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Worldwide time trends for symptoms of rhinitis and conjunctivitis: Phase III of the International Study of Asthma and Allergies in Childhood

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In Phase III of the International Study of Asthma and Allergies in Childhood (ISAAC) time trends in the prevalence of rhinoconjunctivitis symptoms were analysed. Cross-sectional questionnaire surveys with identical protocols and questionnaires were completed a mean of 7 yr apart in two age groups comprising 498,083 children. In the 13- to 14-yr age group 106 centres in 56 countries participated, and in the 6- to 7-yr age group 66 centres in 37 countries participated. A slight worldwide increase in rhinoconjunctivitis prevalence was observed, but the variations were large among the centres and there was no consistent regional pattern. Prevalence increases in the older children exceeding 1% per year were recorded in 13 centres, including 3 of 9 centres in Africa, 2 of 15 in Asia-Pacific, 1 of 8 in India, 3 of 15 in Latin America, 3 of 9 in Eastern Europe and 1 of 34 in Western and Northern Europe. Decreasing rhinoconjunctivititis prevalence of similar magnitude was only seen in four centres. The changes were less pronounced in the 6- to 7-yr-old children and only in one centre did any change exceed 1% per year. The decrease in highest prevalence rates in ISAAC Phase I suggests that the prevalence has peaked in those regions. An increase was recorded in several centres, mostly in low and mid-income countries. The increases were more pronounced in the older age group, suggesting that environmental influences on the development of allergy may not be limited to early childhood.

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The International Study of Asthma and Allergies in Childhood (ISAAC) was designed to allow comparisons of the prevalence of symptoms of asthma, rhinitis and eczema between populations in different countries (1, 2). In Phase I, children in the 13- to 14-yr age group were studied in 155 centres in 56 countries (n = 463,801), and 91 centres in 38 countries in the 6- to 7-yr age group (n = 257,601) (3–6). For the 13- to 14-yr age group, over 20-fold variations in the prevalence of self-reported rhinitis symptoms were observed between centres worldwide (range 3.2–66.6%), with a more than threefold variation observed between the 10th and 90th percentiles (13.3%, 41.5%) (5). The highest 12-month period symptom prevalence of rhinitis in 13- to 14-yr olds were from centres in Argentina (60%, 65%), Paraguay (67%), France (58%) and Brazil (55%), and the lowest from centres in Ethiopia (3%), India (3–9%) and countries in the former Soviet Union (9%, 10%). Phase II involved more intensive investigation of possible etiological factors in 9- to 11-yr-old children in 30 centres in 22 countries using

Table 1. Reported rhinitis, hay fever and rhinoconjunctivitis in 13- to 14-yr-old children for each centre by region participating both in ISAAC Phase I and Phase III. The change in reported symptoms per year is also shown

		Rhinitis ever		Rhinitis in past year		Hay fever ever		Rhinoconjunctivitis in past year		Severe rhinoconjunctivitis in past year	
Centre	Phase III sample size	%	Change per year (%)	%	Change per year (%)	%	Change per year (%)	%	Change per year (%)	%	Change per year (%)
Africa (English speaking)											
Ethiopia											
Addis Ababa	3195	48.1	−0.24	27.8	−0.21	4.4	−0.38	9.9	−0.09	0.7	−0.03
Kenya											
Eldoret	3289	43.0	1.77	31.4	1.82	38.9	3.84	22.4	1.72	2.6	0.24
Nairobi	3023	45.5	0.20	34.8	0.61	36.6	1.85	19.8	0.62	2.7	0.02
Country total	6312	44.2	0.72	33.0	1.02	37.8	2.76	21.2	0.94	2.6	0.14
Nigeria											
Ibadan	3142	43.8	−1.90	33.6	−1.94	19.2	0.51	16.4	−3.88	1.9	−0.17
South Africa											
Cape Town	5037	49.0	1.61	38.5	1.17	41.5	1.77	20.7	0.80	2.7	0.09
Region total	17,686	46.2	0.45	33.7	0.44	29.5	0.39	18.2	0.25	2.2	0.00
Africa (French speaking)											
Algeria											
Wilaya of Algiers (West Algiers)	4203	40.8	3.84	33.2	3.07	10.4	−0.47	20.7	1.80	3.5	0.08
Morocco											
Casablanca	1777	52.7	2.76	42.9	2.72	30.3	0.49	28.1	2.11	4.7	0.42
Marrakech	1689	35.7	0.86	26.4	1.00	16.5	−0.64	14.7	0.62	2.7	0.19
Country total	3466	44.4	1.92	34.9	1.84	23.6	−0.4	21.6	1.12	3.8	0.25
Tunisia											
Sousse	3042	74.4	2.96	61.8	2.59	34.2	0.89	23.2	−2.52	2.4	0.44
Region total	10,711	51.5	2.68	41.9	2.34	21.4	−0.26	21.7	1.07	3.2	0.31
Asia-Pacific											
China											
Beijing	3530	46.1	0.66	35.8	0.30	7.6	0.23	10.2	0.33	0.4	0.05
Guangzhou	3514	53.2	0.99	45.6	0.87	4.1	0.17	10.7	0.33	0.3	0.03
Country total	7044	49.7	0.77	40.7	0.53	5.9	0.19	10.4	0.33	0.3	0.04
Hong Kong											
Hong Kong	3321	48.9	−0.46	40.9	−0.52	1.5	−0.46	22.6	−0.21	0.2	−0.04
Indonesia											
Bandung	2826	36.7	−4.18	19.1	−2.25			4.8	−0.08	0.6	−0.08
Japan											
Fukuoka	2520	60.7	1.00	45.8	0.59	30.6	0.99	17.6	0.34	1.0	0.02
Malaysia											
Alor Setar	2941	49.6	0.14	40.2	0.40	24.3	−1.34	16.3	−0.06	1.0	−0.07
Klang Valley	3025	51.9	0.88	43.0	1.24	41.4	3.59	19.8	0.87	1.7	0.03
Kota Bharu	2989	47.4	1.46	34.9	0.88	29.2	1.49	12.5	0.46	1.0	−0.06
Country total	8955	49.6	0.69	39.4	0.86	31.7	1.32	16.2	0.53	1.2	−0.04
Philippines											
Metro Manila	3658	30.2	−0.82	22.1	−0.71	47.5	2.14	11.0	−0.61	0.7	−0.05
Singapore											
Singapore	4217	48.4	−0.23	40.8	−0.05			16.5	0.20	1.3	0.02
South Korea											
Provincial Korea	7375	38.6	0.65	32.4	0.72	13.1	1.16	11.5	0.30	0.4	0.03
Seoul	2888	36.7	−0.43	31.0	−0.24	13.3	0.97	11.9	0.24	0.2	−0.05
Country total	10,263	38.1	0.04	32.0	0.18	13.1	1.08	11.6	0.28	0.3	0.01
Taiwan											
Taipei	6378	52.9	2.75	43.3	2.24	33.5	−0.14	17.8	1.02	2.8	0.30
Thailand											
Bangkok	4669	64.9	2.41	57.4	2.36	40.0	1.55	23.9	1.41	4.2	0.41
Chiang Mai	3538	57.0	1.67	46.6	1.37	23.8	−0.17	17.2	0.26	1.3	−0.02
Country total	8207	61.5	2.14	52.7	1.98	33.0	0.68	21.0	0.84	2.9	0.12
Region total	57,389	48.1	0.71	38.9	0.53	23.9	0.24	15.1	0.32	1.2	0.02

