

Changes in the Prevalence of Asthma and Allergic Diseases among Brazilian Schoolchildren (13–14 years old): Comparison between ISAAC Phases One and Three

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Summary

The present study is aimed to describe the changes in the prevalence of symptoms of asthma, rhinitis and eczema among Brazilian adolescents (AD, 13–14 years old) between Phases 1 and 3 of the International Study of Asthma and Allergies in Childhood (ISAAC). The prevalence of self-reported symptoms of asthma, rhinitis and eczema in AD from five Brazilian cities (Curitiba, Porto Alegre, Recife, Salvador and São Paulo), obtained during ISAAC Phase 1 ($n = 15\,419$) and Phase 3 ($n = 15\,684$), was compared to determine the trend of prevalence in a 7-year interval. There was a trend to reduction in the current prevalence of wheezing and increasing of nocturnal cough when averaging figures from the five cities. The prevalence of wheezing in the last 12 months was 27.7 vs. 19.9% ($p < 0.01$); asthma ever 14.9 vs. 14.7% ($p > 0.05$); severe episode of wheezing 5.2 vs. 5.2%; nocturnal cough 32.6 vs. 34.9% ($p < 0.01$); exercise wheezing 23.6 vs. 23.0% ($p > 0.05$) and awake with wheezing 11.8 vs. 11.2% ($p > 0.05$). Similar things were observed with the prevalence of current symptoms of rhinitis and eczema. In Brazil, there was a small but significant mean decrease in the prevalence of two asthma-related symptoms, wheezing and nocturnal cough, though this trend was not consistent in the surveyed cities. The prevalence of asthma symptoms in Brazil, despite its mean trend to a decrease, is still one of the highest in Latin America.

Keywords: asthma, eczema, epidemiology, prevalence, rhinitis

Introduction

Although asthma is the most common chronic disease in childhood, only recently has the global information on its prevalence, which includes developed and developing areas of the world, become available [1, 2]. A main finding has been the wide variation in the prevalence of asthma, rhinitis and eczema among children and adults from different places in the world, even between cities in same countries, suggesting that distinct environmental factors play a role as the determinant of such observed variability [2, 3].

Recently, the International Study of Asthma and Allergies in Childhood (ISAAC) has provided, for the first time, data on symptoms prevalence of asthma and allergies in several developing regions of the world [1, 2]. In Latin America, some countries as Costa Rica, Peru and Brazil had the highest prevalence in the continent and were among the top eight of the world [4, 5]. It was also clear from ISAAC Phase 1 data that the wide variation in prevalence observed between countries was present within countries also [1, 2, 4]. In Brazil, the prevalence of symptoms of asthma, rhinitis and eczema ranged from 2.3 to 46.9%, 11.3 to 68.2% and 0.2 to 14.0%, respectively [6–8].

Although several studies have shown increase in the prevalence of asthma and other allergic diseases in the last 25 years in developed countries [9–14],

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it was not everywhere [15]. In contrast, there is very little information on the temporal trends of respiratory and allergic symptoms in developing areas of the world where prevalence rates and temporal trends may be determined by factors different from those reported in developed nations [5, 16–19].

This study describes the changes in the prevalence of asthma, rhinitis, atopic eczema and related symptoms occurred in a 7-year interval in five large Brazilian cities.

Subjects and Methods

Data on the prevalence of symptoms related to asthma, allergic rhinitis and atopic eczema among schoolchildren aged 13–14 years, living in five Brazilian cities that participated in ISAAC Phases 1 (1994–95) and 3 (2001–03), were compared. The cities and the number of children studied were as follows: Recife (Pernambuco, northeast, Phase 1 [1994], $n=3086$ and Phase 3 [2002], $n=2865$); Salvador (Bahia, northeast, Phase 1 [1995], $n=3119$ and Phase 3 [2002], $n=3022$); São Paulo (São Paulo, southeast, Phase 1 [1995], $n=3008$ and Phase 3 [2002], $n=3161$); Curitiba (Paraná, south, Phase 1 [1995], $n=3008$ and Phase 3 [2001], $n=3628$) and Porto Alegre (Rio Grande do Sul, south, Phase 1 [1994], $n=3198$ and Phase 3 [2003], $n=3008$) (Fig. 1).

The methodology for ISAAC Phases 1 and 3 has been extensively described elsewhere [20–23]. Briefly, the participating schoolchildren aged 13–14 years were randomly selected from schools, according to data given by the respective Education Secretary, for each phase of the study at each city. During Phase 3, researchers were oriented to apply the ISAAC written questionnaire (WQ) in the same schools participating in Phase 1. The WQ had been previously translated to Portuguese (Brazilian culture), translated back to English and validated [24–26].

