

Worldwide variations in the prevalence of asthma symptoms: the International Study of Asthma and Allergies in Childhood (ISAAC)

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

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ABSTRACT: The International Study of Asthma and Allergies in Childhood (ISAAC) was designed to allow comparisons between populations in different countries.

ISAAC Phase One, reported here, used standardized simple surveys which were conducted among representative samples of school children from centres in most regions of the world.

Two age groups (13-14 and 6-7 yrs) with approximately 3,000 children in each group were studied in each centre. The 13-14 yr olds (n=463,801) were studied in 155 centres (56 countries) and the 6-7 yr olds (n=257,800) were studied in 91 centres (38 countries).

There were marked variations in the prevalence of asthma symptoms with up to 15-fold differences between countries. The prevalence of wheeze in the last 12 months ranged from 2.1-32.2% in the older age group and 4.1-32.1% in the younger age group and was particularly high in English speaking countries and Latin America. A video questionnaire completed in the older age group in 99 centres (42 countries) showed a similar pattern.

The major differences between populations found in the International Study of Asthma and Allergies in Childhood Phase One are likely to be due to environmental factors. The results provide a framework for studies between populations in contrasting environments which are likely to yield new clues about the aetiology of asthma.

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There is considerable concern that the prevalence of asthma and allergic diseases is increasing in Western and developing countries. However, the aetiology of these conditions remains poorly understood, despite a large volume of clinical and epidemiological research within populations that has been directed at explaining why some individuals and not others develop asthma and allergies. Investigation of the reasons for variations in prevalence between populations may be a more fertile source of new aetiological clues, but little is known about worldwide variations in the prevalence of asthma and allergic diseases. Phase One of the International Study of Asthma and Allergies in Childhood (ISAAC) developed simple methods for measuring the prevalence of childhood asthma, allergic rhinitis and atopic eczema for international comparisons, suitable for different geographical locations and languages [1, 2]. ISAAC is a unique project which has attracted worldwide interest and large scale participation.

The aims of ISAAC Phase One were: 1) to describe the prevalence and severity of asthma, rhinitis and eczema in children living in different centres and to make comparisons within and between countries; 2) to obtain baseline measures for assessment of future trends in the prevalence and severity of these diseases; and 3) to provide a framework for further aetiological research into lifestyle, environmental, genetic and medical care factors affecting these diseases.

This publication describes the results of the worldwide ISAAC study of the prevalence of symptoms of asthma. The prevalence of symptoms of allergic rhinoconjunctivitis and atopic eczema, and an overview of all three conditions are described in other publications [3, 4].

Materials and methods

ISAAC Phase One uses core questionnaires designed to assess the prevalence and severity of asthma and allergic disease in defined populations. The methods are described in the ISAAC manual and a previous paper concerning rationale and methods [2]. Each centre obtained the necessary approval from an ethics committee before the start of the study.

Collaborating centres and registration

ISAAC was open to any collaborator who agreed to adhere to the protocol. Countries in which there was little existing information about asthma and allergies were particularly encouraged to participate. Each collaborating centre was responsible for completing a registration document and obtaining its own funding. Included in this first worldwide analysis are a total of 155 centres for the 13-14 yr

old age group and 91 centres for the 6–7 yr old age group. For each centre included, the data were received and verified by the ISAAC International Data Centre by June 30, 1996. The data-checking processes and a detailed report on study design and methods were completed by November 24, 1997. The first centre began its survey in 1991, but most centres undertook the data collection in 1994 and 1995. A small number of other centres, where the ISAAC questionnaire was used, are not included in this worldwide analysis. Reasons included that the data checking and report were not completed or because of low number of participating children (<1,000), low response rate of children within schools, or other important departures from the protocol.

Sampling frame

The sampling frame was schoolchildren of two age groups (13–14 and 6–7 yrs old) within a specified geographical area (ISAAC centre), for which a detailed map was provided. The ISAAC centre was most commonly an urban area (a city) and therefore may not be representative of the country. Within centres there was no attempt to select affluent *versus* poor districts. A minority of ISAAC centres were regions within a country (*e.g.* in the UK), or a whole country (*e.g.* Costa Rica, Malta and Republic of Ireland). In a small number of the 246 centre/age groups there was further definition of the sampling frame by school type (17%), ethnic group (1%) and language (3%). In 31% of centres some schools were excluded from the sampling frame before selection or excluded after selection for a variety of reasons, including recent participation in a similar study, children with disabilities unable to complete the questionnaires and very small numbers of children. The school selection within the sampling frame was representative of the geographical area, without selection by urban or rural residence or variations in socioeconomic status, and it included either all schools with children within the age group (26% of centres) or a random sample of such schools (74% of centres). A minority (19%) used stratification of the sample before random selection. Among the 90 centres studying both age groups the strategies used for the sampling frame and selection of sample were similar for both age groups.

Selection of subjects

Subjects aged 13–14 yrs were selected because they were able to self-complete the written and video questionnaires. The younger age group, 6–7 yrs, was chosen as this is the youngest age when children are usually at school. The majority of centres (74%) chose the school grade with children mostly of the desired age group, choosing one (26%), two (71%) or three or more grades (3%). A minority of centres (24%) chose children by their actual age, regardless of the grade within the school. The age of children was checked against the age calculated from the date of birth, but where there were inconsistencies or missing data the given age was used.

The participation rates of schools were calculated as the number of participating schools divided by the number of schools approached for participation. The response rate of children was calculated as the number of children for whom there was a completed written questionnaire in the

participating schools divided by the number of children approached. A high response rate was sought and the majority of centres achieved >80%.

Sample size

The recommended sample size was 3,000 to ensure good prevalence estimates for severe asthma. For a sample size of 3,000 the 95% confidence interval (CI) around an estimate of 1% would be 0.64–1.33 and around an estimate of 30% would be 28.4–31.6 [5]. Centres with limited resources or small populations were included in the prevalence comparisons, providing that the sample size was at least 1,000 per age group.

Phase One core questionnaire modules

The ISAAC core questionnaires have been published previously [2], and used in a pilot study [1]. Most of the questions used for asthma symptoms are based on questions used in previous respiratory epidemiological studies and include both sensitive and specific indicators of asthma [6]. Questions about the date of completion of the questionnaire, child's date of birth, age and sex were also included. Some centres added questions on ethnicity and other questions (*e.g.* on environment) after the core questions, but analyses of these are not included in this paper.

Written questionnaire. Use of written questionnaires on wheezing, allergic rhinitis and atopic eczema for the 13–14 yr old group was a requirement for participation in ISAAC Phase One. Written questionnaires to parents for the 6–7 yr old group were strongly recommended and used in 59% of centres. The questionnaires were completed by the children in the older age group and by the parents in the younger age group. The severity of asthma symptoms was assessed by three questions that asked about the following symptoms in the last 12 months: number of attacks of wheezing; sleep disturbed due to wheezing; and wheezing severe enough to limit speech to only one or two words at a time between breaths.

Translation. In 81% of centres the written questionnaire was translated from English into one (88%) or more (12%) local languages. The method of translation was standardized according to guidelines developed in Germany [7] and adapted for ISAAC (ISAAC Document 41). These guidelines included the use of translators familiar with asthma terminology (98% of centres that used translations), consultation with the local community (60%) and back-translation into English by an independent translator (99%). The written questionnaires were used in 41 different languages. English was used most commonly (32% of centres), followed by Spanish (15%), Italian (9%), Hindi (7%), Chinese (6%), Portuguese (6%), Marathi (5%) and Malay (4%) and other languages made up the remainder.

Video questionnaire. A video using the audiovisual presentation of young people with clinical symptoms and signs of asthma was completed, where possible, by the 13–14 yr old group [8, 9]. After completing the written questionnaire, the children themselves were shown the video and answered questions at the time. The video elicited information without using written language terms to

describe asthma symptoms. It was used in 99 centres with the original "European" English-language version in 33 centres and the revised "International" version in 66 centres. Both versions show five sequences of young persons with different manifestations of asthma. Two scenes were the same in both versions: the first scene, of a young person wheezing while at rest, and the fourth scene, of a young person waking at night with coughing. The European version showed only European children and the questions were written in English, with local verbal translation of instructions where appropriate. The International version showed scenes with children of different ethnic groups, there was no written language and the questions were asked verbally in the local language. This version has been validated in children in a Hong Kong population [10].

Data management and analysis

Information on the questionnaires was entered, by each collaborating centre or a national centre, on to the computer exactly as recorded by the child or parent (except for six centres where data was recoded to eliminate inconsistent responses). The entry of data was checked by using double entry (68% centres) or other acceptable data-checking methods (24%), but 8% of centres used only single data entry. Data were transferred to the ISAAC International Data Centre (Auckland) using the protocol described in the ISAAC Coding and Data Transfer Manual.

The two age groups were analysed separately. Symptom prevalences in each centre were calculated by dividing the number of positive responses to each question by the number of completed questionnaires for the written and video questionnaires separately. Thus, apparent inconsistencies between responses to the stem and branch questions were accepted and not recoded. Basic descriptive summaries of the data were compiled by centre and country, in both age groups, along with correlations between variables. In centres where a random sample of schools was taken, the effect of cluster sampling by schools was examined in the correlations [11]. The effects of cluster sampling were small and hence ignored, allowing the use of the more robust Spearman correlations.

The within-country and between-country variances were estimated using a generalized linear mixed model in which country, and centre within country, are random effects. With this model, the ratio of the 95% CI of prevalences (between country to within country) were calculated. The ratio of the proportions responding "yes" for males and females in each centre was assessed, using the same generalized linear mixed model with the addition of sex as a fixed effect and a sex by country term to investigate any interaction [12].

Quality-control measures

The Steering Committee required documentation of the procedures for the study from each centre as a prerequisite for inclusion in publications of ISAAC worldwide results. Centres completed a Registration Document before starting the study and followed the protocol described in the published ISAAC Manual and ISAAC Coding and Data Transfer Manual. All data submitted to the ISAAC Inter-

national Data Centre were checked. Coding errors, omissions and inconsistencies in the demographic information were corrected with the assistance of the collaborator. A final report on all aspects of methodology actually used was completed for each centre and agreed between the ISAAC International Data Centre and the collaborators. This report included information about the sampling frame, sampling methods, participation rate of schools and of children within schools, the data entry method and details of translation. Some centres departed from the protocol (see footnotes to tables) but were included in the analysis if the methodology was otherwise sound.

Results

Participants

The requirements for analysis were met by 156 collaborating centres in 56 countries, with a total of 721,601 participating children. The principal investigators of the ISAAC collaborating centres are listed in the appendix. In the 13–14 yr age group, 155 centres from 56 countries participated, with a total of 463,801 participating children. The video questionnaire was completed in 99 collaborating centres in 42 countries, with a total of 304,796 children. For the 6–7 yr olds there were 91 collaborating centres in 38 countries, with a total of 257,800 participating children.

Information on the study sample is published elsewhere [3, 4]. More than 85% of centres had a high rate of both participation by schools and response rate by pupils; in <10% of centres there was a high rate of nonparticipation by schools, but there was a good response by pupils within schools. Participation rates of schools in the older age group averaged 94% (range 37–100%), and in the younger age group averaged 97% (range 57–100%). Response rates of children within participating schools in the older age group averaged 92% (range 67–100%) and in the younger age group averaged 89% (range 61–100%).

The age range of children within each age group varied because of variations in methods of selection within schools. In the older age group 85% of centres had more than 70% of children aged 13 and 14 yrs. In the younger age group 93% of centres had more than 70% of children aged 6 and 7 yrs. In neither age group did the variations in age affect the general pattern of results.