Table 1. Continued

Centre	Phase III sample size	Rhinitis ever		Rhinitis in past year		Hay fever ever		Rhinoconjunctivitis in past year		Severe rhinoconjunctivitis in past year	
		%	Change per year (%)	%	Change per year (%)	%	Change per year (%)	%	Change per year (%)	%	Change per year (%)
Eastern Mediterranean											
Iran											
Rasht	3004	27.6	0.98	20.2	0.90	5.5	0.13	7.2	0.18	0.3	0.03
Tehran	3119	33.4	0.86	25.1	0.65	10.5	1.46	12.3	0.50	0.3	−0.02
Country total	6123	30.5	0.91	22.7	0.78	8.1	0.60	9.8	0.31	0.3	0.01
Kuwait											
Kuwait	2882	39.7	−0.44	27.6	−0.59	19.4	0.30	10.7	−0.32	0.0	−0.27
Malta											
Malta	4136	50.4	−0.33	42.8	−0.66	40.7	1.20	20.9	−1.15	0.7	−0.05
Pakistan											
Karachi	2999	36.4	0.27	28.4	−0.24	24.0	0.51	16.8	−0.22	1.3	−0.05
Sultanate of Oman											
Al-Khod	3747	42.1	1.25	29.7	0.98	14.2	0.62	15.2	0.63	1.6	0.05
Region Total	19,887	39.1	0.54	29.8	0.36	20.1	0.66	14.3	0.18	0.8	−0.01
Indian sub-continent											
India											
Borivali	1004	14.3	0.32	10.4	0.21	6.5	−0.22	3.9	0.09	0.2	−0.01
Chandigarh	3122	37.9	4.62	30.5	3.74	18.5	1.93	13.6	1.37	0.5	0.04
Chennai (3)	2181	29.2	0.76	21.1	1.33	8.2	0.12	5.6	0.34	0.3	0.00
Jodhpur	2341	39.0	1.81	34.9	1.85	23.8	1.31	13.0	0.43	0.6	−0.03
Kottayam	3685	36.8	−1.58	26.9	−1.54	11.3	−0.64	13.2	−1.16	0.0	−0.06
Mumbai (18)	2982	20.0	0.72	13.4	0.28	12.7	0.80	6.3	0.41	0.8	0.05
New Delhi (7)	3469	26.5	−1.36	24.7	−0.57	25.9	2.02	11.6	0.20	0.7	0.06
Pune	1983	17.4	0.95	13.7	0.87	10.3	0.84	5.1	0.51	0.6	0.07
Region total	20767	29.3	1.07	23.4	0.99	15.8	0.74	10.0	0.43	0.5	0.01
Latin America											
Argentina											
Córdoba	3445	49.3	−0.25	40.0	0.19	12.7	−2.40	16.9	−0.09	0.8	0.03
Brazil											
Curitiba	3628	48.2	1.24	39.2	1.57	12.2	0.72	17.0	0.47	0.6	0.01
Porto Alegre	3007	44.5	−0.98	32.1	−0.97	42.1	1.97	14.2	−0.38	0.9	0.02
Recife	2865	48.3	1.67	35.8	1.47	15.8	−0.32	14.2	0.36	1.0	−0.01
Salvador	3020	53.6	−2.10	44.2	−1.54	24.2	−0.07	21.1	−0.56	1.2	0.07
São Paulo	3161	41.4	−0.55	27.4	−0.94	32.2	0.06	12.1	−0.07	0.6	−0.01
Brazil cont.											
Country total	15,681	47.2	0.00	35.8	−0.02	24.9	0.61	15.8	−0.05	0.9	0.01
Chile											
Punta Arenas	3044	40.9	2.58	32.3	2.10	7.2	−0.69	14.1	0.64	0.7	0.00
South Santiago	3026	51.9	2.90	39.1	2.63	23.9	2.22	26.3	2.27	2.0	0.33
Valdivia	3105	51.2	4.38	42.8	3.68	24.4	2.04	26.3	2.35	1.3	0.01
Country total	9175	48.0	3.09	38.1	2.59	18.5	0.55	22.2	1.12	1.3	0.07
Costa Rica											
Costa Rica	2436	39.6	0.05	34.4	0.43			17.7	0.43	1.1	0.07
Mexico											
Cuernavaca	1431	30.6	−3.54	20.8	−0.17	10.6	0.65	7.1	−0.28	0.2	0.03
Panama											
David	3183	36.1	0.39	28.6	0.76	39.4	6.03	11.7	0.40	0.5	0.02
Paraguay											
Asunción	3000	89.5	1.80	80.6	2.80	44.4	1.21	45.1	2.12	4.0	0.47
Peru											
Lima	3022	44.1	0.36	34.1	−0.05			18.7	−0.12	1.0	−0.06
Uruguay											
Montevideo	3177	33.4	−2.27	24.6	−1.24	15.2	−1.23	10.6	−0.67	0.4	0.02
Region total	44,550	47.4	0.54	37.6	0.80	23.7	1.03	18.5	0.17	1.1	0.03

Table 1. Continued

Centre	Phase III sample size	Rhinitis ever		Rhinitis in past year		Hay fever ever		Rhinoconjunctivitis in past year		Severe rhinoconjunctivitis in past year	
		%	Change per year (%)	%	Change per year (%)	%	Change per year (%)	%	Change per year (%)	%	Change per year (%)
North America											
Barbados											
Barbados	2498	26.3	0.77	20.0	0.72	43.2	0.99	11.8	0.16	1.5	−0.04
USA											
Seattle	2422	35.0	−0.49	31.0	0.19	23.1	−1.32	19.1	0.71	1.9	0.15
Region total	4920	30.6	0.42	25.4	0.55	33.3	−1.12	15.4	0.41	1.7	0.08
Northern & Eastern Europe											
Albania											
Tiranë	2983	21.0	0.39	15.6	0.47	5.2	0.49	5.5	0.24	0.6	0.05
Estonia											
Tallinn	3603	34.6	0.14	24.5	0.18	7.2	−1.11	6.3	0.22	0.3	0.01
Finland											
Kuopio County	3051	51.5	0.70	40.1	0.55	28.4	−0.10	15.5	0.04	0.4	−0.04
Georgia											
Kutaisi	2650	19.2	0.04	15.3	0.42	3.8	−0.12	4.5	−0.01	0.5	0.04
Latvia											
Riga	1283	31.3	0.23	18.6	−0.29	8.0	0.46	4.5	−0.08	0.2	−0.05
Lithuania											
Kaunas	2723	28.8	−1.51	20.1	−1.26	6.2	0.28	4.6	−0.17	0.1	−0.01
Poland											
Krakow	2545	41.1	2.13	33.1	1.70	29.9	1.45	19.3	1.07	2.2	0.15
Poznan	1875	39.6	2.57	32.8	2.38	32.6	2.57	18.4	1.49	1.9	0.16
Country total	4420	40.4	2.43	33.0	2.13	31.0	1.81	18.9	1.35	2.1	0.16
Romania											
Cluj	3019	50.0	5.01	37.1	3.66	3.1	0.13	14.3	1.29	0.6	0.05
Russia											
Novosibirsk	3769	41.4	0.39	32.5	0.48	3.2	0.08	11.7	0.65	0.9	0.05
Sweden											
Linköping	2679	27.7	0.17	20.2	0.05	23.1	−0.11	10.4	−0.09	0.4	−0.04
Ukraine											
Kharkiv	2428	28.9	0.54	19.4	−0.33	5.8	−0.35	11.2	−0.01	0.7	0.00
Region total	32,608	35.1	1.03	26.3	0.81	12.3	0.19	10.5	0.28	0.7	0.01
Oceania											
New Zealand											
Auckland	2870	48.9	0.18	40.2	0.06	33.3	−0.04	18.8	−0.01	1.3	0.05
Bay of Plenty	1976	37.9	−1.27	31.5	−1.07	35.3	0.30	15.3	−0.38	0.8	−0.04
Christchurch	3116	39.2	−0.33	31.4	−0.55	45.3	0.48	15.9	−0.36	0.5	−0.04
Nelson	2305	40.3	−0.29	32.3	−0.37	43.1	0.70	15.3	−0.21	0.5	0.02
Wellington	3050	56.1	1.05	46.6	0.74	40.6	0.39	23.2	0.43	0.9	−0.03
Region total	13,317	45.2	−0.11	37.0	−0.17	39.8	0.48	18.0	−0.13	0.8	−0.01
Western Europe											
Austria											
Urfahr-Umgebung	1439	29.7	0.55	21.3	0.03	17.0	0.36	9.7	0.06	0.2	−0.02
Belgium											
Antwerp	3250	47.3	0.37	40.6	0.60	20.0	0.42	16.9	0.34	1.3	0.02
Channel Islands											
Guernsey	1248	41.2	−0.51	32.5	−0.30	36.7	0.30	16.3	−0.29	0.7	−0.04
Jersey	773	35.4	−1.73	27.4	−1.58	33.5	−0.47	12.9	−0.66	0.5	−0.03
Country total	2021	39.0	−0.89	30.5	−0.66	35.5	−0.12	15.0	−0.45	0.6	−0.04
Germany											
Münster	4132	41.0	0.90	31.6	0.58	24.0	0.58	15.0	0.12	0.4	−0.02
Isle of Man											
Isle of Man	1716	43.7	−1.09	36.7	−0.45	42.1	0.96	20.2	0.02	1.0	0.04
Italy											
Cosenza	925	18.9	−1.93	15.1	−1.15	14.8	−0.57	9.3	−0.43	0.0	0.00
Emilia-Romagna	1347	44.7	0.28	34.4	0.40	23.4	0.84	13.5	−0.27	0.1	−0.01