The cumulative and current (last 12 months) prevalence of symptoms of asthma, rhinitis and eczema were obtained from the children who responded positively to the questions related to each of the mentioned conditions. The questions on 'ever' asthma, rhinitis or eczema were considered as diagnostic labels [20–23].

Phase 1 and Phase 3 data were entered manually into a database (Epi-Info) using a double-entry method. To check the significance of differences between proportions in the two surveys, the chi-square test was performed. Odds ratio (OR) with 95% confidence interval (CI) was also calculated using Phase 1 as the base.

To express changes observed in Phase 3 when compared with Phase 1 in a selected number of variables, a relative percentage was calculated as

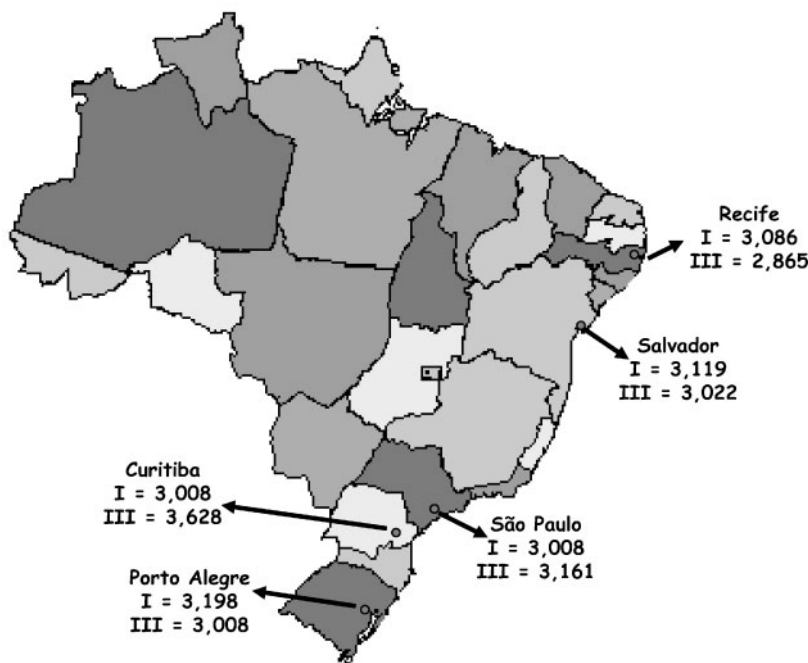


FIG. 1. Brazilian's ISAAC centers.

follows: $[(\text{Phase 3 prevalence} - \text{Phase 1 prevalence}) / \text{Phase 1 prevalence}] \times 100$. The significance of the changes was tested using the OR and its 95%CI. A P -value <0.05 was considered statistically significant.

The study was approved by local Ethical Committees and full informed consent for participation was obtained from parents or guardians.

Results

The return of filled ISAAC WQ varied from 93 to 98% in both phases. The number of participating children and the figures on prevalence of symptoms of asthma, and prevalence OR between Phases 1 and 3 from the five cities are shown in Table 1. There was not a uniform pattern towards a decrease or an increase in the prevalence of symptoms related to asthma, as to rhinitis and eczema (Table 2) among participating centers. Also, the decrease or increase in the prevalence of symptoms of asthma, rhinitis and eczema within each center was not consistent (Tables 1 and 2).

Asthma symptoms

In Porto Alegre, there was a more consistent trend to a decrease in several of the asthma-related symptoms, except for 'asthma ever' and 'severe wheezing limiting speech' (Table 1; Fig. 2A–D). With respect to the prevalence of 'wheeze in the last year' in all centers, except in Recife and Curitiba, there was a significant reduction. The same was observed considering all centers together (Brazil) (Table 1, Fig. 2A).

Considering Brazil, there was a significant mean relative percentage decrease in the prevalence of current wheezing of 12.3% (Table 1, Fig. 2A).

The prevalence of 'wheeze disturbs sleep' significantly increased in Recife and Salvador and decreased in the other centers (Table 1, Fig. 2B). The prevalence of 'severe wheezing limiting speech' increased in Recife and decreased in São Paulo and Curitiba (Table 1, Fig. 2C). There was a significant reduction in the prevalence of physician-diagnosed asthma (asthma ever) in Recife but not in the other cities (Table 1, Fig. 2D).

On an average, in Brazil there was a non uniform decrease on the mean prevalence of asthma symptoms between Phases 1 and 3, except for nocturnal cough that increased (Table 1).