Written questionnaires

13–14 yr old group. The prevalence rates for symptoms of asthma are presented by centre and country in table 1. Thirty countries were represented by more than one centre. The geographic distribution of prevalence is illustrated, by centre on a world map (fig. 1), for positive answers to the question "Have you had wheezing or whistling in the chest in the last 12 months?". For this question there was a very wide range of prevalences, up to 15-fold differences, between countries, ranging from 2.1–4.4% in Albania, China, Greece, Georgia, Indonesia, Romania and Russia, to 29.1–32.2% in Australia, New Zealand, Republic of Ireland and the UK. These countries also tended to be at the extremes for the other questions. The two centres at the extremes, Akola (1.6%) and Scotland (36.7%), had

Table 1. — Summary of self-completed wheezing questionnaire (written) data, 13–14 yr old age group

Centre ^a	12-month prevalence						Ever had asthma	n
	Wheeze	≥4 Attacks	Wheeze disturbs sleep	Severe wheeze limiting speech	Exercise wheeze	Night cough		
<i>Africa</i>								
Ethiopia	6.2	3.2	1.4	4.1	13.9	14.5	2.5	5978
Addis Ababa	10.7	5.6	2.5	7.3	27.2	27.3	2.8	2951
Jimma ^{c,f}	1.9	0.9	0.3	1.0	1.0	2.0	2.2	3027
Kenya	13.9	3.8	4.2	5.8	24.0	27.3	11.2	6267
Eldoret	10.4	2.3	1.9	3.0	17.4	18.4	6.8	3024
Nairobi	17.1	5.2	6.3	8.4	30.2	35.6	15.4	3243
Nigeria								
Ibadan ^b	10.7	3.2	3.7	7.6	43.4	31.7	18.4	3057
South Africa								
Cape Town	16.1	3.3	3.6	5.2	21.4	23.6	13.1	5173
Regional total	11.7	3.4	3.1	5.4	23.3	23.3	10.2	20475
<i>Africa (French speaking)</i>								
Algeria								
Algiers ^f	7.8	2.0	1.8	3.5	13.6	19.6	6.4	1173
Regional total	7.8	2.0	1.8	3.5	13.6	19.6	6.4	1173
<i>Asia-Pacific</i>								
China	4.2	0.9	0.3	0.7	21.7	15.0	6.1	19008
Beijing	5.1	1.5	0.2	0.9	25.2	15.7	6.9	4167
Chongqing	4.7	0.8	0.2	0.4	25.1	11.1	7.1	4296
Guangzhou	3.4	0.7	0.3	0.5	17.4	18.9	3.9	3855
Shanghai	3.3	0.4	0.2	0.7	15.8	6.9	7.1	3483
Wulumuqi	4.0	1.0	0.3	0.8	24.3	23.4	5.4	3207
Hong Kong								
Hong Kong	12.4	4.4	0.5	2.4	29.1	27.7	11.2	4666
Indonesia								
Bandung ^f	2.1	0.4	0.8	0.9	2.3	4.0	1.6	2249
Japan								
Fukuoka	13.4	4.2	0.6	2.1	27.3	14.0	18.9	2831
Malaysia	9.6	2.7	0.8	1.8	14.0	24.0	10.9	18636
Alor Setar ^d	8.9	2.1	0.4	1.8	16.4	28.3	10.2	3298
Ipoh ^{f,h}	10.0	2.8	0.8	1.7	10.3	23.4	11.4	3313
Klang Valley	12.3	3.8	1.0	2.3	15.7	25.3	13.9	6079
Kota Bharu	6.8	1.7	0.4	1.3	9.9	21.6	8.6	3113
Muar ^f	7.1	2.0	1.0	1.4	16.4	19.4	7.4	2833
Philippines								
Metro Manila	12.3	2.4	2.0	4.1	21.4	34.3	17.6	3207
Singapore								
Singapore	9.7	2.1	1.3	2.4	13.2	11.3	20.9	4206
South Korea	7.7	1.6	0.2	2.7	12.4	8.6	2.4	9983
Provincial Korea ^{a,d}	7.5	1.5	0.2	2.7	11.9	8.3	2.2	6990
Seoul ^{a,d}	8.3	2.0	0.3	2.6	13.6	9.2	2.8	2993
Taiwan								
Taipei ^a	5.2	1.6	0.4	0.8	8.2	10.4	9.0	11400
Thailand	13.0	4.0	1.1	3.5	14.5	28.4	11.6	7640
Bangkok ^b	13.5	4.1	1.3	3.9	15.6	28.4	14.1	3713
Chiang Mai	12.6	3.8	1.0	3.2	13.5	28.5	9.3	3927
Regional total	8.0	2.2	0.6	1.8	16.0	17.8	9.4	83826
<i>Eastern Mediterranean</i>								
Iran	10.9	2.3	1.8	2.6	11.3	13.8	2.7	5873
Rasht	9.7	2.3	1.7	2.3	9.1	13.2	2.7	3182
Tehran	12.4	2.2	2.0	3.0	13.8	14.6	2.6	2691
Kuwait								
Kuwait ^{b,f}	17.0	6.3	5.7	10.6	24.7	30.5	17.5	1056
Lebanon								
Beirut ^f	14.4	4.1	5.0	7.0	16.1	22.4	11.6	2993
Malta								
Malta	16.0	4.6	2.4	3.6	20.6	31.8	11.1	4184
Morocco	7.5	2.1	2.2	2.7	17.9	17.6	11.7	9359
Casablanca	9.9	3.1	3.0	3.4	18.9	19.8	12.1	3183
Marrakech	5.6	1.5	1.0	2.2	21.1	18.6	17.1	2900
Rabat	6.8	1.7	2.7	2.4	14.2	14.5	6.6	3276
Oman								
Al-Khod	8.9	2.6	2.9	4.0	19.2	20.9	20.7	3174
Pakistan								
Karachi	8.5	2.0	1.6	3.9	15.1	17.6	7.3	1829
Regional total	10.7	2.9	2.6	3.8	16.9	20.2	10.7	28468
<i>Latin America</i>								
Argentina	10.9	3.1	2.1	3.8	15.1	39.1	7.3	6004
Buenos Aires	9.9	2.8	1.9	3.1	13.8	36.2	6.6	2996
Rosario	11.8	3.4	2.4	4.4	16.5	41.9	7.9	3008
Brazil	22.7	4.4	3.7	4.7	23.6	32.6	14.9	15454
Curitiba	18.4	3.5	2.7	4.6	19.8	30.1	8.6	3004
Porto Alegre	24.7	4.5	4.5	5.7	29.0	39.2	21.9	3195
Recife	19.7	3.8	4.6	4.8	20.5	30.9	20.9	3086
Salvador ^f	27.0	6.0	3.0	5.4	27.6	29.6	12.5	3162
São Paulo ^f	23.3	4.4	3.5	2.7	20.5	33.0	10.0	3007
Chile	10.2	1.5	1.4	2.5	15.9	21.6	10.7	12708
Central Santiago ⁱ	11.7	1.7	1.3	2.0	15.0	23.1	12.4	2944
Punta Arenas	6.8	1.1	0.8	1.3	6.3	15.5	7.3	3482

Table 1. - continued.

Centre*	12-month prevalence						Ever had asthma	n
	Wheeze	≥4 Attacks	Wheeze disturbs sleep	Severe wheeze limiting speech	Exercise wheeze	Night cough		
South Santiago	11.1	1.2	2.2	4.9	25.3	32.8	11.5	3051
Valdivia	11.5	2.1	1.2	2.2	18.0	16.2	11.9	3231
Costa Rica								
Costa Rica	23.7	5.3	3.5	10.1	24.2	31.1	18.5	3200
Mexico								
Cuernavaca ^l	6.6	1.5	1.6	2.4	4.0	13.6	5.5	3102
Panama								
David-Panamá ^f	17.6	3.4	2.0	6.7	14.6	21.7	16.9	2885
Paraguay								
Asunción	19.4	3.4	3.0	5.2	15.3	31.3	12.2	2966
Peru								
Lima	26.0	4.8	3.3	6.9	35.9	33.6	28.0	3158
Uruguay								
Montevideo ^f	19.0	5.4	2.6	5.1	18.4	28.1	15.3	3072
Regional total	16.9	3.4	2.6	4.5	19.1	28.6	13.4	52549
<i>North America</i>								
Canada								
Hamilton ^h	28.1	9.1	2.1	8.1	34.3	36.3	16.5	4952
Saskatoon ^h	30.6	10.0	2.2	8.9	36.5	37.5	19.2	3051
USA								
Saskatoon ^h	24.0	7.7	2.0	6.7	30.8	34.4	12.2	1901
Chicago (3) ^{a, g, h}	21.7	6.5	4.2	10.0	28.7	31.9	16.5	7508
Chicago (4) ^g	24.6	8.8	3.0	5.5	27.4	29.4	17.8	1422
Seattle ^{a, h}	19.8	5.6	5.9	13.3	29.5	35.5	16.1	3756
Regional total	22.9	6.7	2.4	7.4	28.2	27.6	16.4	2330
Regional total	24.2	7.6	3.4	9.2	30.9	33.7	16.5	12460
<i>Northern and Eastern Europe</i>								
Albania								
Tiranë	2.6	0.3	0.3	0.8	4.5	5.7	1.6	2957
Estonia	10.8	1.7	1.1	2.1	12.6	15.6	3.0	4984
Narva	16.7	2.0	2.2	4.0	21.2	18.6	2.5	1424
Tallinn	8.5	1.5	0.7	1.3	9.1	14.4	3.3	3560
Finland	16.0	3.5	0.5	3.1	20.6	16.5	6.6	11895
Helsinki	19.8	5.1	0.8	5.1	25.1	19.5	7.4	2855
Kuopio County	13.1	2.8	0.6	2.0	17.6	14.5	4.6	2878
Lapland Area	16.1	3.3	0.2	2.7	20.6	15.6	6.6	3077
Turku and Pori County	15.0	2.9	0.5	2.7	19.2	16.3	7.8	3085
Georgia	3.6	0.7	0.7	0.8	6.4	7.8	3.1	6746
Kutaisi	3.6	0.7	0.5	0.7	8.2	9.0	3.8	3297
Tbilisi	3.7	0.8	0.8	1.0	4.7	6.6	2.4	3449
Latvia	8.4	1.2	0.9	1.6	10.7	14.8	4.3	6149
Riga	8.3	1.1	0.7	1.4	8.6	12.3	3.9	3004
Rural Latvia	8.6	1.4	1.2	1.8	12.8	17.3	4.6	3145
Poland	8.1	1.9	0.9	1.7	9.3	14.8	2.4	10167
Krakow (1993)	8.8	2.1	0.7	1.9	9.7	15.9	2.9	3750
Krakow (1995)	7.5	1.9	0.9	1.8	9.9	16.1	2.3	2786
Poznan	7.9	1.7	1.0	1.5	8.3	12.6	2.0	3631
Romania								
Cluj	3.0	0.7	0.4	0.7	6.9	4.4	3.7	3396
Russia								
Moscow	4.4	0.7	0.1	0.8	6.6	5.6	2.4	3411
Sweden	12.9	3.9	0.8	2.0	19.3	12.0	10.4	6452
Linköping	11.2	3.5	0.7	1.7	17.4	10.2	10.0	3377
Stockholm/Uppsala ^e	14.8	4.5	0.9	2.3	21.4	14.0	10.8	3075
Uzbekistan	9.2	0.7	0.2	2.1	11.1	9.7	1.7	4662
Samarkand ^f	14.4	1.1	0.3	3.8	15.1	15.8	2.3	1758
Tashkent ^f	6.0	0.5	0.1	1.1	8.7	6.1	1.4	2904
Regional total	9.2	1.9	0.6	1.8	12.3	12.2	4.4	60819
<i>Oceania</i>								
Australia								
Adelaide	29.4	10.0	3.0	8.3	37.0	28.3	28.2	12278
Melbourne	33.5	12.8	3.3	8.7	41.4	27.8	30.4	3030
Perth ^h	27.3	9.9	3.3	8.2	35.7	27.7	26.6	2759
Sydney	31.4	9.6	2.3	8.7	38.9	28.6	30.2	3650
New Zealand	24.7	7.5	3.1	7.3	31.0	29.0	24.8	2839
Auckland	30.2	9.9	3.2	8.0	40.3	30.0	24.4	19023
Bay of Plenty	26.5	8.0	2.7	8.1	36.1	29.7	22.9	3206
Christchurch	29.5	9.0	3.3	7.1	39.4	31.3	22.3	2813
Hawke's Bay	29.6	9.7	2.9	7.5	40.3	27.4	25.9	3191
Nelson	32.4	11.0	4.6	8.6	42.4	33.2	25.7	3550
Wellington	30.9	10.2	2.6	8.2	43.3	26.3	20.2	1839
Regional total	31.6	11.1	3.0	8.3	41.1	30.3	26.3	4424
Regional total	29.9	9.9	3.1	8.1	39.0	29.3	25.9	31301
<i>South-east Asia</i>								
India								
Akola	6.0	1.6	1.1	3.0	9.5	14.1	4.5	37171
Bombay (16)	1.6	0.5	0.5	1.0	2.7	3.8	2.6	2138
Bombay (17) ^h	1.9	1.2	0.8	1.0	2.6	6.5	3.6	4225
Bombay (18)	10.6	1.8	1.3	3.2	11.1	22.4	6.5	2226
Borivali	3.6	1.0	0.8	1.4	7.4	14.9	5.2	3178
Chandigarh	3.4	0.6	0.4	1.6	5.3	10.2	5.9	3878
Jodhpur	4.2	1.5	0.7	2.7	8.0	8.0	3.3	3139
Kottayam	10.7	3.5	1.7	4.8	15.9	18.4	6.4	1094
	17.8	1.7	1.8	13.5	17.9	32.2	12.4	2047