Table 1. Continued

Centre	Phase III sample size	Rhinitis ever		Rhinitis in past year		Hay fever ever		Rhinoconjunctivitis in past year		Severe rhinoconjunctivitis in past year	
		%	Change per year (%)	%	Change per year (%)	%	Change per year (%)	%	Change per year (%)	%	Change per year (%)
Empoli	1229	45.6	−0.15	33.1	−0.09	21.5	0.47	12.2	−0.45	0.2	−0.02
Firenze	1383	45.3	−0.08	33.0	−0.18	24.3	0.71	15.7	−0.34	0.2	0.00
Milano	1410	44.1	−0.14	31.9	−0.06	28.0	0.87	18.5	0.27	0.3	0.00
Roma	1325	49.3	1.23	37.7	0.94	26.8	1.30	22.2	0.93	0.5	0.01
Siena	1082	40.5	−0.76	38.4	0.59	23.1	0.81	20.0	0.29	0.4	0.03
Torino	1180	50.5	1.05	38.0	1.11	22.4	0.47	17.5	0.30	0.3	0.02
Trento	1311	27.5	−0.19	17.5	−0.10	16.2	0.52	9.8	0.11	0.1	0.00
Country total	11,192	41.4	0.18	31.3	0.27	22.6	0.71	15.5	0.07	0.2	0.00
Portugal											
Funchal	3161	32.6	0.40	21.4	0.03	8.7	−0.03	8.7	0.15	0.5	0.04
Lisbon	3024	39.7	0.93	29.0	0.93	6.4	0.14	10.5	0.44	0.4	0.03
Portimao	1109	34.4	0.74	21.7	0.26	7.3	0.52	7.1	−0.21	0.1	0.01
Porto	3336	41.8	1.71	31.7	1.27	5.0	0.12	10.3	0.57	0.3	−0.01
Country total	10,630	37.7	1.06	26.8	0.88	6.8	0.15	9.5	0.40	0.3	0.02
Republic of Ireland											
Republic of Ireland	3089	45.1	−0.44	37.0	−0.60	31.5	0.83	15.5	−0.48	0.9	0.00
Spain											
Barcelona	3066	34.7	−0.08	23.4	−0.30	9.3	0.08	10.5	−0.14	0.1	−0.02
Bilbao	3401	35.1	−1.92	27.3	−1.13	16.1	0.73	14.5	−0.38	0.2	−0.02
Cartagena	3998	42.8	−0.11	32.0	−0.08	11.0	0.42	15.6	−0.14	0.2	−0.01
Castellón	4024	47.1	0.59	35.8	0.75	7.1	0.05	15.9	0.31	0.2	−0.01
Madrid	2652	36.9	0.68	28.7	1.09	19.7	1.73	18.7	1.11	0.5	0.06
Pamplona	2932	31.1	−2.66	39.4	0.56	7.4	0.20	15.8	0.16	0.3	0.03
Valencia	3132	36.6	−0.57	26.3	−0.17	14.1	−0.05	12.6	0.08	0.2	0.00
Valladolid	2944	45.9	0.09	35.1	0.42	8.6	0.11	17.1	0.55	0.2	0.01
Country total	26,149	39.2	−0.41	31.1	−0.01	11.4	0.21	15.0	0.10	0.2	0.00
United Kingdom											
North Thames	2356	42.2	−0.23	34.5	0.09	39.6	0.50	15.0	−0.14	0.8	−0.01
Scotland	4662	41.7	−0.97	34.4	−0.81	34.0	0.11	15.1	−0.75	0.6	−0.05
South Thames	2432	41.2	−0.81	31.9	−0.75	38.2	−0.03	14.5	−0.30	0.7	−0.04
Sunderland	2193	25.7	−1.45	22.9	−1.18	25.4	−0.07	14.3	−0.69	1.4	−0.01
Surrey/Sussex	5082	38.3	−0.72	32.5	−0.50	41.2	0.13	17.6	−0.49	0.6	−0.09
Wales	2501	40.2	−0.79	31.8	−0.71	38.5	0.83	12.7	−0.83	0.6	−0.06
Country total	19,226	38.8	−0.83	32.0	−0.64	36.7	0.18	15.3	−0.57	0.7	−0.05
Region total	82,844	39.8	−0.06	31.3	0.09	21.2	0.31	14.5	0.02	0.5	0.00
Global total	304,679	42.1	0.37	33.2	0.40	22.1	0.3	15.1	0.18	1.0	0.01

standardized child contact modules including examination of flexural dermatitis, skin prick testing, bronchial challenge, blood sampling and dust sampling (7).

In many of the countries participating in Phase I and Phase III, there has been little previous information on allergy prevalence and only a few, mostly industrialized affluent countries had undertaken time trends analyses. ISAAC Phase III aimed at examining time trends in the prevalence of symptoms of asthma, rhinoconjunctivitis and eczema in centres and countries which participated in Phase I (Phase III A) and at describing the prevalence and severity of these conditions in centres and countries which are of interest but did not participate in Phase I (Phase III B). Recently, worldwide trends in the prevalence of asthma, rhinoconjunctivitis and eczema were summarized (8).The present publication describes the detailed findings for time trends in the prevalence of rhinitis and conjunctivitis symptoms, as well as of perceived hay fever, in those centres that participated in both Phase I and Phase III.

Methods

The methods used in Phase III were the same as to those used in Phase I (9, 10). Briefly, two age groups of children (13- to 14-yr olds and 6- to 7-yr olds) were chosen from a randomly selected sample of schools from a defined geographic

Table 2. Reported rhinitis, hay fever and rhinoconjunctivitis in 6- to 7-yr-old children for each centre by region participating both in ISAAC Phase I and Phase III. The change in reported symptoms per year is also shown