Rhinitis symptoms

The prevalence of 'rhinitis in the last year' significantly increased in Recife and Curitiba and decreased in São Paulo and Porto Alegre (Table 2, Fig. 3A).

There was a significant increase in the prevalence of 'rhinitis in the last year with itchy-watery eyes' (rhinoconjunctivitis in the last year) in Recife and Curitiba (Table 2, Fig. 3B) and the prevalence of 'physician-diagnosis of rhinitis' increased

significantly in Porto Alegre and decreased in Recife and Curitiba (Table 2). Considering all data, we observed a significant increase in the 'physician-diagnosed rhinitis' in Brazil (Table 2) and again the pattern for this increase was nonhomogeneous among participating centers.

Eczema symptoms

The prevalence of 'rash in the last 12 months' decreased significantly in Salvador and Curitiba while the prevalence of 'atopic eczema' decreased significantly only in Salvador (Table 2, Fig. 3C and D). There was a significant increase in the prevalence of 'severe eczema' in Recife and Salvador, and a significant decrease was observed in Curitiba. The analysis of total data shows that, in Brazil, there was a significant decrease in 'rash in the last 12 months' and 'atopic eczema' (Table 2, Fig. 3C and D), and a significant increase in 'severe eczema' (Table 2).

Discussion

Despite evidence on the sustained and important increase in the prevalence of symptoms of asthma, rhinitis and eczema in developed countries, very little is known about the trends of these diseases in developing regions [16–19]. The possibility to compare data on the prevalence of symptoms of asthma, rhinitis and eczema, obtained by ISAAC in its Phases 1 and 3 [14, 15, 18, 19, 27], allows the pattern of changes in different regions of the world to be studied.

This study shows that in Brazil, there was an overall decrease in the mean prevalence of 'wheeze ever' and 'wheeze in the last 12 months', but not in 'asthma ever' 'nocturnal wheezing', 'severe wheezing limiting speech' and 'wheezing with exercise'. The exception was the prevalence of nocturnal dry cough that showed a significant increase.

However, when analyzing the prevalence of asthma-related symptoms in each of the five centers surveyed, it was evident that they clearly differed in the magnitude and direction of prevalence changes and no specific or consistent trend was apparent.

It is worth mentioning that the figures of prevalence of asthma-related symptoms in Phase 3 was quite close to that reported in Phase 1: those centers with higher and lower prevalence in Phase 1 remains the ones with higher and lower prevalence, respectively, in Phase 3. This observation suggests that factors involved in determining the prevalence in the centers analyzed may have not changed over the time elapsed between the two phases. Less likely, the time employed to contrast the prevalence between the two phases may have not been enough to identify changes.

TABLE 1
Prevalence of asthma-self-reported symptoms (%), and prevalence odds ratios (OR; 95% confidence interval) between ISACC Phase 1 (base, I) and ISAAC Phase 3 (III) among 13–14-year-old schoolchildren from different cities in Brazil

Question	Recife		Salvador		São Paulo		Curitiba		Porto Alegre		Total	
	I (n = 3086)	III (n = 2865)	I (n = 3119)	III (n = 3022)	I (n = 3008)	III (n = 3161)	I (n = 3008)	III (n = 3628)	I (n = 3198)	III (N = 3008)	I (n = 15 419)	III (n = 15 684)
Wheeze ever	39.0 0.95 (0.86–1.06)	37.8	44.4 1.09 (0.99–1.21)	46.6	45.4 0.97 (0.88–1.07)	44.6	40.4 1.01 (0.92–1.12)	40.7	46.9* 0.53 (0.48–0.59)**	36.2	43.3* 0.92 (0.88–0.96)**	41.2
Wheeze last 12 months	19.7 0.96 (0.85–1.10)	19.1	27.1* 0.88 (0.78–0.99)**	24.6	23.3* 0.76 (0.67–0.86)**	18.7	18.4 1.04 (0.91–1.17)	18.9	24.7* 0.68 (0.60–0.77)**	18.2	22.7* 0.85 (0.80–0.89)**	19.9
Wheezing disturbs sleep	13.1 1.33 (1.15–1.54)**	16.7*	9.6 1.37 (1.17–1.61)**	12.7*	12.0* 0.82 (0.70–0.97)**	10.1	9.1* 0.77 (0.65–0.93)**	7.1	15.1* 0.68 (0.58–0.78)**	10.7	11.8 0.94 (0.88–1.01)	11.2
Severe wheezing limiting speech	4.8 2.25 (1.84–2.77)**	10.2*	5.4 1.10 (0.89–1.37)	5.9	5.7* 0.49 (0.38–0.64)**	2.9	4.6* 0.67 (0.52–0.86)**	3.1	5.7 0.83 (0.67–1.04)	4.8	5.2 1.00 (0.91–1.11)	5.2
Asthma ever	21.0* 0.83 (0.73–0.94)**	18.0	12.6 1.10 (0.95–1.28)	13.7	10.0 1.05 (0.89–1.23)	10.4	8.6 1.08 (0.91–1.28)	9.2	21.9 0.99 (0.87–1.12)	21.1	14.9 0.99 (0.93–1.05)	14.7
Exercise wheeze	20.6 1.15 (1.02–1.30)**	23.0*	27.6 1.39 (1.25–1.55)**	34.6*	20.5* 0.79 (0.70–0.90)**	17.0	19.8 0.96 (0.85–1.08)	19.1	29.0* 0.71 (0.63–0.80)**	22.4	23.6 0.97 (0.92–1.02)	23.0
Night cough	31.0 1.32 (1.19–1.47)**	37.3*	29.7 1.24 (1.11–1.38)**	34.3*	33.0 1.01 (0.91–1.23)	33.3	30.1 1.23 (1.11–1.36)**	34.7*	39.1* 0.84 (0.76–0.93)**	35.0	32.6 1.11 (1.06–1.16)	34.9*