Table 1. - continued.

Centre*	12-month prevalence						Ever had asthma	n
	Wheeze	≥4 Attacks	Wheeze disturbs sleep	Severe wheeze limiting speech	Exercise wheeze	Night cough		
Madras (2)	8.4	1.9	1.5	2.9	7.7	14.6	2.8	1903
Madras (3) ^h	6.0	3.3	2.0	3.6	7.4	11.5	1.8	3086
New Delhi	13.0	3.0	1.9	4.8	18.4	25.8	5.3	3026
Neyveli	6.0	1.9	1.0	2.5	23.2	16.9	2.4	3281
Orissa	3.8	0.8	0.8	2.1	6.8	13.5	2.8	1248
Pune	1.8	0.8	0.7	1.3	4.0	9.4	4.9	2702
Regional total	6.0	1.6	1.1	3.0	9.5	14.1	4.5	37171
<i>Western Europe</i>								
Austria	11.6	2.5	0.8	3.6	18.0	13.3	6.0	4886
Salzburg	11.5	2.3	0.8	3.0	17.5	13.3	6.3	3371
Urfahr-Umgebung	11.7	3.0	0.9	5.0	19.0	13.3	5.3	1515
Belgium								
Antwerp	12.0	3.5	1.5	2.6	13.1	21.2	8.1	1515
France	13.5	4.1	1.1	2.8	20.8	26.5	12.6	18544
Marseilles	14.9	4.0	1.2	2.8	22.8	26.9	14.4	3494
Montpellier	18.2	6.6	1.9	4.2	25.4	29.8	14.2	3384
Pessac ^{a,b}	12.8	3.9	1.0	1.8	19.3	24.3	15.0	3302
Strasbourg	10.2	2.6	0.6	2.4	17.9	26.2	10.1	5403
West Marne	13.3	4.2	1.4	2.9	20.1	25.4	10.7	2961
Germany	13.8	3.4	1.2	5.7	22.0	20.8	5.7	7172
Greifswald	13.3	3.0	1.1	5.1	23.0	21.5	4.2	3169
Münster	14.1	3.7	1.3	6.1	21.2	20.2	7.0	4003
Greece								
Athens	3.7	0.7	0.7	0.7	3.6	6.7	4.5	2561
Italy	8.9	2.0	0.6	2.0	14.5	21.2	9.9	26477
Ascoli Piceno	2.7	0.7	0.4	0.8	5.5	9.8	7.7	1130
Cosenza	7.1	1.4	0.0	2.3	14.8	22.4	8.1	1068
Cremona	9.2	1.7	0.7	1.6	13.2	19.7	8.1	1201
Emilia-Romagna	10.4	2.6	0.6	2.0	17.1	21.5	10.2	3961
Empoli	13.5	2.3	0.8	2.5	17.6	28.6	12.0	1046
Firenze	10.5	2.6	0.9	2.6	15.7	21.3	9.6	1171
Frosinone ^h	7.4	1.7	0.6	2.3	15.7	19.0	11.3	1147
Milano	10.6	2.3	0.7	2.5	18.0	27.3	10.7	3373
Roma	9.8	2.0	0.4	2.6	14.4	23.0	11.3	3323
Siena	13.0	3.0	1.2	3.0	20.8	26.4	11.0	1181
Torino	8.6	2.3	0.6	2.9	18.8	23.3	9.4	1242
Trento ^d	5.9	1.3	0.3	1.3	9.4	17.6	7.5	4426
Verona	7.5	2.0	0.4	1.3	12.0	15.9	11.8	2208
Portugal	9.5	2.4	1.4	2.2	13.9	17.0	12.1	10751
Funchal	10.6	2.7	1.8	2.7	16.6	19.8	13.1	3532
Lisbon	11.1	2.8	1.3	2.4	14.1	17.5	12.3	3030
Portimao ^h	8.1	2.0	1.4	1.9	14.8	18.1	10.3	1058
Porto	7.4	1.7	1.0	1.6	10.5	13.1	11.3	3131
Republic of Ireland								
Republic of Ireland	29.1	8.1	2.6	6.0	25.2	33.9	15.2	3147
Spain	10.3	2.7	1.1	2.4	16.1	22.4	10.5	25021
Barcelona	14.3	3.4	1.4	2.7	18.3	20.5	11.1	3031
Bilbao	11.9	4.2	1.5	3.0	19.8	25.6	16.3	3212
Cartagena	10.5	3.4	1.8	2.9	14.9	20.4	10.5	3017
Castellón	7.1	1.8	0.5	1.1	12.8	22.3	7.8	3094
Cádiz	15.4	3.2	1.9	4.2	20.2	28.0	11.2	3270
Pamplona	5.5	1.7	0.5	1.1	12.2	17.6	8.7	3040
Valencia	11.0	2.6	1.1	2.8	17.2	21.2	12.1	3179
Valladolid ^f	6.1	1.5	0.5	1.4	13.1	22.9	6.3	3178
UK	32.2	9.3	3.5	8.5	29.1	42.3	20.7	35485
Anglia and Oxford ^h	34.3	10.2	2.9	9.0	30.3	43.3	22.8	2324
Guernsey	35.0	9.6	4.0	8.6	31.7	44.9	21.4	1170
Isle of Man	33.4	9.1	3.4	8.5	30.7	41.5	18.8	1467
Jersey	35.2	10.7	2.7	8.5	30.7	45.1	18.8	1135
North East and Yorkshire	34.1	9.3	4.3	8.7	28.7	47.1	20.3	3709
North Thames ^h	30.5	7.4	3.3	7.7	25.9	47.1	18.2	2220
North West	30.0	9.0	3.5	7.9	26.1	46.1	19.8	3029
Scotland	36.7	11.6	4.7	10.0	31.4	42.3	21.4	4444
South Thames ^h	31.3	9.7	3.4	8.8	26.8	45.5	20.5	2297
South and West ^h	35.3	10.9	3.1	9.6	30.9	43.1	20.8	2707
Sunderland	19.9	6.2	2.4	5.0	24.2	21.0	22.2	2092
Surrey/Sussex	26.8	8.6	2.3	6.9	38.6	26.6	19.0	2114
Trent ^h	33.6	8.8	3.6	8.2	27.8	45.6	22.3	2207
Wales ^h	33.6	9.0	3.7	9.0	29.7	43.6	21.8	2351
West Midlands ^h	30.0	8.0	3.7	8.5	25.1	46.8	20.7	2219
Regional total	16.7	4.6	1.7	4.2	20.0	27.1	13.0	135559
Global total	13.8	3.7	1.7	3.8	18.8	22.3	11.3	463801

All data are presented as percentages of the study children. ^a: data recoded to eliminate inconsistent responses; ^b: response rate <80%; ^c: no age or date of birth on questionnaire; ^d: no age on questionnaire; ^e: no date of interview or date of birth on questionnaire; ^f: single data entry; ^g: no eczema questionnaire; ^h: <10 schools if ≥10 schools in sampling frame; ⁱ: no sex information provided; ^j: 90% children 11-12 yrs old. *: numbers in parenthesis indicate International Study of Asthma and Allergies in Childhood (ISAAC) registration number for that centre, as given by the national coordinator.

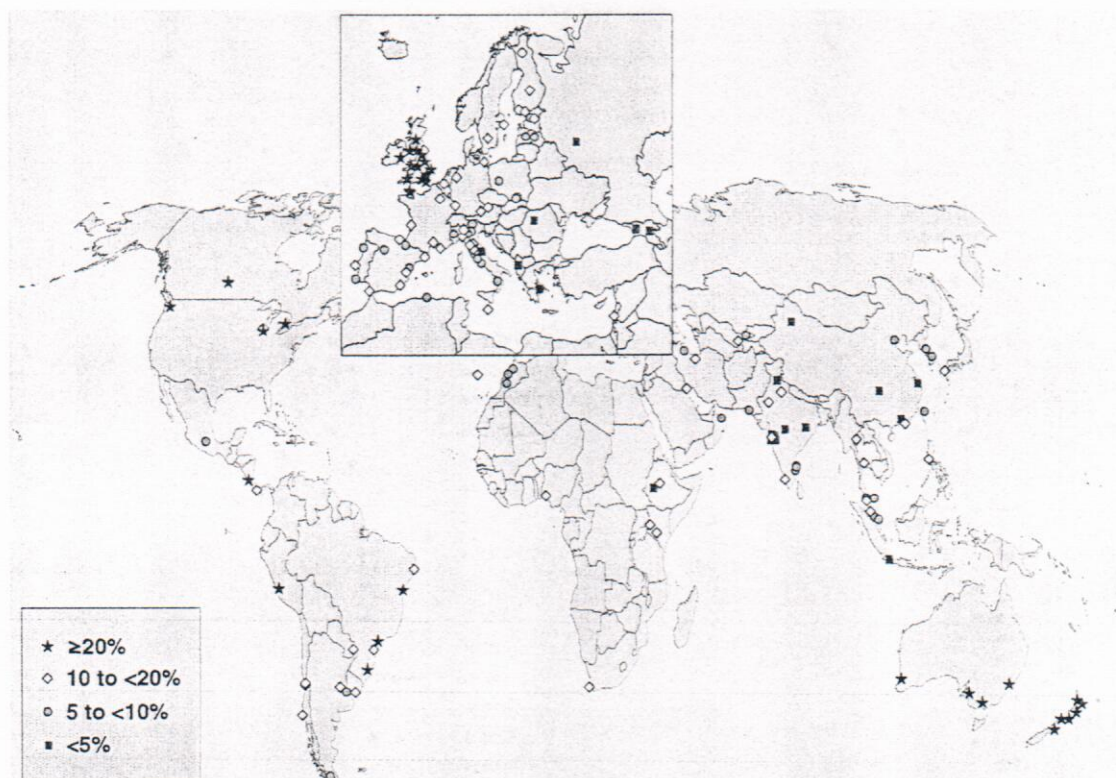


Fig. 1. - World map for the 13-14 yr old age group, showing the percentage of children who answered "yes" to the written question "Have you had wheezing or whistling in the chest in the last 12 months?". Each point represents the prevalence for one collaborating centre, with distinct colour symbols used for different prevalence ranges.

over 20-fold differences. Other countries that had a prevalence of 12 month wheeze under 10% were found mainly in Asia, Northern Africa, Eastern Europe and the Eastern Mediterranean regions and those over 20% were found mainly in North America, Latin America and Oceania.