Centre	Phase III sample size	Rhinitis ever		Rhinitis in past year		Hay fever ever		Rhinoconjunctivitis in past year		Severe rhinoconjunctivitis in past year	
		%	Change per year (%)	%	Change per year (%)	%	Change per year (%)	%	Change per year (%)	%	Change per year (%)
Africa (English speaking)											
Nigeria											
Ibadan	2396	14.1	0.50	11.7	0.23	14.4	0.52	3.6	−0.01	0.3	−0.03
Region total	2396	14.1	0.50	11.7	0.23	14.4	0.52	3.6	−0.01	0.3	−0.03
Asia-Pacific											
Hong Kong											
Hong Kong	4448	42.4	0.99	37.3	0.74	1.5	0.05	17.7	0.67	0.3	0.02
Indonesia											
Bandung	2503	18.1	−0.5	10.9	−1.58			3.6	−0.04	0.5	0.07
Japan											
Fukuoka	2958	37.9	0.89	33.1	0.93	14.5	0.59	10.6	0.35	0.4	0.00
Malaysia											
Alor Setar	3786	15.9	−0.13	13.3	0.04	10.9	0.30	4.2	0.09	0.6	0.00
Klang Valley	3044	20.4	0.68	17.8	0.67	15.0	0.56	6.2	0.21	1.0	0.01
Kota Bharu	3110	16.9	−0.31	14.1	−0.17	17.8	0.31	4.2	0.06	0.7	−0.03
Country total	9940	17.6	0.16	14.9	0.19	14.3	0.40	4.8	0.11	0.7	−0.01
Singapore											
Singapore	5389	29.4	0.01	25.6	−0.10			8.7	0.02	0.5	0.02
South Korea											
Provincial Korea	4258	30.0	−0.93	25.0	−0.86	18.7	0.76	8.6	−0.14	0.4	−0.07
Seoul	1760	31.8	−1.18	27.8	−1.12	21.2	1.14	9.0	−0.38	0.3	−0.05
Country total	6018	30.5	−0.99	25.8	−0.92	19.5	0.87	8.7	−0.18	0.3	−0.07
Taiwan											
Taipei	4832	46.4	1.41	42.0	1.60	39.4	0.65	24.2	1.37	3.3	0.34
Thailand											
Bangkok	4209	47.9	1.93	43.4	1.81	31.9	0.47	13.4	0.58	1.4	0.04
Chiang Mai	3106	26.9	1.01	23.5	0.84	19.7	0.30	6.2	0.24	0.8	0.04
Country total	7315	38.9	1.24	35.0	1.03	26.7	0.32	10.4	0.30	1.1	0.04
Region total	43,403	31.6	0.34	27.5	0.26	19.6	0.20	10.6	0.18	0.9	0.02
Eastern Mediterranean											
Iran											
Rasht	3057	14.1	1.06	11.2	1.00	2.4	0.02	2.4	0.21	0.1	0.02
Tehran	3008	11.2	0.23	8.9	0.23	2.1	0.26	1.9	0.00	0.1	0.00
Country total	6065	12.6	0.63	10.1	0.59	2.2	0.18	2.2	0.12	0.1	0.01
Malta											
Malta	3795	29.0	0.78	24.6	0.54	22.3	1.08	8.9	0.24	0.4	−0.01
Sultanate of Oman											
Al-Khod	4130	29.2	1.20	19.2	0.70	5.4	−0.34	7.0	0.13	0.6	−0.03
Region total	13,990	22.0	0.75	16.7	0.60	8.6	0.14	5.4	0.14	0.3	0.00
Indian sub-continent											
India											
Jodhpur	2114	14.4	0.44	12.3	0.37	6.5	−0.01	2.9	0.05	0.2	0.01
Kottayam	2619	19.3	−1.25	15.1	−1.25	9.2	0.47	8.6	−0.13	0.0	−0.07
Mumbai (16)	2865	9.4	−0.08	7.4	−0.10	5.2	0.02	2.1	−0.07	0.0	−0.02
Mumbai (18)	4862	14.0	0.82	11.2	0.65	7.1	0.52	3.5	0.25	0.2	0.00
New Delhi (7)	3706	16.0	0.12	14.8	0.22	16.1	1.47	4.5	0.15	0.2	−0.01
Pune	2711	9.8	0.42	7.4	0.24	4.7	0.30	1.8	0.04	0.1	0.01
Region total	18,877	13.9	0.17	11.4	0.13	8.5	0.26	3.9	0.05	0.1	−0.01
Latin America											
Brazil											
São Paulo	3047	35.8	−0.60	28.2	−0.81	29.2	0.07	12.0	−0.07	1.1	0.04
Chile											
Punta Arenas	3052	34.1	0.83	28.1	0.69	14.0	0.39	11.2	0.35	1.1	0.04
South Santiago	3075	31.0	1.34	25.3	1.10	12.6	0.48	13.7	0.87	1.4	0.10

Table 2. Continued

Centre	Phase III sample size	Rhinitis ever		Rhinitis in past year		Hay fever ever		Rhinoconjunctivitis in past year		Severe rhinoconjunctivitis in past year	
		%	Change per year (%)	%	Change per year (%)	%	Change per year (%)	%	Change per year (%)	%	Change per year (%)
Valdivia	3183	31.4	1.58	28.1	1.53	13.5	0.37	11.9	0.56	1.9	0.14
Country total	9310	32.1	1.24	27.2	1.09	13.4	0.40	12.3	0.56	1.5	0.09
Costa Rica											
Costa Rica	3234	40.4	0.96	34.9	1.04			15.9	0.54	1.1	0.07
Mexico											
Cuernavaca	2579	25.4	−4.93	20.9	−0.29	4.7	0.13	7.2	−0.17	0.5	0.07
Panama											
David	2942	35.7	1.26	28.0	1.25	39.2	5.90	11.7	0.77	0.5	0.01
Region total	21,112	33.6	0.00	27.9	0.74	16.2	0.59	12.1	0.32	1.1	0.06
North America											
Barbados											
Barbados	2759	14.6	0.40	11.2	0.35	34.8	1.07	6.4	0.15	0.7	0.04
Canada											
Saskatoon	1255	30.7	0.56	27.0	0.49	12.3	0.56	10.8	0.29	0.3	0.00
Region total	4014	19.6	0.47	19.1	0.41	27.8	0.67	7.8	0.21	0.5	0.02
Northern & Eastern Europe											
Albania											
Tiranë	2896	16.4	0.00	13.7	0.13	3.3	0.09	3.9	−0.03	0.4	0.01
Estonia											
Tallinn	2385	18.3	0.47	13.0	0.20	3.5	0.12	4.2	0.11	0.1	−0.02
Georgia											
Kutaisi	2666	11.1	0.05	8.7	0.10	2.8	−0.41	2.8	−0.16	0.2	−0.01
Lithuania											
Kaunas	2772	28.4	0.46	21.9	0.26	2.4	0.15	3.8	0.08	0.2	0.01
Poland											
Krakow	2497	33.6	0.76	28.3	0.55	21.1	0.91	14.5	0.72	1.6	0.03
Poznan	1999	31.3	2.30	25.4	1.77	19.5	1.83	11.1	0.81	1.4	0.09
Country total	4496	32.6	1.87	27.0	1.40	20.4	1.61	13.0	0.78	1.5	0.07
Russia											
Novosibirsk	2730	26.4	−0.13	20.9	−0.27	5.2	0.18	4.7	−0.16	0.8	0.02
Sweden											
Linköping	2089	14.7	−0.35	12.2	−0.31	8.3	0.01	6.9	−0.14	0.3	−0.09
Ukraine											
Kharkiv	1950	29.2	0.60	16.3	−0.69	7.6	0.32	7.7	−0.51	0.5	−0.09
Region total	21,984	23.0	0.53	17.8	0.34	7.7	0.23	6.4	0.10	0.6	0.00
Oceania											
Australia											
Melbourne	2968	27.6	0.22	25.1	0.23	19.8	0.54	12.9	0.34	0.5	0.02
New Zealand											
Auckland	3541	26.9	−0.09	23.5	−0.14	14.8	0.27	11.0	0.14	0.5	−0.06
Bay of Plenty	2150	28.6	−0.07	24.4	−0.14	15.9	0.48	11.3	0.30	0.6	0.03
Christchurch	3315	28.0	0.06	24.8	0.05	20.4	0.58	12.9	0.17	0.5	0.02
Nelson	1867	23.2	0.48	19.7	0.32	17.2	0.71	9.3	0.18	0.2	0.00
Country total	10,873	26.9	0.10	23.4	0.01	17.2	0.51	11.4	0.19	0.5	0.00
Region total	13,841	27.1	0.12	23.8	0.05	17.7	0.51	11.7	0.21	0.5	0.01
Western Europe											
Austria											
Kärnten	4847	12.2	0.27	10.8	0.25	4.3	0.06	5.7	0.14	0.2	0.01
Urfahr-Umgebung	2029	14.1	0.40	12.5	0.32	4.3	0.04	7.1	0.17	0.2	0.01
Country total	6876	12.8	0.30	11.3	0.26	4.3	0.06	6.1	0.15	0.2	0.01
Belgium											
Antwerp	5645	22.6	0.51	18.0	0.47	6.0	0.14	5.8	0.13	0.6	0.02
Germany											
Münster	3830	18.5	0.71	16.1	0.73	6.4	0.09	6.9	0.30	0.3	0.01
Italy											
Emilia-Romagna	2265	22.2	0.42	17.0	0.51	7.7	0.22	6.4	0.13	0.1	0.00