n, Number of schoolchildren.

chi-square: * $p < 0.05$.

OR (95% CI): ** $p < 0.05$.

TABLE 2

Prevalence of self-reported symptoms (%) of rhinitis and atopic eczema, and prevalence odds ratios (OR; 95% confidence interval) between ISACC Phase 1 (base, I) and ISAAC Phase 3 (III) among 13–14-year-old schoolchildren from different cities in Brazil

Question	Recife		Salvador		São Paulo		Curitiba		Porto Alegre		Total	
	I (n = 3086)	III (n = 2865)	I (n = 3119)	III (n = 3022)	I (n = 3008)	III (n = 3161)	I (n = 3008)	III (N = 3628)	I (n = 3198)	III (n = 3008)	I (n = 15 419)	III (n = 15 684)
Sneezing, runny, blocked nose without a cold ever	35.0	48.3*	58.2*	53.6	45.3*	41.4	40.8	48.2*	53.4*	44.5	46.7	47.2
	1.74 (1.56–1.93)**		0.83 (0.75–0.92)**		0.85 (0.77–0.94)**		1.35 (1.23–1.49)*		0.70 (0.63–0.71)**		1.02 (0.98–1.07)	
Sneezing, runny, blocked nose without a cold, last 12 months	24.1	35.8*	46.0	44.2	34.0*	27.4	29.8	39.2*	40.8*	32.1	35.0	34.5
	1.76 (1.57–1.97)*		0.93 (0.84–1.03)		0.73 (0.66–0.82)*		1.52 (1.37–1.68)*		0.69 (0.62–0.76)*		0.98 (0.93–1.03)	
Nasal symptoms plus itchy–watery eyes	11.3	14.5*	25.0	24.4	14.4	12.2	14.1	17.2*	17.6	15.9	16.5	16.8
	1.34 (1.14–1.55)**		0.97 (0.85–1.03)		0.82 (0.72–0.96)**		1.27 (1.11–1.45)**		0.88 (0.77–1.01)		1.02 (0.96–1.09)	
Rhinitis ever	18.3*	15.8	24.7	24.2	31.7	32.2	7.9*	2.8	24.4	42.1*	21.4	22.8*
	0.84 (0.72–0.96)**		0.97 (0.86–1.09)		1.02 (0.92–1.14)		0.34 (0.27–0.43)**		2.25 (2.02–2.51)**		1.09 (1.03–1.15)**	
Rash in the last year	11.4	12.2	3.7*	2.2	14.0	12.7	10.0*	4.1	12.6	11.7	10.3*	8.4
	1.08 (0.92–1.27)		0.59 (0.43–0.81)**		0.89 (0.77–1.03)		0.39 (0.32–0.47)**		0.92 (0.79–1.08)		0.80 (0.74–0.86)**	
Atopic eczema	4.6	5.0	9.2*	6.5	3.7	3.6	3.9	3.7	4.8	5.0	5.3*	4.5
	1.09 (0.86–1.38)		0.68 (0.57–0.83)**		0.98 (0.75–1.27)		0.95 (0.74–1.22)		1.04 (0.82–1.31)		0.84 (0.76–0.93)**	
Severe eczema	0.6	4.1*	0.2	0.6*	0.3	0.2	0.6*	0.2	0.9	0.5	0.5	1.0*
	6.93 (4.26–11.29)**		3.11 (1.23–7.84)**		0.64 (0.23–1.78)		0.32 (0.14–0.77)**		0.55 (0.29–1.02)		2.02 (1.53–2.65)**	

n, number of schoolchildren.

chi-square: * $p < 0.05$.

