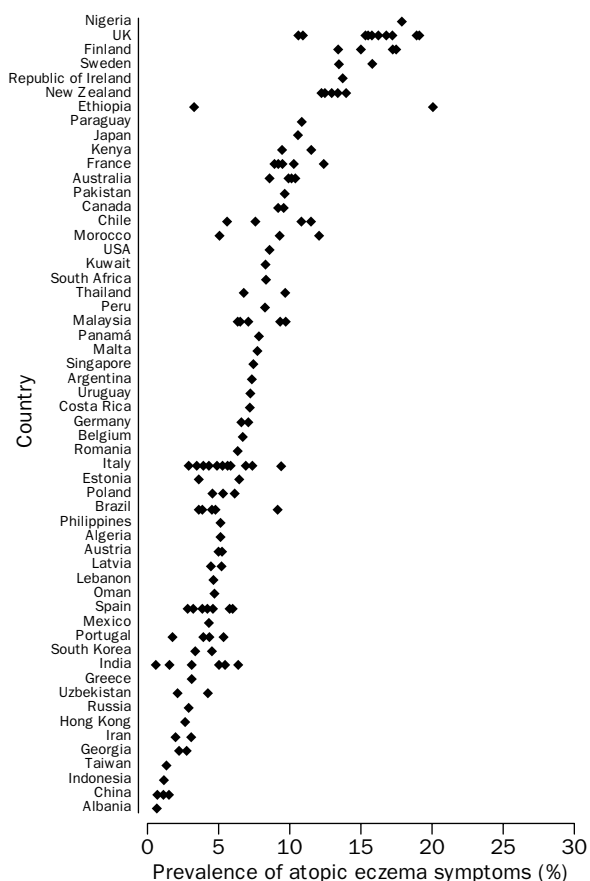


Figure 4: **12-month prevalences of atopic eczema symptoms**

than our study showed little evidence of response bias. Our response rates were high for most centres, and after exclusion of the few centres with response rates of less than 80%, the overall global patterns changed little. Therefore, response bias is unlikely to have seriously affected this study.

The international patterns of prevalences of these disorders should be considered with these potential biases in mind. For asthma symptoms, the highest prevalences from the written and video questionnaires were from the centres in the UK, New Zealand, Australia, Republic of Ireland, followed by most centres in North, Central, and South America. The lowest prevalences were reported from centres in several Eastern European countries, Indonesia, Greece, China, Taiwan, Uzbekistan, India and Ethiopia. Although asthma symptom prevalence rates were generally similar in centres within the same country, in some countries, such as India, Ethiopia, Italy, and Spain, large variations were seen between centres. There were also wide variations within regions, especially within Europe and Asia. Therefore, in addition to analyses of the global ecological patterns, there are opportunities for investigation of possible causative factors within countries and regions.

We believed that by showing rather than describing the signs and symptoms of asthma to children the video questionnaire would provide more accurate recognition of clinical asthma, which would be useful to compare information between populations with different cultures and languages.<sup>11-13</sup> Some differences in the findings for the written and video questionnaires for some centres in