The between-country variation (56 countries) was greater than the within-country variation (30 countries with more than one centre) for all questions: 12 month wheeze was 1.7 times larger; four or more attacks of wheezing in the last 12 months 2.8; waking on one or more nights a week 2.8; wheezing severe enough to limit speech to only one or two words at a time between breaths 1.9; wheeze with exercise 1.3; dry cough at night 1.5; and reported asthma ever 3.7 times larger.

The ranking of countries for sleep disturbance due to wheezing on ≥ 1 night week⁻¹ in the last 12 months is illustrated in figure 2. The seven countries with the highest prevalence of positive answers to this question were Brazil, Kenya, Kuwait, Lebanon, Nigeria, South Africa and the USA, which were not the countries ranking highest for the prevalence of 12 month wheeze. The seven countries with the lowest prevalence of positive answers to this question were Albania, China, Romania, Russia, South Korea, Taiwan and Uzbekistan, which were similar to the centres ranking lowest for the prevalence of 12 month wheeze. A similar ranking of highest centres was found for wheezing severe enough to limit speech to only one or two words at a time between breaths, but for ≥ 4 attacks of wheezing the ranking of highest centres was similar to 12 month wheeze.

Correlations between prevalence and severity were also examined. However, because the severity questions are

not independent of the 12 month wheeze question the correlations were assessed between the proportion of the population wheezing in the last 12 months and the proportion of the population of wheezers in that centre answering positively to questions on severity in the last 12 months. The correlations examining relative severity were: four or more attacks of wheezing ($r=0.25$, $p=0.0016$); sleep disturbance due to wheezing on one or more nights per week ($r=-0.097$, $p=0.23$); and wheezing severe enough to limit speech to only one or two words at a time between breaths ($r=0.012$, $p=0.89$), indicating that the proportion of wheezers with severe symptoms changed little with increasing prevalence of wheeze.

Every country had some children who reported having "asthma" at some time in their lives, but the range in prevalence was very large, ranging from 1.6-3.0% in Albania, Estonia, Ethiopia, Indonesia, Iran, Poland, Russia, South Korea and Uzbekistan to 20.7-28.2% in Australia, New Zealand, Oman, Peru, Singapore and the UK. The correlation between the proportion of the population wheezing in the last 12 months and the proportion of the population reporting "asthma ever" was $r=0.76$ ($p<0.0001$). In some countries the reporting of 12 month wheeze was much higher than the reporting of "asthma ever" (e.g. Ethiopia 6.2%, 2.5%; Iran 10.9%, 2.7%; Brazil 22.7%, 14.9%; Canada 28.1%, 16.5%; Germany 13.8%, 5.7%; "wheeze", "asthma", respectively), whereas in other countries there was much more "asthma" than "wheeze" (e.g. China 4.2%, 6.1%; Nigeria 10.7%, 18.4%; Japan 13.4%, 18.9%; Singapore 9.7%, 20.9%; "wheeze", "asthma", respectively).

Exercise wheeze in the last 12 months was reported more frequently than wheeze in the last 12 months in all

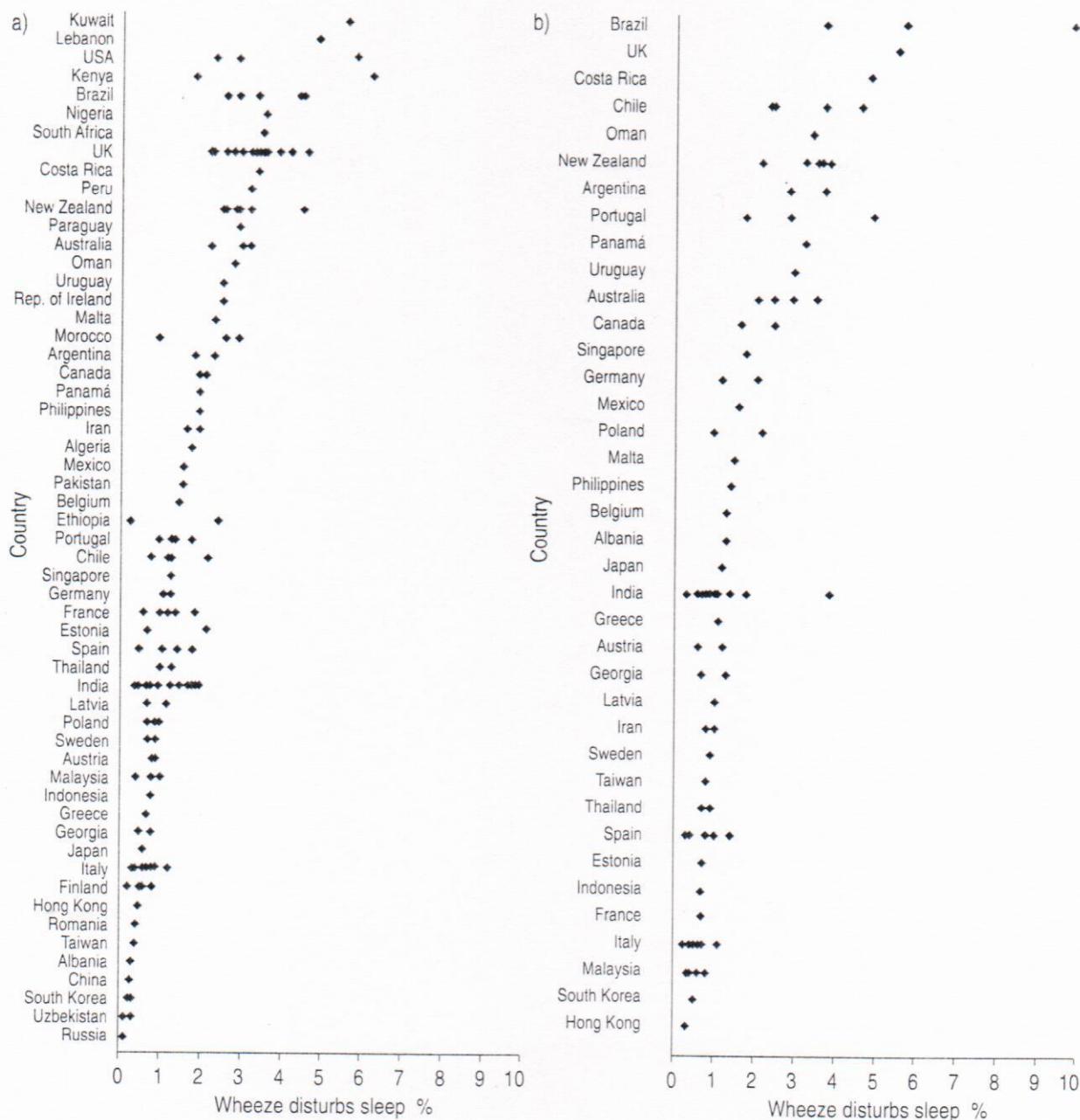


Fig. 2. — Ranking of participating countries for the percentage who answered positively to the question "In the last 12 months, how often, on average, has your (child's) sleep been disturbed due to wheezing?: one or more nights per week" for: a) the 13–14 yr olds; and b) the 6–7 yr olds.

countries except for Greece, Mexico, Panama, Paraguay, Republic of Ireland, the UK and Uruguay, with a correlation of $r=0.83$ ($p<0.0001$) between these variables. The proportion of children reporting wheezing with exercise in the last 12 months ranged from 2.3% in Indonesia to 43.4% in Nigeria.

Dry night cough in the last 12 months was reported more frequently than 12 month wheeze in all countries except for Australia, New Zealand and Sweden, with a correlation of $r=0.81$ ($p<0.0001$) between these variables. The proportion of children reporting dry night cough in the last 12 months ranged from 4.0% in Indonesia to 42.3% in the UK.

The proportion of females and males studied varied among the centres, from 34.1 to 69.9% males. The pattern

of responses to questions between sexes was not consistent. On average females showed a higher prevalence than males for all questions except for reported "asthma ever", where males were higher than females. However, there was a significant interaction with country ($p<0.0001$), with many countries having a greater proportion of positive responses in males than in females.

6–7 yr old group. The prevalence rates for asthma symptoms are presented by centre and country in table 2. Eighteen countries were represented by more than one centre. The geographic distribution of prevalence is illustrated, by centre on a world map (fig. 3), for positive answers to the question "Has your child had wheezing or whistling in the chest in the last 12 months?". There was more than

Table 2. — Summary of parent-completed wheezing questionnaire (written) data, 6–7 yr-old age group