OR (95% CI): ** $p < 0.05$.

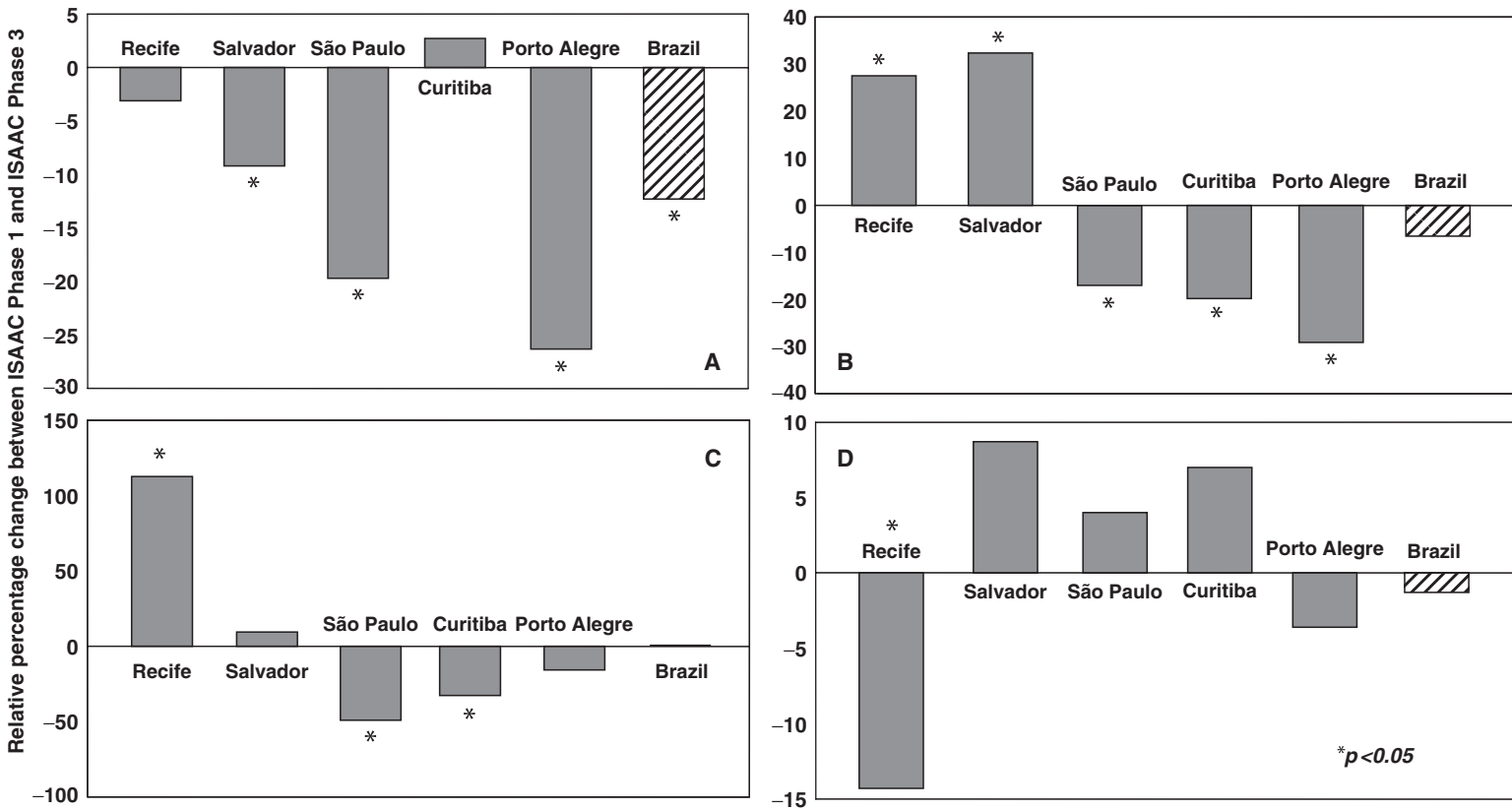


FIG. 2. Relative percentage change in the prevalence of wheezing in the last 12 months (A), wheezing disturbs sleep in the last 12 months (B), severe wheezing limiting speech in the last 12 months (C), and asthma ever (D) between ISAAC Phase 1 and Phase 3 in 13-14-year-old schoolchildren from different cities in Brazil.