Table 2. Continued

Centre	Phase III sample size	Rhinitis ever		Rhinitis in past year		Hay fever ever		Rhinoconjunctivitis in past year		Severe rhinoconjunctivitis in past year	
		%	Change per year (%)	%	Change per year (%)	%	Change per year (%)	%	Change per year (%)	%	Change per year (%)
Empoli	1152	25.2	0.59	17.1	0.52	12.7	0.63	6.6	0.28	0.3	0.02
Firenze	1036	24.7	0.44	18.4	0.32	10.5	0.48	6.4	0.01	0.1	−0.01
Milano	2249	26.5	0.76	18.7	0.56	8.0	0.18	7.1	0.16	0.1	−0.01
Roma	2224	26.6	0.92	20.1	0.83	10.5	0.49	6.4	0.16	0.1	0.00
Torino	2361	25.2	0.74	18.8	0.75	9.8	0.52	6.2	0.13	0.1	−0.01
Country total	11,287	25.1	0.67	18.5	0.61	9.5	0.39	6.5	0.15	0.1	0.00
Portugal											
Funchal	1819	27.0	0.45	21.6	0.15	6.7	−1.31	9.2	−0.29	0.8	−0.06
Lisbon	2477	31.2	0.62	26.3	0.41	2.7	−0.03	10.0	0.19	0.7	0.03
Portimao	1069	28.0	1.42	23.1	1.20	3.6	0.15	7.9	0.41	0.7	0.00
Country total	5365	29.2	0.73	24.1	0.56	4.2	−0.14	9.3	0.16	0.7	0.01
Spain											
Bilbao	3157	23.7	−0.46	20.1	0.19	8.9	0.33	8.9	0.34	0.2	0.00
Cartagena	2948	21.4	−0.15	17.1	0.09	7.8	0.14	8.1	0.15	0.1	0.01
Castellón	3915	19.2	0.60	14.4	0.56	8.0	0.55	6.3	0.31	0.2	0.01
Madrid	2347	28.6	1.30	23.3	1.15	10.7	0.74	11.1	0.51	0.2	0.01
Pamplona	3176	14.1	−0.21	17.1	0.93	8.2	0.49	6.6	0.43	0.1	0.00
Valencia	3398	20.5	0.39	16.3	0.57	7.2	0.26	7.5	0.39	0.1	0.00
Country total	18,941	20.9	0.14	17.7	0.50	8.4	0.36	7.9	0.33	0.1	0.00
United Kingdom											
Sunderland	1843	23.9	0.04	21.6	0.05	13.9	0.69	10.1	0.05	0.7	0.07
Western Europe cont.											
Region total	53,787	21.7	0.38	17.7	0.49	7.5	0.24	7.3	0.22	0.3	0.00
Global total	193,404	24.9	0.34	20.7	0.39	11.8	0.27	8.3	0.17	0.6	0.01

area. A simple questionnaire with questions related to symptoms of wheezing, rhinoconjunctivitis and eczema was completed by the older children and by parents of the younger children.

The Phase III A centres completed Phase III at least 5 yr after Phase I, and were required to conduct Phase III in the same way as Phase I (11). Questionnaires were translated if necessary from English into the local language for self-completion by the 13- to 14-yr olds and for completion by the parents of the 6- to 7-yr-old children. Respondents were asked:

1 Have you (has your child) ever had a problem with sneezing or a runny or blocked nose, when you (he or she) DID NOT have a cold or 'the flu'?
2 In the past 12 months, have you (has your child) had a problem with sneezing or a runny or blocked nose, when you (he or she) DID NOT have a cold or 'the flu'?
3 In the past 12 months, has this nose problem been accompanied by itchy-watery eyes?
4 In which of the past 12 months did this nose problem occur?
5 In the past 12 months, how much did this nose problem interfere with your (child's) daily activities? (Not at all, a little, a moderate amount, a lot).
6 Have you (has your child) ever had hay fever?

This article will focus in particular on rhinitis with itchy eyes in the past year (rhinoconjunctivitis), i.e. affirmative responses to both questions 2 and 3. This combination of symptoms was selected as those which best predict allergic rhinitis (12), both in adults and children. Severe rhinoconjunctivitis was based on the combination of the two questions for rhinoconjunctivitis combined with the answer 'a lot' to question 5. The data from the question concerning months of nose symptoms were excluded because of concerns regarding bias in the responses (17).

Adequate documentation of the procedures for the study from each centre was a prerequisite for inclusion in publications of ISAAC worldwide results. Centres completed a Registration Document before starting the study and followed the published ISAAC Phase III Manual (10). Centres were expected to obtain ethics approval and

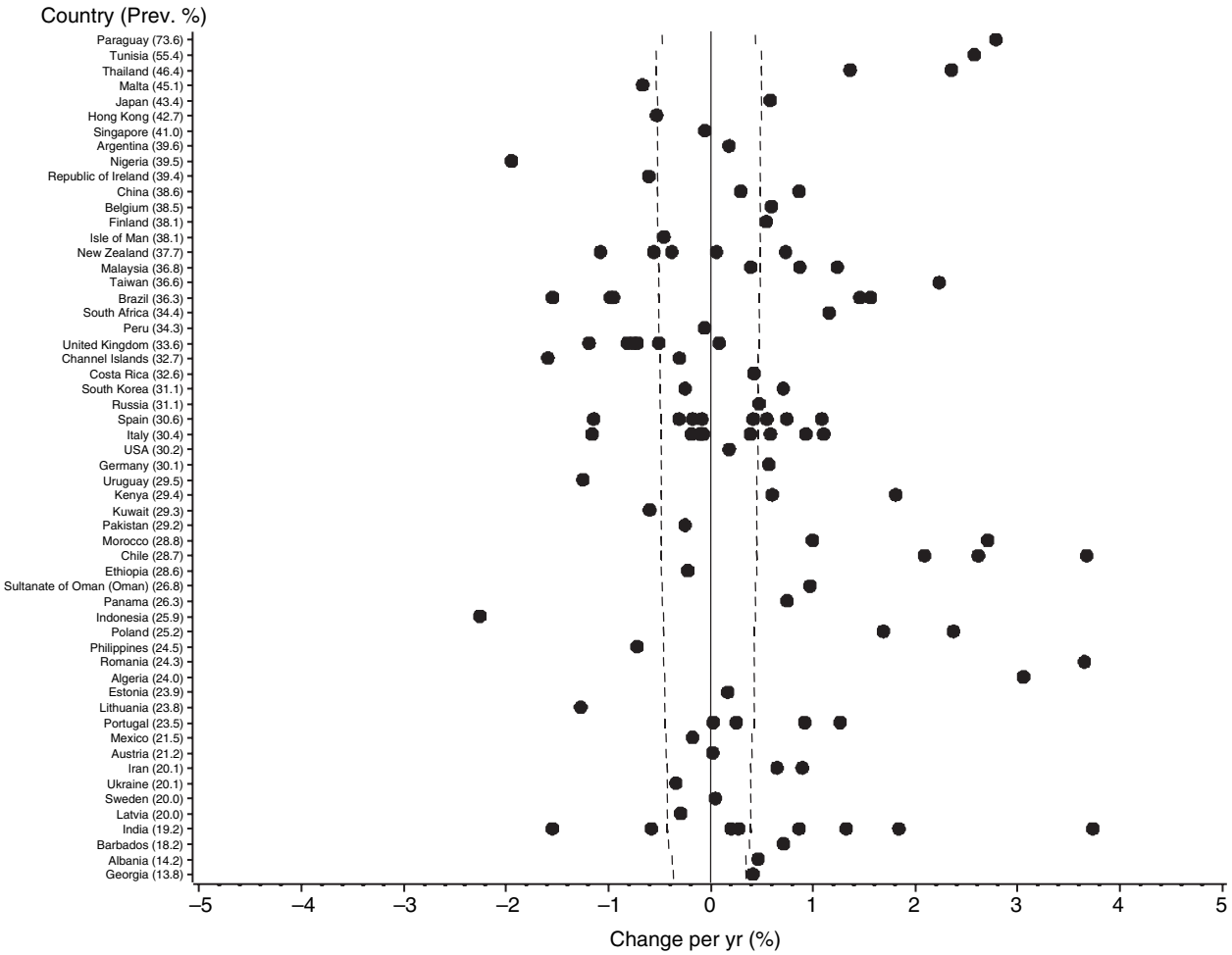

Fig. 1. Ranking plot showing the change per year of symptoms of rhinitis in 13- to 14-yr-old children for each centre by country, with countries ordered by their average prevalence (for all centres combined) across Phase I and Phase III. The plot also shows the confidence interval about zero change for a given level of prevalence, given a sample size of at least 3000 and no cluster sampling effect.

parental consent according to the requirements of the country, and to fund their own study.