Centre ^a	12-month prevalence						n	
	Wheeze	≥4 Attacks	Wheeze disturbs sleep	Severe wheeze limiting speech	Exercise wheeze	Night cough		Ever had asthma
<i>Asia-Pacific</i>								
Hong Kong								
Hong Kong	9.1	2.3	0.3	1.1	6.9	21.7	7.7	3618
Indonesia								
Bandung ^{c, f}	4.1	0.8	0.7	0.8	3.1	9.1	6.6	1390
Japan								
Fukuoka	17.3	5.4	1.2	1.8	5.3	9.5	18.2	2900
Malaysia	6.1	1.4	0.5	1.1	4.3	16.2	10.4	15285
Alor Setar	6.2	1.6	0.8	1.4	4.7	15.8	13.4	2978
Ipoh ^c	6.3	1.2	0.3	1.0	4.6	12.6	10.3	2506
Klang Valley	7.8	2.1	0.6	1.4	4.9	17.9	11.1	3109
Kota Bharu	5.6	1.1	0.4	1.0	4.0	21.0	10.4	3819
Muar ^c	4.5	1.2	0.4	0.8	3.6	11.7	6.4	2873
Philippines								
Metro Manila	11.3	1.4	1.4	2.4	6.7	30.6	16.4	3558
Singapore								
Singapore	15.7	3.5	1.8	1.9	8.2	15.0	18.5	2353
South Korea	13.3	1.7	0.5	2.0	4.4	17.4	8.5	8109
Provincial Korea ^a	12.4	1.9	0.5	2.0	4.5	17.4	8.3	5527
Seoul ^a	15.1	1.5	0.5	2.0	4.1	17.3	9.0	2582
Taiwan								
Taipei ^a	9.6	2.9	0.8	1.2	6.0	17.0	12.7	4806
Thailand	8.2	2.4	0.8	1.3	3.9	18.4	6.7	7457
Bangkok	11.0	3.4	0.9	1.7	5.1	22.8	9.3	3629
Chiang Mai	5.5	1.5	0.7	0.9	2.8	14.2	4.2	3828
Regional total	9.6	2.2	0.7	1.5	5.0	17.6	10.7	49476
<i>Eastern Mediterranean</i>								
Iran	5.4	1.0	0.9	0.9	1.8	5.9	3.0	5469
Rasht	5.3	1.0	1.0	1.1	1.8	5.7	4.1	3013
Tehran	5.5	1.0	0.8	0.8	1.7	6.0	1.7	2456
Malta								
Malta	8.8	1.7	1.5	1.2	4.1	19.1	7.5	3493
Oman								
Al-Khod	7.1	2.5	3.5	3.2	6.9	19.6	10.5	3891
Regional total	6.8	1.7	1.8	1.7	4.0	13.6	6.5	12853
<i>Latin America</i>								
Argentina	16.4	3.8	3.4	4.3	6.2	39.5	5.3	6012
Buenos Aires	15.4	3.2	2.9	3.2	4.9	37.5	4.1	3005
Rosario	17.3	4.4	3.8	5.4	7.5	41.5	6.5	3007
Brazil	23.3	5.3	5.8	4.4	7.5	34.2	13.1	7261
Porto Alegre	23.5	5.0	5.8	4.0	6.9	33.8	16.8	2846
Recife ^f	27.2	8.3	10.0	9.6	13.0	34.8	20.4	1410
São Paulo ^c	21.3	4.1	3.8	2.3	5.5	34.2	6.1	3005
Chile	17.9	2.9	3.5	3.0	11.0	25.7	12.1	10838
Central Santiago	16.5	1.6	2.4	1.9	8.0	23.7	9.7	1458
Punta Arenas	17.1	2.1	2.5	2.6	10.1	29.5	10.4	3060
South Santiago	16.9	2.6	3.8	3.6	9.3	24.0	10.5	3182
Valdivia	20.5	4.5	4.7	3.3	15.2	24.7	16.5	3138
Costa Rica								
Costa Rica	32.1	7.3	4.9	11.3	16.1	38.3	26.9	2942
Mexico								
Cuernavaca	8.6	1.3	1.6	2.8	4.0	19.9	5.1	3097
Panama								
David-Panamá ^c	23.5	4.1	3.3	6.2	12.3	29.3	19.3	3043
Uruguay								
Montevideo ^{b, c}	18.0	4.6	3.0	3.3	7.0	26.4	12.0	3071
Regional total	19.6	4.0	3.8	4.5	9.1	30.6	12.4	36264
<i>North America</i>								
Canada	17.6	5.5	2.2	3.0	9.6	25.1	14.7	5755
Hamilton	20.1	6.2	2.5	3.3	10.7	27.7	17.2	3337
Saskatoon	14.1	4.5	1.7	2.6	8.1	21.5	11.2	2418
Regional total	17.6	5.5	2.2	3.0	9.6	25.1	14.7	5755
<i>Northern and Eastern Europe</i>								
Albania								
Tiranë	7.6	1.0	1.3	2.4	4.8	9.3	3.1	2981
Estonia								
Tallinn	9.3	1.5	0.7	0.7	1.6	11.7	1.4	3070
Georgia	7.6	1.5	1.0	1.3	3.3	7.0	3.1	6770
Kutaisi	9.3	2.0	1.3	1.5	4.5	8.7	4.5	3356
Tbilisi	5.9	1.0	0.7	1.1	2.1	5.4	1.8	3414
Latvia								
Riga	7.3	1.3	1.0	0.9	2.2	7.8	1.6	3003
Poland	10.9	3.0	1.5	2.1	3.8	18.5	2.5	4974
Krakow (1995)	14.3	3.8	2.2	2.4	4.9	25.1	4.1	2264
Poznan	8.1	2.3	1.0	1.7	2.9	13.0	1.3	2710

Table 2. — continued.

Centre*	12-month prevalence							n
	Wheeze	≥4 Attacks	Wheeze disturbs sleep	Severe wheeze limiting speech	Exercise wheeze	Night cough	Ever had asthma	
Sweden								
Stockholm/Uppsala	10.4	3.3	0.9	1.5	6.2	14.6	8.0	3029
Regional total	8.8	2.0	1.1	1.5	3.6	11.4	3.2	23827
Oceania								
Australia	24.6	8.7	2.8	3.9	14.8	29.8	27.1	10899
Adelaide	26.2	9.2	3.6	4.4	15.5	30.4	27.5	3063
Melbourne	27.2	9.1	2.5	4.2	15.8	32.2	28.6	2840
Perth	22.0	9.0	3.0	4.4	15.3	29.7	28.4	2192
Sydney	22.3	7.5	2.1	2.6	12.5	26.7	24.4	2804
New Zealand	24.5	9.0	3.5	5.1	16.5	29.2	26.5	18569
Auckland	22.5	7.9	3.7	5.3	14.8	27.5	23.8	3526
Bay of Plenty	24.0	8.2	3.6	4.8	15.9	28.9	25.7	2681
Christchurch	27.2	10.2	3.9	5.0	19.2	32.2	28.4	3318
Hawke's Bay	27.0	9.9	3.7	5.6	17.7	30.7	28.3	3338
Nelson	18.7	7.1	2.2	4.6	13.2	21.1	17.6	1868
Wellington	25.1	9.8	3.3	4.7	16.9	31.1	30.8	3838
Regional total	24.6	8.9	3.2	4.6	15.9	29.4	26.8	29468
South-east Asia								
India	5.6	1.5	1.2	1.9	3.6	12.3	3.7	31697
Akola	0.8	0.6	0.3	0.6	1.0	3.3	1.3	2030
Bombay (16)	3.8	1.3	1.0	1.6	3.0	12.6	3.8	3967
Bombay (17) ^c	5.4	1.0	1.0	1.3	4.3	16.1	2.9	1148
Bombay (18)	1.8	0.7	0.6	0.7	1.8	8.3	2.3	3568
Borivali	5.2	2.0	1.4	1.7	3.1	12.3	3.4	1672
Chandigarh	5.4	1.9	1.8	2.8	3.8	10.7	2.8	2891
Jodhpur	3.5	1.3	1.0	1.4	2.9	13.6	4.1	1104
Kottayam	24.6	4.7	3.9	7.5	13.3	27.0	14.4	2156
Madras (2)	7.2	2.1	0.9	1.4	2.5	16.4	1.4	1466
Madras (3)	8.5	2.4	1.4	2.5	3.8	15.4	2.2	2491
New Delhi	6.9	1.4	0.7	1.6	4.1	14.6	3.7	2938
Neyveli	1.5	0.1	0.3	0.3	1.4	8.1	1.0	1498
Orissa	4.1	1.4	1.1	2.2	3.8	8.7	3.8	1520
Pune	2.3	1.0	0.8	1.3	2.5	9.5	4.2	3248
Regional total	5.6	1.5	1.2	1.9	3.6	12.3	3.7	31697
Western Europe								
Austria	8.9	1.6	1.0	2.0	5.3	14.2	3.9	5787
Salzburg	9.7	1.8	1.2	2.5	5.7	16.4	4.2	3658
Urfahr-Umgebung	7.7	1.2	0.6	1.1	4.6	10.4	3.3	2129
Belgium								
Antwerp	7.3	2.0	1.3	1.2	3.6	14.8	4.2	6533
France								
Pessac ^a	8.1	2.6	0.7	0.7	3.3	16.4	9.3	3202
Germany	8.5	1.9	1.7	2.0	5.1	11.1	3.6	6592
Greifswald	7.2	1.4	1.2	1.8	3.8	8.0	2.9	2853
Münster	9.6	2.2	2.1	2.1	6.0	13.5	4.1	3739
Greece								
Athens	7.6	1.4	1.1	0.7	2.4	12.8	5.4	1654
Italy	7.3	1.4	0.6	1.1	1.8	17.9	8.6	20815
Cremona	5.7	0.8	0.7	0.6	1.0	12.9	4.6	1392
Emilia-Romagna	7.4	1.4	0.7	1.1	1.5	16.1	6.9	4472
Empoli	8.7	0.8	0.5	0.8	1.0	19.2	7.8	1434
Firenze	9.9	1.9	1.1	1.3	2.5	19.8	8.8	1138
Milano	7.0	1.5	0.6	1.3	2.2	22.6	9.1	3616
Roma	7.2	1.5	0.5	1.1	1.8	18.2	10.3	4027
Torino	6.4	1.2	0.5	1.4	1.4	17.7	7.6	1429
Verona	7.4	1.7	0.4	1.1	3.2	16.1	11.7	2076
Viterbo ^d	6.7	1.5	0.2	1.0	1.5	16.0	8.4	1231
Portugal	13.2	3.8	3.4	4.5	7.9	28.3	11.0	5129
Funchal	14.7	5.2	5.0	7.2	11.4	34.9	17.5	1797
Lisbon	13.1	3.5	2.9	3.1	6.7	26.3	8.3	2143
Portimao	11.0	2.1	1.8	3.1	4.6	22.0	6.2	1189
Spain	6.2	1.4	0.8	1.0	2.9	12.2	6.2	16884
Bilbao	8.0	2.1	1.0	1.3	4.7	15.9	10.1	3019
Cartagenab	8.4	1.6	1.4	1.5	3.1	16.0	6.2	3335
Castellón	4.7	0.9	0.8	0.8	2.1	8.5	4.3	3594
Pamplona	3.5	0.7	0.3	0.4	1.5	9.7	4.3	2996
Valencia	6.2	1.5	0.4	1.0	2.9	11.5	6.2	3940
UK								
Sunderland	18.4	6.8	5.6	3.4	13.5	28.1	22.9	1864
Regional total	8.1	1.9	1.2	1.5	3.7	16.1	7.2	68460
Global total	11.8	3.1	1.8	2.4	6.2	19.1	10.2	257800

All data are presented as percentages of the study children. ^a: data re-coded to eliminate inconsistent responses; ^b: response rate <70%; ^c: <10 schools if ≥10 schools in sampling frame; ^d: 13–14 yr age group not included in this paper; ^e: single data entry; ^f: no date of interview or date of birth on questionnaire; ^g: no eczema questionnaire. *: numbers in brackets indicate International Study of Asthma and Allergies in Childhood (ISAAC) registration number for that centre, as given by the national coordinator.

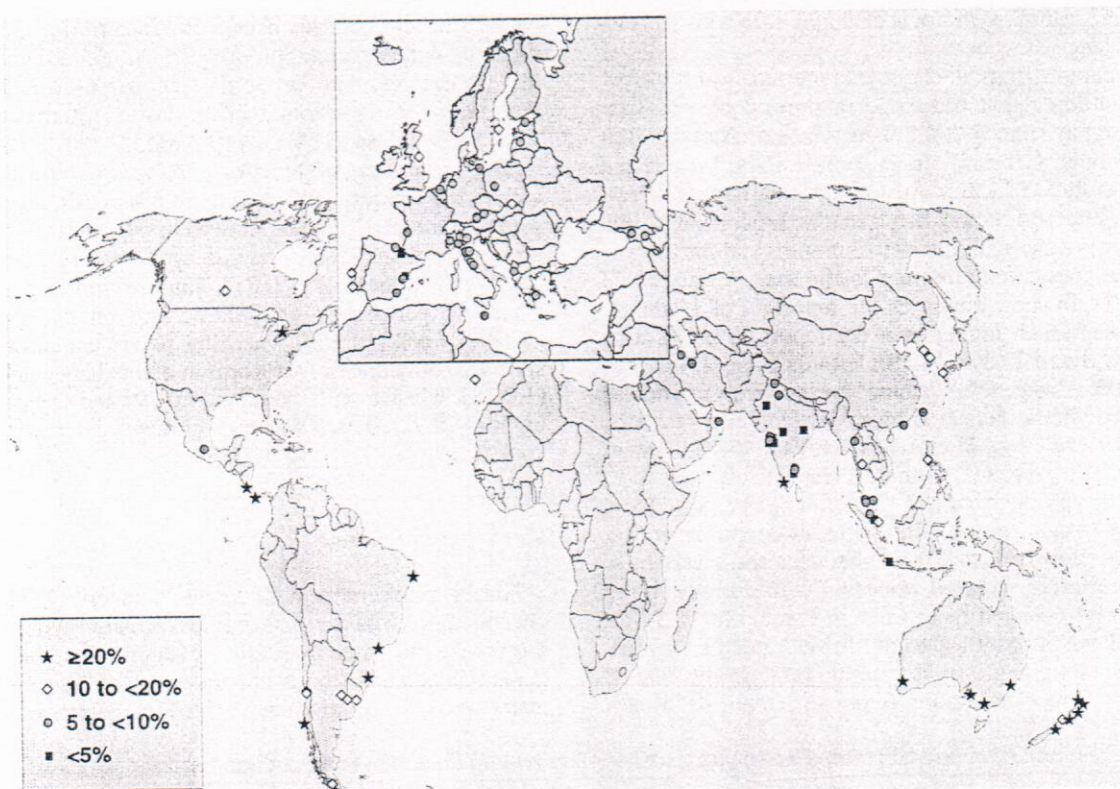


Fig. 3. — World map for the 6–7 yr old age group, showing the percentage of parents who answered "yes" to the written question "Has your child had wheezing or whistling in the chest in the last 12 months?". Each point represents the prevalence for one collaborating centre, with distinct colour symbols used for different prevalence ranges.

a fivefold difference in prevalence between countries (4.1–32.1%), with lowest rates in India, Indonesia, Iran and Malaysia and highest rates in Australia, Brazil, Costa Rica, New Zealand and Panama. Some centres in countries with extreme values in the older age group did not provide data for the younger age group.