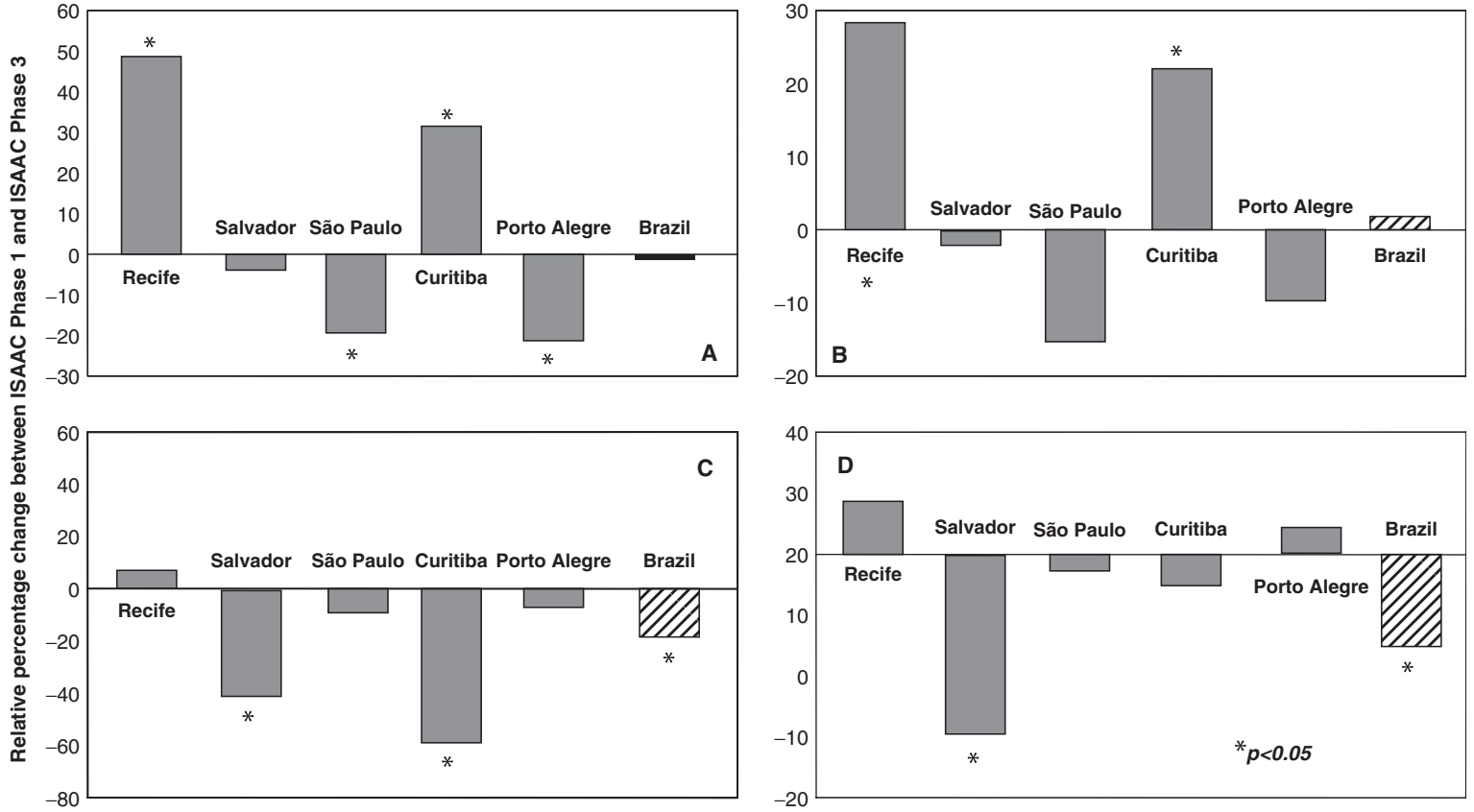


FIG. 3. Relative percentage change in the prevalence of sneezing without a cold in the last 12 months (A), nasal symptoms plus itchy-watery eyes in the last 12 months (B), rash in the last 12 months (C), and atopic eczema (D) between ISAAC Phase 1 and Phase 3 in 13-14-year-old schoolchildren from different cities in Brazil.