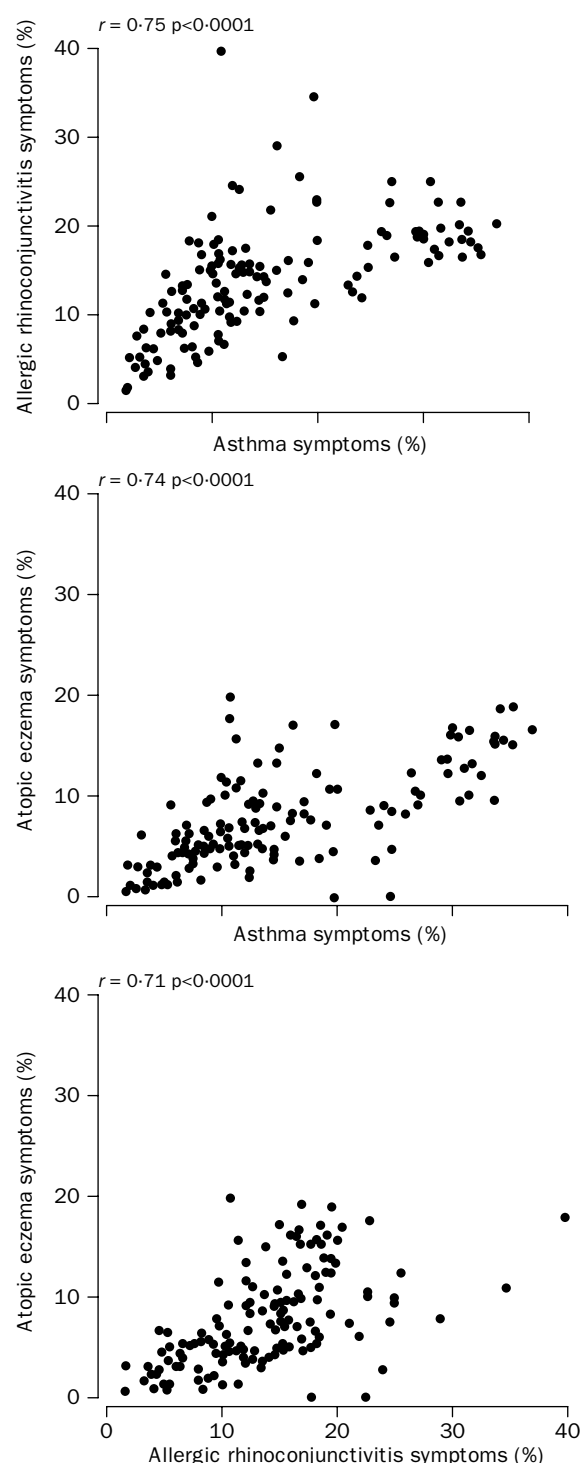


Figure 5: Scatter plots of 12-month prevalences of symptoms from written questionnaires

non-English-speaking countries, suggest that language factors may have led to differences in symptom prevalences. The highest prevalences for asthma symptoms were found mainly in English-speaking centres in western countries. These findings raise the possibility that environmental factors related to living conditions in these countries may be important. This hypothesis will need further study.

By contrast with asthma findings, the highest prevalences of allergic-rhinoconjunctivitis symptoms were reported from centres scattered across the world.

Several centres with the highest symptom prevalences were not represented among the centres with the highest asthma prevalences; therefore, the major risk factors for these related disorders may differ or may involve different latency periods and time trends.

For atopic eczema, the highest symptom prevalences included centres from many regions of the world, including some from Scandinavia and Africa not represented among the highest asthma rates. The centres with low prevalences of atopic-eczema symptoms were generally the same as those with low prevalences of asthma and allergic-rhinoconjunctivitis symptoms.

The interpretation of these large between-country differences for allergic rhinoconjunctivitis and atopic eczema is likely to be partly influenced by validity of the written questionnaires, despite the translation guidelines,<sup>10,14</sup> and the avoidance of diagnostic labels such as allergic rhinoconjunctivitis and atopic eczema in the written questionnaires. For example, some of the high or low values for atopic-eczema prevalences could relate to differences in the interpretation of the written questionnaire based on the presence of a flexural itchy rash, or differences in the frequency of other skin disorders, such as ectoparasites, which involve the skin flexures in children. Findings from the validation study of the rhinitis questionnaire led to the use of the symptoms of rhinoconjunctivitis rather than rhinitis alone since it was more closely related to positive skin-test reactivity.<sup>18</sup> Further validation exercises and studies that include objective clinical assessment (planned for phase two of ISAAC) will be required to better understand these international differences and the large variations seen within some countries.

When self-reported symptoms of more than one atopic disorder were taken into account, the highest prevalences were observed predominantly in English speaking Western countries, decreasing prevalences were found in northwest to southeast Europe, higher prevalences were seen among many Spanish-speaking and Portuguese-speaking communities in Latin America than in centres in Spain and Portugal, and widely differing prevalences were found between centres with populations of similar ethnic origins within countries such as China (including Taiwan and Hong Kong), India, Italy, and Ethiopia. These findings were dominated to some extent by the asthma and allergic-rhinoconjunctivitis results, because of their relatively higher symptom prevalences.

We looked at the relation between the different disorders in individual children; most symptomatic children had had symptoms of only one disorder in the previous year, which indicates that many different risk factors may be required for the clinical expression of these related disorders. Studies from China and Africa have shown that striking differences in asthma prevalences may occur in populations, despite similar prevalences of atopic sensitisation.<sup>20,21</sup> These findings support the view that in addition to atopic sensitisation, other risk factors may be important in the development of asthma, allergic rhinoconjunctivitis, and atopic eczema in susceptible populations.

Despite the difficulties in interpretation of our findings, there is substantial potential for ecological analyses. For example, the global pattern of asthma prevalences was consistent with evidence that air pollution is not a major risk factor for the development