As in Phase I, the 13–14 yr and the 6–7 yr age groups were analyzed separately. The symptom prevalence of each condition in each centre was calculated by dividing the number of positive responses to each individual question by the number of completed questionnaires. Thus, apparent inconsistencies between responses to the stem and branch questions were accepted and not recoded. The annual change in prevalence was calculated by taking the difference between the Phase I and Phase III prevalence values and dividing by the number of years between the two surveys.

The data are presented in tabular form with the Phase I and Phase III prevalence and the annual change in prevalence for each question. For the national, regional and global summaries, the data for each centre were weighted by the number of participating children with the exception of the summary change per year values which were weighted by the inverse of the variance of the centre level change per year. The key findings are also presented as ranked change per year plots, with focus on the change in prevalence between Phase I and Phase III, rather than the absolute level of prevalence. Thus, the ranked change per year plot shows the change in prevalence of a symptom (e.g. rhinitis, current and severe rhinoconjunctivitis) for each centre by country, with countries ordered by their average prevalence (for all centres combined) across Phase I and Phase III. The average prevalence (rather than the Phase I prevalence) was used to order countries as this is statistically independent from the change in prevalence (between Phase I and Phase III) (14–16). The ranked change per year plots also show the confidence interval about zero change for a given

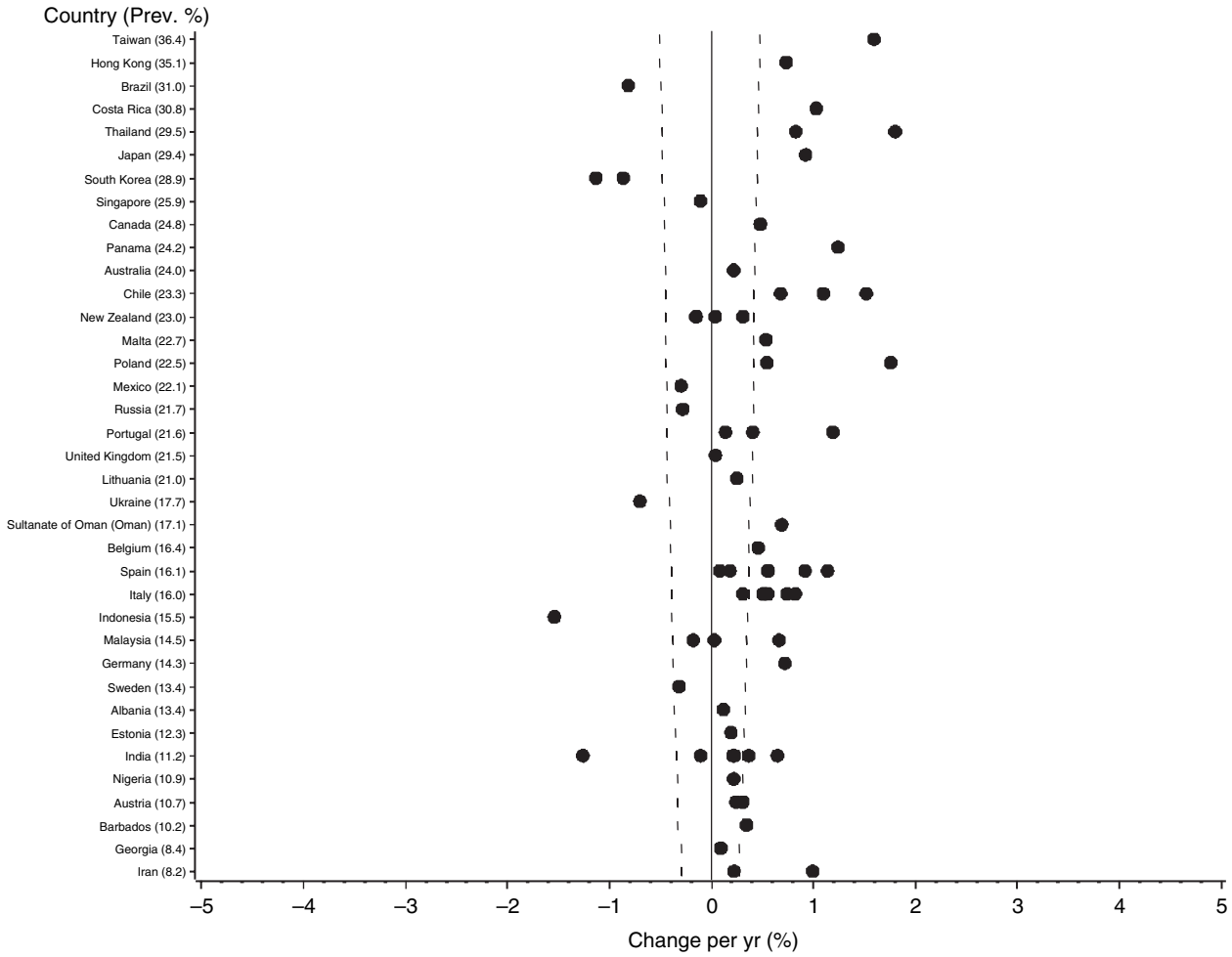

Fig. 2. Ranking plot showing the change per year of symptoms of rhinitis in 6- to 7-yr-old children for each centre by country, with countries ordered by their average prevalence (for all centres combined) across Phase I and Phase III (c.f. Fig. 1).

level of prevalence (i.e. the average prevalence across Phase I and Phase III) given a sample size of 3000 and no cluster sampling effect.

Results

The details of the participating centres including years of data collection and response rates are listed in a separate Phase III overview paper (8). Of the centres that participated in Phase I, 106 centres from 56 countries completed the Phase III survey, thus allowing time trends analyses, with a total of 304,679 participating children in the 13- to 14-yr age group. In the 6- to 7-yr age group, 66 centres in 37 countries (a total of 193,404 children) also completed the survey and met the requirements for the time trends analyses. Data were collected within 1 yr for each centre within each Phase, but the year of study varied among centres between 1991 and 1998 (mostly 1994–95) for Phase I and between 1999 and 2004 (mostly 2002–03) for Phase III. The time period between Phase I and Phase III averaged 7 yr (range 5–10 yr).

The Phase I and Phase III prevalence rates and prevalence per year for symptoms of nose symptoms and rhinoconjunctivitis in 13- to 14-yr olds are presented by centre and country in Table 1. The symptom prevalence of rhinoconjunctivitis increased among the 13- to 14-yr-old children in 62 centres and decreased in 44 centres. The changes were mostly small and there was no consistent pattern in any of the regions. Increases exceeding 1% per year were recorded in three of nine African centres while a decrease of similar magnitude was observed in two centres. The corresponding figures for Asia-Pacific were 2 of 15 centres and no centre, respectively. In the Eastern Mediterranean region one centre showed