Studies with ISAAC method in children have shown an increasing in the prevalence of current wheezing, asthma-related symptoms and in physician-diagnosed asthma [5, 14, 18]. Lee *et al.*, [19] in China, did not report on changes in the prevalence of current wheezing and physician-diagnosed asthma but on an increase in severe asthma. On the other hand, Robertson, *et al.* [12] observed a decrease in the prevalence of current asthma (from 27.2% in 1993 to 20.0% in 2002), associated with a reduction in the consumption of asthma drugs, the visits to emergency department for asthma and hospitalizations due to asthma in 6–7 year-old Australian school-children, which could be representing a true decrease in asthma prevalence in Australia, one of the countries with highest prevalence of asthma in the world. Similar results were observed by others [26–30].

The prevalence of current rhinitis remained stable in Brazil although it had clearly increased in Recife and Curitiba and decreased in São Paulo and Porto Alegre, showing again a nonhomogeneous trend of prevalence in the five cities. Lee, *et al.* [19] observed a significant reduction in the prevalence of current rhinitis (from 37.4% in 1995 to 35.1% in 2001) as in rhinoconjunctivitis (from 17.2 to 13.6%). Other authors did not report on changes in the prevalence of allergic rhinoconjunctivitis [15, 18, 30]. On the other hand, Maziak *et al.* [14] observed a significant increase in the prevalence of nasal symptoms in the last year: from 12.5% in 1994–95 to 16.3% in 1999–2000. Selnes *et al.* [27] found a significant increase in the prevalence of allergic rhinoconjunctivitis in three cross-sectional questionnaire-based studies from 1985 to 2000: 16.5 to 29.6%.

In comparison with Phase 1 results, we observed a significant decrease in the prevalence of 'rash in the last 12 months' in Salvador and Curitiba, and in Brazil, in an average from 10.3 to 8.4%. The same was observed regarding prevalence of atopic eczema (from 5.3 to 4.5%), although an increase in its severity occurred. These data are contrary to others showing increase in the prevalence of reported eczema [12, 14, 20, 26] and in flexural eczema [14, 20, 28]. Lee *et al.* [19] observed a significant reduction in the prevalence of atopic eczema.

Based on our data, there was not a characteristic evolutionary pattern of these diseases that allowed us to identify the possible causes involved in the observed changes. The variation towards a decrease or increase in prevalence of the symptoms of asthma, rhinitis and eczema found between and within centers, suggests that differences in environmental exposures may be the most likely explanation.

Considering the maintenance of the figures of asthma ever (diagnostic label) in all centers, except

Recife, occasional improvement or worsen in making diagnosis of the disease and the actual knowledge of the patient on his/her symptoms should be also considered for interpretation.

The wide variation found in the prevalence of symptoms of asthma, rhinitis and eczema, reported by ISAAC Phase 1, which occurred between and within countries throughout the world would reinforce that factors other than genetics, cultural or medical modalities, are playing a major role as determinants for the variability of trends in our centers, and probably in others with a similar or a lower degree of development.

All centers participating in this study are state capitals and two of them are coastal cities (Recife and Salvador) that not only have a low level of atmospheric pollution but also have high proportion of people living in low socioeconomic conditions. We think that the high prevalence of these diseases found in these two cities may be more related with the environmental exposures associated to low socioeconomic conditions than racial or genetic factors.

In both phases of the ISAAC study, only in Recife the prevalence of 'wheezing in the last year' was quite similar to doctor-diagnosed asthma (asthma ever). Although we do not have a definitive explanation for this observation, the high prevalence of symptoms may be reflecting a true high prevalence and severity of disease that should result in a higher demand for the medical care due to asthma. Under these circumstances, the diagnosis of asthma should be easily transmitted by physician and health personnel to parents and children.

Excepting Porto Alegre and Recife, in the other centers, the prevalence of current wheezing almost doubled that of doctor-diagnosed asthma, suggesting that misdiagnosing and also differences in medical/patient, awareness of asthma might be some of the possible causes.

In conclusion, in Brazil, although the mean trend for asthma symptoms showed a mild but significant trend to a decrease between Phases 1 and 3, it was not consistently observed in each of the five participant centers. The latter also occurred for rhinitis and eczema where the time trend in prevalence of nasal and skin symptoms, or disease labels, was not consistent among centers.

The different trends in the prevalence of symptoms of asthma, rhinitis and eczema found among participating centers may have been mainly determined by different environmental exposures related with socioeconomic conditions of the surveyed populations. The prevalence of asthma symptoms in Brazil, despite its mean trend to a decrease, is still one of the highest in Latin America.