The between-country variation (38 countries) was greater than the within-country variation (18 countries with >1 centre) for all questions: 12 month wheeze was 1.1 times larger; four or more attacks of wheezing in the last 12 months 1.8; waking one or more nights a week 2.0; wheezing severe enough to limit speech to only one or two words at a time between breaths 1.5; wheeze with exercise 1.7; dry cough at night 1.6, and reported asthma ever 2.0 times larger.

Both age groups were studied in 90 centres and the correlations between the two age groups for the different symptoms ranged from $r=0.61$ to $r=0.89$. The question about wheezing in the last 12 months is illustrated in figure 4 ($r=0.71$, $p<0.0001$), with 57 centres having a lower prevalence in the younger age group and 33 centres having a higher prevalence in the younger age group. The 6–7 yr age group also had lower prevalences than the 13–14 yr age group for all the other symptoms except for any sleep disturbance due to wheezing.

The ranking of countries for sleep disturbance due to wheezing on one or more nights per week is illustrated in figure 2. The countries with the highest prevalence of positive answers to this question were Brazil, Costa Rica and the UK, and the lowest were Hong Kong, Malaysia and South Korea. A similar pattern was found for wheezing severe enough to limit speech to only one or two words at

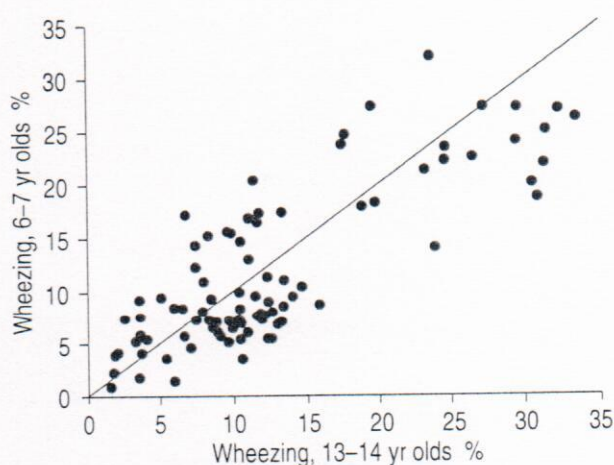


Fig. 4. — Scatter plots for centres for the percentage of children who have had "wheezing or whistling in the chest in the last 12 months". The x-axis shows self-reported wheezing in 13–14 yr olds and the y-axis wheezing reported by parents in 6–7 yr olds. The line of identity is shown.

a time between breaths, but for ≥ 4 attacks of wheezing the pattern was similar to 12 month wheeze.

Correlations done between these variables, examining relative severity (as described above for the 13–14 yr age group), were similar to the older age group: four or more attacks of wheezing ($r=0.12$, $p=0.25$); sleep disturbance due to wheezing on one or more nights per week ($r=-0.04$, $p=0.74$); and wheezing severe enough to limit speech to only one or two words at a time between breaths ($r=-0.13$, $p=0.21$), indicating that the proportion of wheezy children

with severe asthma symptoms changed little with increasing prevalence of wheeze.

Some parents from all countries reported "asthma ever" in their children, but the range in prevalence was very large, ranging from 1.4–4.2% in Albania, Austria, Belgium, Estonia, Germany, India, Iran, Latvia, Poland and Georgia to 26.5–27.1% in Australia, Costa Rica and New Zealand. The correlation between the proportion of the population wheezing in the last 12 months and the proportion of the population reporting "asthma ever" was $r=0.73$ ($p<0.0001$). In some countries the reporting of 12 month wheeze was much higher than the reporting of "asthma ever" (e.g. Brazil 23.3%, 13.1%; Estonia 9.3%, 1.4%; Iran 5.4%, 3.0%; "wheeze", "asthma", respectively), whereas in other countries there was more "asthma ever" than 12 month wheeze (e.g. Philippines 11.3%, 16.4%; Oman 7.1%, 10.5%; "wheeze", "asthma", respectively).

Exercise wheeze in the last 12 months was reported less frequently than 12 month wheeze in all countries, with a correlation of $r=0.84$ ($p<0.0001$) between these variables. The proportion of reported wheezing with exercise in the last 12 months ranged from 1.6% in Estonia to 16.5% in New Zealand. In contrast to the lower rates of exercise wheeze in this age group, dry night cough in the last 12 months was reported more frequently than 12 month

wheeze in all countries except for Japan, Singapore and Georgia, with a correlation of $r=0.82$ ($p<0.0001$) between these variables. The proportion of parents of children reporting dry night cough in the last 12 months ranged from 5.9% in Iran to 39.5% in Argentina.

The proportion of females and males studied varied among the centres, from 40.0 to 58.6% males, and a clear pattern emerged. Males showed a significantly higher prevalence than females in this age group ($p<0.001$) for 12 month wheezing (1:0.81), four or more attacks of wheezing per week (1:0.76), waking on one or more nights a week (1:0.92), wheezing severe enough to limit speech to only one or two words at a time between breaths (1:0.78), wheeze with exercise (1:0.79) and dry cough at night (1: 0.92). There was no significant interaction with country.

Video questionnaire

Ninety-nine centres in 42 countries undertook the video questionnaire. The prevalence rates for video symptoms of asthma are presented by centre and country in table 3. The geographic distribution is illustrated, by centre on a world map (fig. 5), for positive answers to the scene of wheezing

Table 3. – Summary of self-completed wheezing questionnaire (video) data, 13–14 yr-old age group

Centre	Video	Prevalence in the last year					n
		Wheeze	Exercise wheeze	Night wheeze	Night cough	Severe wheeze	
<i>Africa</i>							
Kenya		11.4	15.0	6.7	16.2	7.5	6257
Eldoret	I	3.5	5.0	1.4	0.0	1.4	3016
Nairobi	I	18.7	24.3	11.7	31.2	13.1	3241
South Africa							
Cape Town	I	6.5	11.5	3.9	11.6	5.0	5164
Regional total		9.2	13.4	5.4	14.1	6.3	11421
<i>Asia-Pacific</i>							
China		2.0	5.1	0.6	4.9	1.2	18985
Beijing	I	3.3	4.7	0.6	6.8	1.4	4165
Chongqing	I	1.3	5.2	0.4	3.3	0.8	4289
Guangzhou	I	2.0	6.9	0.7	5.4	1.1	3854
Shanghai	I	1.6	3.5	0.9	1.8	1.1	3470
Wulumuqi	I	1.8	5.4	0.4	7.4	1.6	3207
Hong Kong							
Hong Kong	I	10.1	15.3	3.8	24.6	6.9	4665
Indonesia							
Bandung	I	1.3	2.8	0.6	1.8	0.8	2246
Japan							
Fukuoka	I	10.2	16.5	3.7	7.2	5.3	2820
Malaysia		5.9	9.2	2.5	8.4	3.6	15571
Alor Setar	I	5.3	8.6	2.1	8.6	2.7	3295
Ipoh	I	6.5	10.8	3.2	9.9	5.8	3271
Klang Valley	I	6.9	9.7	2.7	9.0	3.7	5966
Kota Bharu	I	3.9	7.0	1.8	5.2	2.2	3039
Philippines							
Metro Manila	I	9.6	12.6	3.9	14.6	4.9	3207
Singapore							
Singapore	I	9.9	8.1	3.2	9.0	5.0	4189
South Korea		3.7	6.7	0.5	4.0	1.9	9932
Provincial Korea*	I	3.1	6.0	0.5	3.3	1.6	6972
Seoul*	I	5.2	8.2	0.7	5.8	2.6	2960
Taiwan							
Taipei*	I	4.6	6.0	1.8	3.4	2.8	4211
Thailand		6.9	10.1	2.1	12.3	3.8	7629
Bangkok	I	8.0	12.7	2.7	14.4	4.6	3705
Chiang Mai	I	6.0	7.7	1.7	10.2	3.1	3924
Regional total		5.3	8.3	1.8	8.1	3.1	73455
<i>Eastern Mediterranean</i>							
Iran							
Rasht	I	3.1	6.1	1.1	6.0	2.1	3175
Kuwait							
Kuwait	E	13.3	14.6	9.4	9.7	9.1	1033
Lebanon							
Beirut	I	4.9	8.4	3.6	7.4	3.2	2985

Table 3. - continued.