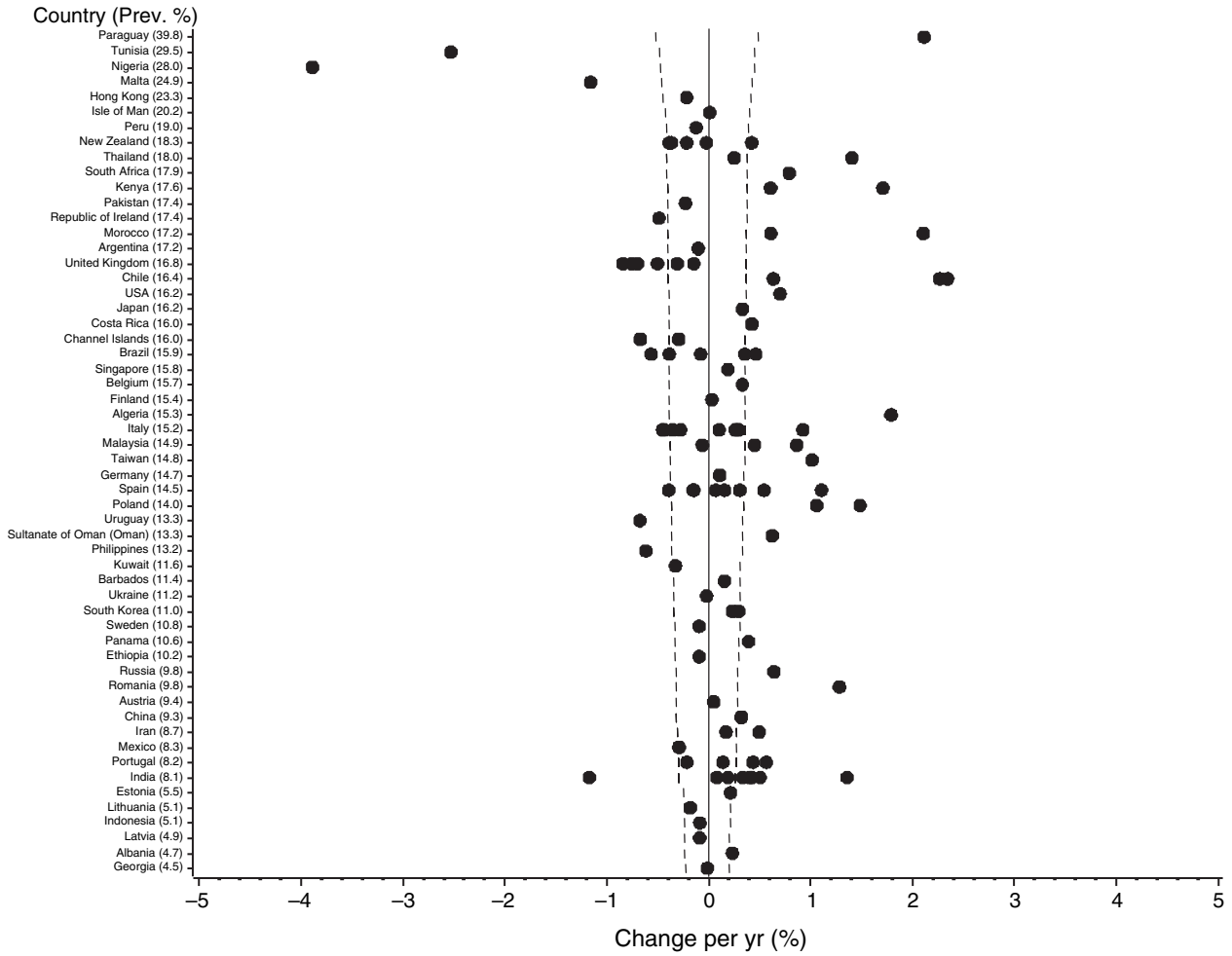

Fig. 3. Ranking plot showing the change per year of symptoms of rhinoconjunctivitis (affirmative responses to both the questions 'In the past 12 months, have you had a problem with sneezing or a runny or blocked nose, when you DID NOT have a cold or 'the flu'?' and 'In the past 12 months, has this nose problem been accompanied by itchy-watery eyes?') in 13- to 14-yr-old children for each centre by country, with countries ordered by their average prevalence (for all centres combined) across Phase I and Phase III (c.f. Fig. 1).

a decrease of more than 1% per year. In the Indian sub-continent one of eight centres showed an increase and one a decrease. In Latin America an increase was recorded in 3 of 15 centres. In Northern and Eastern Europe, 3 of 12 centres showed an increase and no centres showed a decrease, while in Western Europe 1 of 34 centres showed a more than 1% increase and four centres, all in the UK or the Channel Islands, a decrease. No changes of this magnitude were recorded in North America or Oceania.

The findings in the 6- to 7-yr age group largely corroborated the findings in the older children, although the changes generally were smaller, with mostly small increases reported in 51 centres and small decreases reported in 15 centres (Table 2). An increase exceeding 1% per year was only observed in Taipei (Taiwan) which also reported a similar increase among the 13- to 14-yr olds (Table 1).

Figs 1 and 2 give the ranked prevalence plots for the two age groups, showing the change in prevalence of rhinitis in the last 12 months for each centre by country, with countries ordered by their average prevalence (for all centres combined) across Phase I and Phase III. The direction of changes was similar for centres with high and low prevalence in Phase I. The 6- to 7-yr age group showed a pattern of more increases than decreases.

In contrast, for rhinoconjunctivitis, countries with the highest prevalence in Phase I (including most of the English-speaking countries) showed decreases in prevalence in Phase III, whereas some of the countries which previously had a low prevalence showed increases

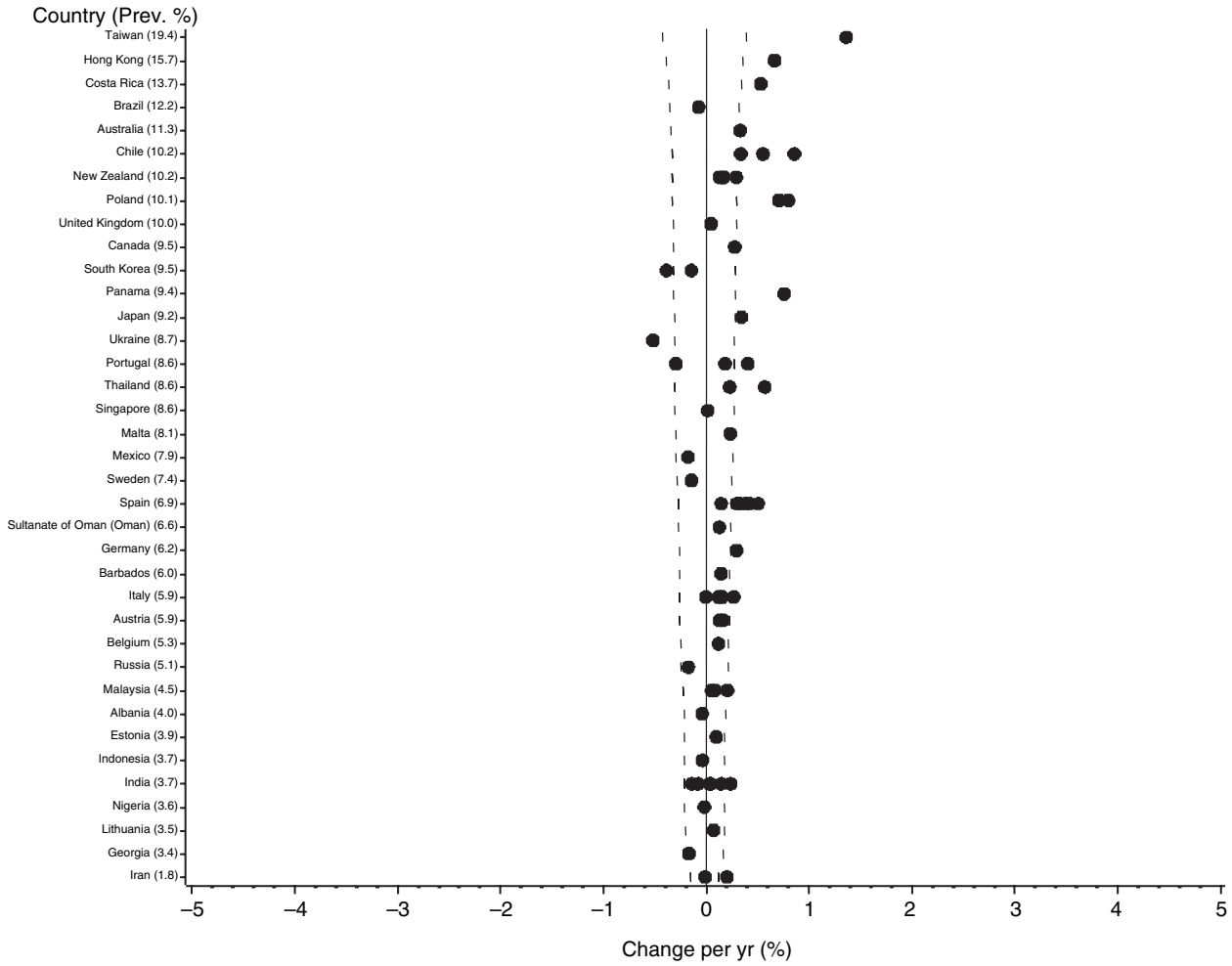

Fig. 4. Ranking plot showing the change per year of symptoms of rhinoconjunctivitis (affirmative responses to both the questions 'In the past 12 months, have you had a problem with sneezing or a runny or blocked nose, when you DID NOT have a cold or 'the flu'?' and 'In the past 12 months, has this nose problem been accompanied by itchy-watery eyes?') in 6- to 7-yr-old children for each centre by country, with countries ordered by their average prevalence (for all centres combined) across Phase I and Phase III (c.f. Fig. 1).