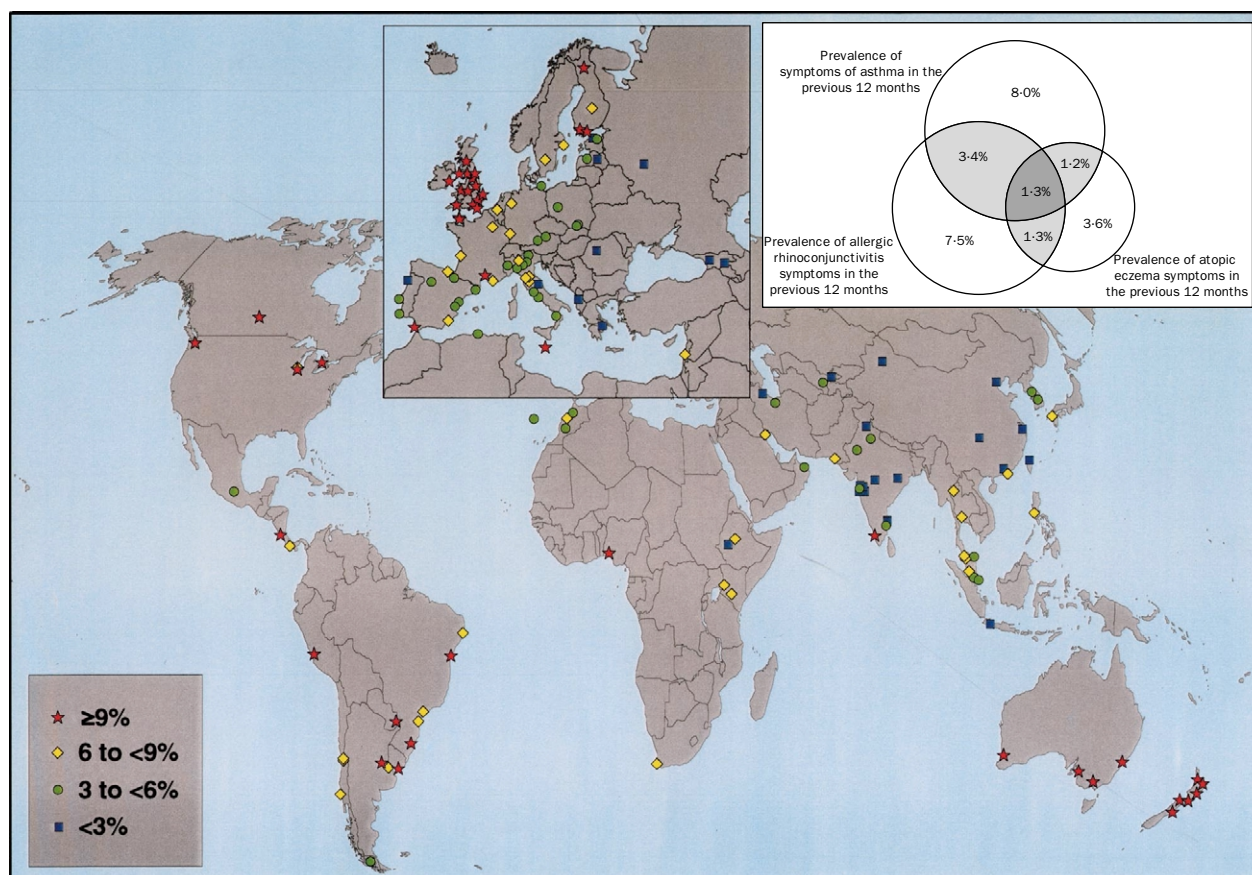


Figure 6: **World map of 12-month prevalences of symptoms of at least two of three disorders**

Venn diagram shows overall proportions of children with symptoms of asthma, allergic rhinoconjunctivitis, or atopic eczema, or combinations of symptoms.

of asthma in populations, although it may exacerbate asthma in individuals.<sup>22-24</sup> Regions such as China and Eastern Europe, with some of the highest degrees of air pollutants such as particulate matter and sulphur dioxide, generally had low rates of asthma prevalence, whereas those such as western Europe and the USA with high degrees of air pollutants such as ozone, had intermediate prevalences of asthma, and some centres with the lowest degrees of air pollution, such as those in New Zealand, had high prevalences of asthma. Ecological analyses will also be possible of the international prevalences of these disorders and other putative risk or protective factors, or their surrogate measures. These analyses will need to be based on standard international public-health, socioeconomic, demographic, and environmental data.

Comprehensive comparisons between ISAAC phase-one findings and those from the ECRHS are difficult since the ECRHS primarily involved centres in western Europe. Nevertheless, the ECRHS also showed the highest asthma-symptom prevalences in the UK, Australia, New Zealand, the Republic of Ireland, and the USA, with lower prevalences in non-English-speaking countries in Europe, North Africa, and India. In addition, the centres with the highest prevalences of atopy (defined as the presence of at least one positive allergen-specific IgE) were mainly in English-speaking populations,<sup>23</sup> which is also consistent with our findings.

Phase one of the ISAAC study has shown a wide variation in the prevalence of symptoms of asthma,

allergic rhinoconjunctivitis and atopic eczema throughout the world, with differing international patterns for the different disorders. Although we acknowledge the limitations of international prevalence comparisons of this kind, we have provided a framework for further aetiological research into the genetic, lifestyle, environmental, and medical-care factors affecting these disorders.

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