Centre	Video	Prevalence in the last year					n
		Wheeze	Exercise wheeze	Night wheeze	Night cough	Severe wheeze	
Malta							
Malta	I	8.8	11.1	4.0	17.8	5.5	4173
Morocco		7.5	9.5	3.8	11.7	5.6	9350
Casablanca	E	10.6	13.0	5.5	14.5	8.3	3182
Marrakech	E	5.6	7.7	2.5	10.6	3.8	2899
Rabat	I	6.2	7.6	3.4	9.9	4.6	3269
Pakistan							
Karachi	I	7.9	6.3	3.1	6.1	4.4	1829
Regional total		7.1	9.1	3.6	10.9	4.8	22545
<i>Latin America</i>							
Argentina		8.3	9.4	4.7	12.8	5.5	5089
Buenos Aires	I	7.8	9.6	4.2	11.0	5.8	2498
Rosario	I	8.8	9.1	5.2	14.5	5.1	2591
Chile		11.2	14.2	3.5	15.4	4.5	6303
Punta Arenas	I	9.5	11.7	2.7	14.7	4.4	3253
South Santiago	I	13.0	16.9	4.4	16.2	4.5	3050
Paraguay							
Asunción	I	10.1	14.5	5.3	12.7	6.1	2966
Peru							
Lima	I	18.5	21.4	6.4	16.8	8.3	3151
Uruguay							
Montevideo	I	15.0	17.6	5.9	19.3	11.0	3069
Regional total		12.0	14.7	4.9	15.1	6.5	20578
<i>North America</i>							
Canada		12.0	28.1	6.5	20.1	8.5	4947
Hamilton	E	13.4	31.0	7.2	21.2	8.6	3047
Saskatoon	I	9.9	23.5	5.4	18.2	8.3	1900
USA							
Seattle*	I	13.0	22.5	4.6	13.5	10.6	2140
Regional total		12.3	26.4	5.9	18.1	9.1	7087
<i>Northern and Eastern Europe</i>							
Albania							
Tiranë	I	1.0	1.3	0.4	1.6	0.6	2362
Estonia							
Tallinn	I	2.1	5.4	1.2	6.1	0.9	3454
Finland		5.1	8.6	1.2	12.5	2.8	11888
Helsinki	I	5.8	9.3	1.5	14.7	2.6	2853
Kuopio County	I	3.8	7.5	0.9	11.1	2.6	2877
Lapland Area	I	5.4	7.6	1.2	11.6	3.4	3074
Turku and Pori County	I	5.2	9.9	1.2	12.5	2.6	3084
Latvia		1.3	2.6	1.1	2.1	0.6	5957
Riga	I	1.3	3.2	0.7	3.3	0.6	2847
Rural Latvia	I	1.3	1.9	1.4	1.1	0.6	3110
Poland							
Poznan	I	3.9	8.6	1.5	8.5	2.3	3238
Russia							
Moscow	E	1.3	1.9	0.8	1.1	0.3	3411
Sweden		5.2	12.0	1.6	8.2	2.9	6418
Linköping	E	5.1	10.4	1.0	7.3	2.5	3363
Stockholm/Uppsala	E	5.3	13.8	2.3	9.2	3.4	3055
Uzbekistan		1.3	1.4	0.6	1.3	0.5	4662
Samarkand	E	1.8	2.3	0.7	2.1	0.4	1758
Tashkent	E	1.0	0.9	0.6	0.8	0.6	2904
Regional total		3.2	6.2	1.1	6.7	1.7	41390
<i>Oceania</i>							
Australia		17.6	27.2	11.0	18.7	11.3	12193
Adelaide	E	19.6	29.5	11.7	20.5	12.5	2990
Melbourne	E	15.5	25.8	10.5	16.9	10.8	2726
Perth	E	16.8	28.0	9.9	18.2	10.6	3641
Sydney	E	18.4	25.1	12.2	19.2	11.6	2836
New Zealand		18.4	30.3	11.7	22.8	12.4	18957
Auckland	E	16.3	28.4	11.3	20.7	11.4	3201
Bay of Plenty	E	18.6	28.4	11.4	25.2	12.8	2810
Christchurch	E	17.4	32.2	11.3	22.4	13.2	3172
Hawke's Bay	E	19.6	29.9	12.7	22.5	9.8	3536
Nelson	E	19.0	32.3	10.5	23.3	11.7	1827
Wellington	E	19.5	31.0	12.2	23.1	14.9	4411
Regional total		18.1	29.1	11.4	21.2	12.0	31150
<i>South-east Asia</i>							
India		2.9	5.5	2.3	3.7	2.5	30043
Bombay (16)	I	0.8	2.2	0.9	0.9	0.7	4178
Bombay (18)	I	1.4	4.1	0.8	3.4	2.3	3128
Borivali	I	2.6	5.3	1.3	3.3	2.0	3869
Chandigarh	I	2.8	5.8	2.6	3.0	1.9	3087
Jodhpur	I	5.8	8.4	4.0	5.4	4.4	1063
Madras (2)	I	4.3	5.7	2.9	5.7	3.7	1764
Madras (3)	I	2.6	6.7	1.6	4.7	2.0	3044
New Delhi	I	7.1	9.1	7.5	7.8	6.2	2818
Neyveli	I	4.3	10.3	3.3	4.8	3.3	3273
Orissa	I	2.3	3.3	1.0	2.6	2.2	1240

Table 3. — continued.

Centre	Video	Prevalence in the last year					n
		Wheeze	Exercise wheeze	Night wheeze	Night cough	Severe wheeze	
Pune	I	0.7	1.4	0.6	0.9	0.9	2579
Regional total		2.9	5.5	2.3	3.7	2.5	30043
<i>Western Europe</i>							
Austria		5.5	15.0	3.3	8.8	3.1	4876
Salzburg	E	5.0	14.7	3.1	9.1	3.2	3370
Urfahr-Umgebung	E	6.5	15.6	3.7	8.2	2.9	1506
France		8.3	22.8	4.4	14.9	4.6	8802
Marseilles	E	9.1	23.1	5.1	15.2	5.5	3409
Strasbourg	E	7.9	22.5	3.9	14.8	4.1	5393
Germany		5.3	16.7	3.6	10.2	3.6	7019
Greifswald	E	4.8	17.2	3.5	9.7	3.0	3020
Münster	E	5.6	16.4	3.8	10.6	4.1	3999
Italy		5.3	16.9	2.1	13.2	2.8	18181
Ascoli Piceno	I	6.0	19.8	1.7	9.6	2.3	1089
Cremona	I	4.1	13.1	1.4	12.0	2.3	1191
Emilia-Romagna	I	5.8	17.5	1.9	12.4	3.0	3778
Empoli	I	5.0	17.7	1.5	17.0	3.2	1038
Firenze	I	3.9	17.8	1.5	14.0	2.3	1167
Milano	I	5.5	19.1	1.9	16.8	3.7	3357
Roma	I	4.8	15.9	1.6	11.8	2.8	3147
Torino	I	5.3	15.7	1.5	14.7	2.3	1239
Verona	I	5.8	14.4	4.8	10.6	2.1	2175
Portugal							
Funchal	E	6.2	14.4	3.3	10.2	5.0	3407
Spain		7.8	25.7	4.8	16.5	3.9	24842
Barcelona	I	7.4	21.9	4.7	16.3	4.1	2984
Bilbao	E	9.8	27.6	6.1	16.7	5.3	3167
Cartagena	E	7.7	22.9	4.1	12.8	3.7	3013
Castellón	E	5.8	18.9	3.9	18.7	2.6	3089
Cádiz	E	8.9	24.5	6.4	16.4	4.3	3238
Pamplona	E	6.9	24.6	3.8	15.8	3.4	3040
Valencia	E	9.6	35.4	5.1	17.9	4.3	3140
Valladolid	E	6.3	29.0	3.9	17.1	3.2	3171
Regional total		6.7	20.6	3.7	13.9	3.7	67127
Global total		7.3	13.7	3.7	11.2	4.5	304796

Data are presented as percentages. E: European version of video; I: International version of video. *: data recoded to eliminate inconsistent responses.

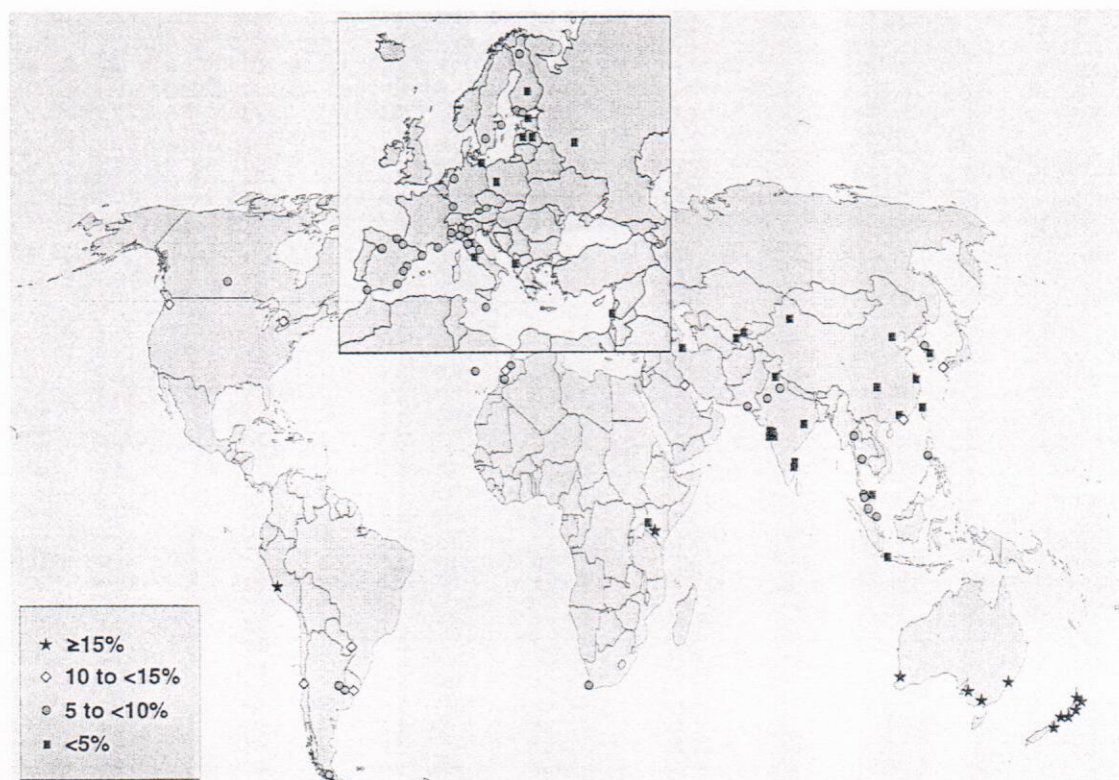


Fig. 5. — World map for the 13–14 yr old age group, for the video scene showing a person wheezing while at rest. The percentage of children who answered "yes" to the question "Has your breathing ever been like this... in the last year?" is shown for each centre, with distinct colour symbols used for different prevalence ranges.

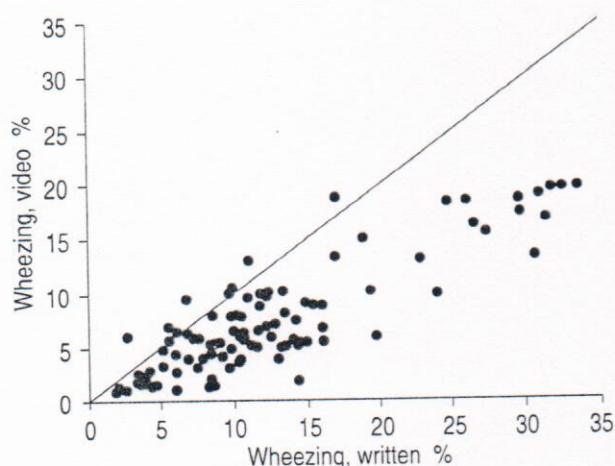


Fig. 6. — Scatter plots for the percentage of the 13–14 yr old age group responding "yes" for wheezing in the last year (video questionnaire) against "wheezing or whistling in the chest in the last 12 months". The x-axis shows wheezing for the written questionnaire and the y-axis wheezing for the video questionnaire. The line of identity is shown.

at rest in the last year, common to both video versions; 33% of these centres used the European version while 67% used the International version. There was a wide range of prevalence rates between countries (1.0–18.5%), showing more than 15-fold differences. The lowest prevalences (<3%) were found in Albania, China, Estonia, India, Indonesia, Latvia, Russia and Uzbekistan and the highest prevalences (>15%) in Australia, New Zealand and Peru. The between-country variation was greater than the within-country variation for all questions in the last 12 months (1.8–2.5 times larger), except for night cough (1.0).

Wheezing with exercise in the last year was more common than wheezing in the last year in all countries except for Pakistan and Singapore. Night cough in the last year was more common than wheezing in the last year in all countries except for Japan, Kuwait, Pakistan, Peru, Russia, Singapore and Taiwan.

The overall pattern of international differences shown by the 13–14 yr olds who took part in both the video and written questionnaires was similar (figs. 1 and 5), with a correlation of $r=0.76$ ($p<0.0001$) (fig. 6). Video prevalence estimates were generally lower than written estimates for comparable questions in centres in the majority ($\geq 75\%$) of countries, except that "severe asthma" on the video questionnaire usually exceeded "severe wheezing limiting speech" on the written questionnaire. Some of the greatest differences (>fivefold) between the video and written questionnaires for wheezing in the last year were found in Latvia and Uzbekistan. Large absolute differences (>13%) were found in centres in Australia, Canada and Finland.