(Figs 3 and 4). However, there were a number of countries, mainly in Eastern Europe, which had a very low prevalence in Phase I and showed little evidence of an increase in Phase III. The prevalence of severe rhinoconjunctivitis in the past year increased in several centres with high prevalence in Phase I, particularly among older children.

There was a correlation (Pearson correlation coefficient $r = 0.43$, $p = 0.0005$) between changes in prevalence in the two age groups, although increases were usually more pronounced in the older children (Fig. 5). Ibadan in Nigeria was an exception with a 3.9% decrease per year in 13- to 14-yr olds and no change in the younger children.

We also analyzed possible gender differences in trends in prevalence of rhinoconjunctivitis among the 13- to 14-yr-old children. In no centre did one gender increase by 0.5% per year while the other gender decreased by this amount. In 66 (62%) of the centres girls and boys showed the same direction of change, 17 being increases by at least 0.5% per year and five being decreases of the same magnitude. There were 23 (22%) centres in which girls had increases by at least 0.5% per year or no change, while the boys had no change or a decrease respectively, and there were 17 (16%) centres in which boys increased or remained the same, while girls showed no change or decreased respectively.

Discussion

There was a slight worldwide increase in the prevalence of rhinoconjunctivitis, both in 13- to

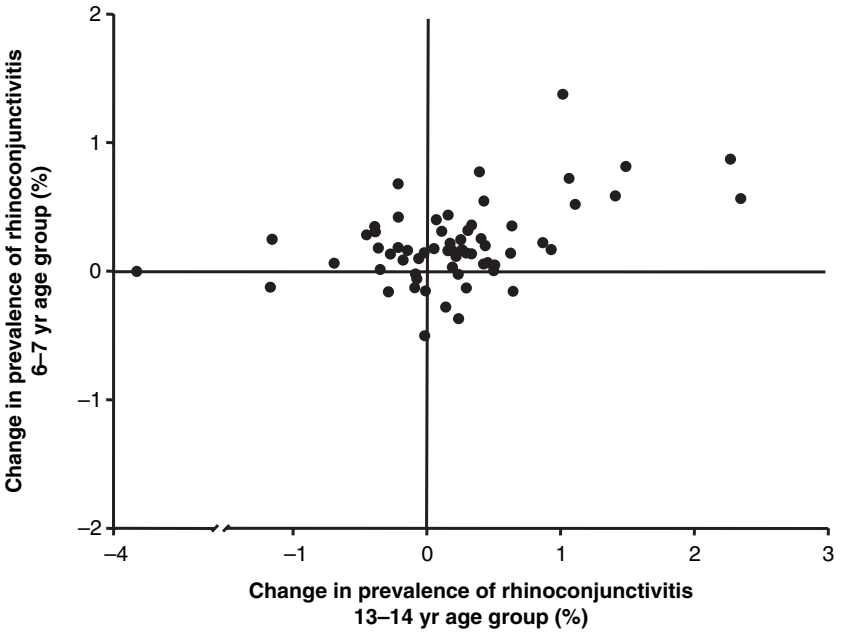

Fig. 5. Scatter plot showing the change per year of symptoms of rhinoconjunctivitis for the 13–14 yr age group and the 6–7 yr age group for centres which included both age groups.

14-yr old and 6- to 7-yr-old children, but the variations were large among the centres and there was no consistent regional pattern. Prevalence increases in the older children exceeding 1% per year were recorded in 13 centres, including 3 of 9 centres in Africa, 2 of 15 in Asia-Pacific, 1 of 8 in India, 3 of 15 in Latin America, 3 of 12 in Northern and Eastern Europe and 1 of 34 in Western Europe. Decreasing prevalence of similar magnitude was seen in four centres. The changes were less pronounced in the 6- to 7-yr-old children and only in one centre did any change exceed 1% per year.

The highest average prevalence for rhinoconjunctivitis among the 13- to 14-yr-old children was recorded in Asunción (Paraguay), Sousse (Tunisia) and Ibadan (Nigeria), and among the younger children in Taipei (Taiwan), Hong Kong and Costa Rica. It should be noted though that only one African centre and rather few centres in Latin America provided data for the 6–7 yr age group. The higher prevalence in these centres when compared with centres in Western Europe and New Zealand raise questions about the specificity of the questionnaire to identify rhinoconjunctivitis. Seasonal rhinitis and rhinoconjunctivitis in the absence of other signs of respiratory infection are strong indicators of IgE-mediated allergy in schoolchildren living in affluent countries with a temperate climate. Much less is known regarding the relationship between respiratory allergy and these symptoms in developing countries and tropical countries. Rhinitis as a single symptom on the other hand is less specific than rhinoconjunctivitis, as it is often triggered by infections, air quality and physical stimuli. This may explain the divergent outcomes for rhinitis when compared with rhinoconjunctivitis. We considered comparing peak months of rhinoconjunctivitis in the centres under the assumption that symptoms reported primarily during the pollen season would suggest allergy, while similar symptoms during the winter months would indicate infectious origin. Such comparisons between countries are reasonable and interesting in a temperate climate, as shown in a previous ISAAC study from Northern and Eastern Europe (17). This approach was not feasible, however, in a global comparison, in which many areas do not have clearly defined pollen seasons.

Over the past 40 yr, there has been a pronounced increase in the prevalence of childhood allergies in industrialized countries. This increase may not yet have peaked, not even in countries with a high prevalence, as indicated by an increase in severe rhinoconjunctivitis among 13- to 14-yr-old children in some centres which already had a high prevalence in ISAAC Phase I.

Several recent studies suggest that environmental factors encountered during the first few years of life may have a major impact on subsequently developing allergic manifestations (18). This hypothesis would have been supported by a more pronounced increase in the younger age group than among the 13–14 yr olds. That was not the case. On the contrary, in centres showing an increasing prevalence of rhinoconjunctivitis, the increasing prevalence was most

obvious in the older children. In particular, in those 13–14 yr olds in countries undergoing a rapid socio-economic transition where changes in environmental factors have been more recent. For example, the children in the older age group in the centres in Eastern Europe were born before the collapse of the socialist system, while the younger children were all born into societies with a different lifestyle, more similar to that in Western Europe. It is reasonable to suggest that the environmental impact on allergy development and induction of tolerance are not limited to the first few years of life.

In contrast to the prevalence of wheezing, English-speaking centres did not show particularly high prevalence figures for rhinitis or rhinoconjunctivitis. The high prevalence of reported wheezing may be explained by the fact that many languages lack a distinct word for 'wheeze'. The fact that English-speaking centres did not demonstrate a correspondingly high prevalence of rhinoconjunctivitis indicates that allergies are not necessarily more common in these centres than in countries with similar environmental conditions.

In conclusion, no consistent global time trends in the prevalence of childhood rhinoconjunctivitis could be identified. A decrease was recorded in most centres with the highest prevalence rates in ISAAC Phase I, suggesting that the prevalence has peaked in those regions. In many countries undergoing rapid socio-economic development an increase was recorded. This was not more pronounced in the young age group, suggesting that environmental influences may not be limited to early childhood.

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Appendix

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The full list of members of the ISAAC International Data Centre, ISAAC Phase Three Principal Investigators and National Coordinators is given in reference #8.