Discussion

The ISAAC study has demonstrated, by means of simple standardized questionnaires, that there are large variations in the prevalence of asthma symptoms throughout the world. The self-reported 12 month prevalence of wheezing among 13–14 yr olds between countries ranged from 2.1% in Indonesia to 32.2% in the UK. Parental

reported 12 month prevalence of wheezing in 6–7 yr olds ranged from 4.1% in Indonesia to 32.1% in Costa Rica. The highest values for 12 month prevalence of wheeze were found in developed English-speaking countries, and some Latin American non-English-speaking countries (*e.g.* Peru and Costa Rica). There were considerable variations within regions, *e.g.* the 12 month prevalence in the 13–14 yr old age group varied within Europe from <5% in centres in Albania, Georgia, Greece, Italy, Romania and Russia to >30% in the UK, and within Latin America from <10% in centres in Argentina, Chile and Mexico to >25% in centres in Brazil and Peru.

The analysis shows that there is consistently more variation between countries than within countries. Three countries with a very large number of centres were represented across the range of prevalences, India with 14 centres representing the low prevalence group, Italy with 14 centres representing the middle prevalence group and the UK with 15 centres representing the high prevalence group. However, it must be remembered that the countries, and centres within countries were self selected, and it is possible that countries with larger within-country variation did not participate.

Although previous international comparisons [1, 13–17] have drawn attention to variations in the prevalence of childhood asthma, the ISAAC project comprises by far the most extensive international survey of asthma symptoms ever performed. Adherence to the protocol ensured that, within centres, there was standardization of the questionnaires and methods of administration and that schools were selected without bias from the defined geographical area. These centres, however, may not represent the prevalence of asthma symptoms throughout the whole country and no comparison could be made between rural and urban areas. Moreover, there may have been important variation within some centres, for example between affluent and poor areas, which the ISAAC Phase One study did not examine. Targets for the sample size ensured there was sufficient precision in the prevalence estimates obtained. By recommending that at least half of the survey be conducted before the main pollen season it was hoped that variation due to seasonal factors would be reduced; in the event, studies in New Zealand [18], the UK and Germany have found that the 12 month period prevalence of the various wheezing symptoms is not significantly affected by the season of the survey.

The only other comparable international survey of asthma is the European Community Respiratory Health Survey (ECHRS) [19, 20], which studied males and females aged 20–44 yrs, mainly from European centres. Among the 13 centres in 10 countries that were reported in both studies, the ranking of prevalence of wheeze in the last 12 months was similar, with the English-speaking countries (Australia, New Zealand, Republic of Ireland and the UK) having the highest and Italy and Greece the lowest rates.

There is, as yet, no accepted definition of asthma and the identification of asthma by questionnaire remains a contentious issue. The ISAAC collaboration agreed that the cardinal symptom of asthma would be that which reflects variable narrowing of the airways and that this is best described (in English) as "wheezing or whistling in the chest". The questionnaire incorporated questions taken from pre-existing questionnaires with sensitive (although

not necessarily specific) questions for asthma and more specific questions which related to the severity of asthma. In recent years a number of studies have compared responses to the ISAAC core wheezing questions with other indicators of asthma, including physician diagnosis [21], other questionnaires [22] and physiological measures [9, 10, 22, 23]. These indicate a level of sensitivity and specificity which is acceptable for the purposes of multicentre international comparisons.

While the significance of very mild wheezing may be questioned, the occurrence of frequent, sleep-disturbing or speech-limiting attacks is accepted widely as clinically important. There were large international variations in the prevalence of these three more specific symptoms and, broadly, the worldwide pattern of prevalence of more severe symptoms followed that of any 12 month wheezing. However, the order of countries ranking highest for the prevalence of "sleep disturbance due to wheezing one or more nights per week in the last 12 months" and "wheeze severe enough to limit speech to only one or two words at a time between breaths" was different from 12 month wheeze, while four or more attacks in the last 12 months was similar to 12 month wheeze. The explanations for the variation between prevalence and severity would be of particular interest and may include differences in the management of asthma between countries, although information on asthma management was not collected in ISAAC Phase One.

The proportion of wheezy children with severe asthma symptoms varied little with the increasing prevalence of wheezy children in the population. This means the high prevalences found in some centres are not explained by excessive inclusion of children with mild wheeze. These findings suggest that factors affecting the prevalence of asthma also affect the severity of asthma, and the factors which especially affect the prevalence of severe asthma should be examined.

The validity of the questionnaire is likely to have varied across cultures and languages. Some languages do not have an equivalent of "wheezing" as understood by English speakers. The high prevalence in English-speaking countries, especially in those most accustomed to using "wheezing" as a term in surveys, suggests there may be some language bias associated with the written questionnaire, as suggested by the findings of the ECHRS [20], or that the population has a higher awareness of asthma. However, high prevalences were also observed in Spanish- and Portuguese-speaking countries in South America, suggesting that other factors are also likely to be important in determining the prevalence of asthma symptoms. There were also large variations in prevalence within Spanish, Portuguese and Chinese languages. The overall pattern of international differences observed with the written questionnaire was maintained among those centres that employed the video questionnaire. Positive responses to the video were generally lower than for similar questions with the written questionnaire. A possible reason is that signs that are obvious enough to be visible or audible on a video are likely to represent more severe symptoms than the full spectrum from mild to severe asthma covered by the written questionnaire. It would be helpful to obtain further validation studies in centres of low prevalence.

There was also considerable variation in the prevalence of a positive response to the question concerning whether

the child had ever had "asthma". This question probably indicates the level of perceived or diagnosed asthma in the various centres but is a less reliable measure for epidemiological purposes [24]. Even in those countries with the lowest prevalences (Albania, Estonia, Indonesia, Latvia and Uzbekistan 1.4–1.7%) asthma is clearly an important medical diagnosis. Over 20% of children in the countries of highest prevalence (Australia, Costa Rica, New Zealand, Oman, Peru, Singapore and the UK) reported "asthma".

The prevalence of exercise-related wheeze in the last 12 months differed from 12 month wheeze in both age groups, being consistently higher in older children and lower in younger children. This may be real or represent under-reporting by parents and over-reporting by adolescents, or different interpretation of wheezing questions. These differences indicate the need for further examination of the validity of these questions. Higher rates of reporting of symptoms by adolescents compared with their parents has been noted in other studies ([25], Strachan personal communication), and rates of symptoms in adolescents are generally similar to those in young adults, suggesting that parental reporting may underestimate true symptoms. In contrast, the prevalence of night cough was consistent in both age groups, and showed a higher prevalence than any other question. Although there was a very strong correlation with wheezing in the last 12 months, the higher prevalence of night cough suggests that this question, in addition to estimating asthma, may be measuring other respiratory conditions. Parents may have a higher awareness of night cough because it disturbs their sleep.

The prevalence of asthma symptoms was greater in males in the younger age group. There was a mixed picture in the older age group, with considerable variation between countries but, on average, females had slightly higher prevalence than males. It is possible that the emergence of a female predominance of asthma in older adolescents and adults may depend on physical maturation, which is likely to occur at different ages in the range of countries studied. This pattern of sex differences has been reported in other studies in Western countries [26], including one large study which used ISAAC questions systematically across the age range 5–17 yrs [27]. It therefore appears unlikely that the present findings with respect to sex differences can be attributed entirely to bias arising from the different methods of questionnaire administration in the younger and older age groups.

A striking feature of these data is the high rates of asthma symptoms in countries whose predominant language is English and further study of possible aetiological factors common to these countries is a high priority. In contrast, while high rates of asthma symptoms were also found in some non-English-speaking countries, rates were not uniformly high among countries sharing the same language. For example, Peru and Costa Rica had a much higher prevalence than Spain, Brazil had a higher prevalence than Portugal and Hong Kong had a higher prevalence than China. The variations are unlikely to be explained entirely by interpretation of language, given the similar trends found between written and video questionnaires, and provide important opportunities for further study.

This large international collaboration, examining the prevalence of reported asthma symptoms in children, has set the framework from which to study a variety of factors contributing to asthma and provides a baseline from which to measure future trends. The most important outcome of ISAAC will be to advance the understanding of the causes of asthma, by studying factors acting at a population level. Although genetic factors are important risk factors for individuals within populations, migrant studies indicate they are unlikely to be responsible for the large variations in asthma which exist between populations and cannot be responsible for the recent upward trends within populations [28]. Environmental factors are likely to be more important and offer the greatest opportunities for prevention. An attractive current theory, supported by experimental evidence, is that increased hygiene and health-care in Western countries has altered the pattern of exposure to infection in early life in such a way as to predispose the immune system towards the atopic response [29, 30]. There are also a number of theories concerning the provocation of asthma by various agents including aeroallergens, diet, indoor and outdoor pollution. The ISAAC group is now using the prevalence data reported here to conduct

ecological studies between populations to test these and other hypotheses.

ISAAC Phase Two studies are now planned or underway in a number of countries and regions. Measures of bronchial hyperresponsiveness are being used to determine whether these support the questionnaire results. Measures of atopy (using allergen skin tests and immunoglobulin E measurements) are being used to determine the extent to which variations in wheezing illness are reflected in variations in atopy. Phase Two studies will also systematically obtain environmental data such as indoor exposure to allergens and pollutants to contribute to the ecological analyses.

This worldwide study of asthma symptoms is a major step forward in using population differences in prevalence to gain new insights into the causes of asthma. The simplicity of the questionnaire method enabled a wide range of countries to participate but was necessarily accompanied by some uncertainty as to international comparability. However, the large variations found are most unlikely to be explained by methodological factors alone. The existence of such wide variation provides an epidemiological opportunity for new investigations into the causes of asthma.

Appendix: Centres and principal investigators

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Algeria Algiers	A. Bezzaoucha, Chu Bab el Oued, Service d'Epidemiologie	Salvador	L.S.dF. Souza, Faculty of Medicine, Federal University of Bahia
Argentina Buenos Aires, Rosario	N. Salmun*, Fundación para el Estudio del Asma y otras Enfermedades Alérgicas	São Paulo	D. Solé*, Division of Allergy, Universidade Federal de São Paulo
Australia Adelaide	D. Kennedy, Respiratory Medicine, Adelaide Children's Hospital	Canada Hamilton	M. Sears*, Firestone Regional Chest & Allergy Unit, St. Joseph's Hospital, McMaster University
Melbourne	C. Robertson*, Dept of Thoracic Medicine, Royal Children's Hospital	Saskatoon	B. Taylor, IWK - Grace Emergency
Perth	L. Landau, Faculty of Medicine and Dentistry, University of Western Australia	Chile Central Santiago	I. Sanchez, Departamento de Pediatría, Universidad Católica de Chile
Sydney (6-7 yr)	J. Peat, Dept of Medicine, University of Sydney	Punta Arenas	L. Amarales, Children's Respiratory Service, Regional Hospital "Lautaro Navarro"
Sydney (13-14 yr)	A. Bauman, School of Community Medicine, University of New South Wales	South Santiago	E. Cortez, Dept of Paediatric Respiratory Medicine, Hospital El Pino, University of Santiago de Chile
Austria Salzburg	J. Riedler*, Kinderspital	Valdivia	M. Calvo-Gil, Instituto de Pediatría, Facultad de Medicina, Universidad Austral de Chile
Urfahr-Umgebung	G. Haidinger, Dept of Epidemiology, Institute of Tumorbiology/Cancer Research, University of Vienna	China Beijing	Y. Chen*, Capital Institute of Pediatrics
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Costa Rica	M.E. Soto-Quirós, Unidad de Enseñanza, Hospital Nacional de Niños, San José		Bombay (17)	U.A. Pai, Pediatrician
Estonia			Bombay (18)	K. Raghavan, L.T.M. Medical College
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India				
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