References

1. ISAAC Steering Committee. Worldwide variations in the prevalence of asthma symptoms: the International Study of Asthma and Allergies in Childhood (ISAAC). *Eur Respir J* 1998;12:315–35.
2. Asher MI, Barry D, Clayton T, *et al.* International Study of Asthma and Allergies in Childhood (ISAAC) Phase One – The burden of symptoms of asthma, allergic rhinoconjunctivitis and atopic eczema in children and adolescents in six New Zealand centers: ISAAC Phase One. *N Z Med J* 2001;114:114–20.
3. Chinn S, Jarvis D, Burney P, *et al.* Increase in diagnosed asthma but not in symptoms in the European Community Respiratory Health Survey. *Thorax* 2004;59:646–51.
4. Mallol J, Solé D, Asher I, *et al.* Prevalence of asthma symptoms in Latin America: the International Study of Asthma and Allergies in Childhood (ISAAC). *Pediatr Pulmonol* 2000;30:439–44.
5. Soto-Quiros ME, Soto-Martinez M, Hanson LA. Epidemiological studies of the very high prevalence of asthma and related symptoms among school children in Costa Rica from 1989 to 1998. *Pediatr Allergy Immunol* 2002;13:342–9.
6. Solé D, Yamada E, Vana AT, *et al.* International Study of Asthma and Allergies in Childhood (ISAAC): prevalence of asthma and asthma-related symptoms among Brazilian schoolchildren. *J Invest Allergol Clin Immunol* 2001;11:123–8.
7. Solé D, Camelo-Nunes IC, Vana AT, *et al.* Prevalence of rhinitis and related-symptoms in schoolchildren from different cities in Brazil. *Allergol Immunopathol (Madr)* 2004;32:7–12.
8. Yamada E, Vanna AT, Naspitz CK, *et al.* International Study of Asthma and Allergies in Childhood (ISAAC): validation of the written questionnaire (eczema component) and prevalence of atopic eczema among Brazilian children. *J Invest Allergol Clin Immunol* 2002;12:34–41.
9. Burr ML, Butland BK, King S, *et al.* Changes in asthma prevalence: two surveys 15 years apart. *Arch Dis Child* 1989;64:1452–6.
10. Barraclough R, Devereux G, Hendrick DJ, *et al.* Apparent but not real increase in asthma prevalence during the 1990s. *Eur Respir J* 2002;20:826–33.
11. Devenny A, Wassall H, Ninan T, *et al.* Respiratory symptoms and atopy in children in Aberdeen: questionnaire studies of a defined school population repeated over 35 years. *Br Med J* 2004;329:489–90.
12. Robertson CF, Roberts MF, Kappers JH. Asthma prevalence in Melbourne schoolchildren: have we reached the peak? *Med J Aust* 2004;180:273–6.
13. Verlato G, Corsico A, Villani S, *et al.* Is the prevalence of adult asthma and allergic rhinitis still increasing? Results of an Italian study. *J Allergy Clin Immunol* 2003;111:1232–8.
14. Maziak W, Behrens T, Brasky TM, *et al.* Are asthma and allergies in children and adolescents increasing? Results from ISAAC phase I and III surveys in Münster, Germany. *Allergy* 2003;58:572–9.
15. Braun-Fahrlander C, Gassner M, Grize L, *et al.* No further increase in asthma, hay fever and atopic sensitisation in adolescents living in Switzerland. *Eur Respir J* 2004;23:407–13.
16. Villarreal AB, Aguirre LHS, Rojo MMT, *et al.* Risk factors for asthma in school children from Ciudad Juarez, Chihuahua. *J Asthma* 2003;40:413–423.
17. Chatkin MN, Menezes AM, Victora CG, *et al.* High prevalence of asthma in preschool children in Southern Brazil: a population-based study. *Pediatr Pulmonol* 2003;35:296–301.
18. Wang XS, Tan TN, Shek LP, *et al.* The prevalence of asthma and allergies in Singapore; data from two ISAAC surveys seven years apart. *Arch Dis Child* 2004;89:423–6.
19. Lee S-L, Wong W, Lan Y-L. Increasing prevalence of allergic rhinitis but not asthma among children in Hong Kong from 1995 to 2001 (Phase 3 International Study of Asthma and Allergies in Childhood). *Pediatr Allergy Immunol* 2004;15:72–8.
20. Asher MI, Keil U, Anderson HR, *et al.* International study of asthma and allergies in childhood (ISAAC): rationale and methods. *Eur Respir J* 1995;8:483–91.
21. Strachan D, Sibbald B, Weiland S, *et al.* Worldwide variations in prevalence of symptoms of allergic rhinoconjunctivitis in children: the International Study of Asthma and Allergies in Childhood (ISAAC). *Pediatr Allergy Immunol* 1997;8:161–76.
22. Williams H, Robertson C, Stewart A, *et al.* Worldwide variations in the prevalence of symptoms of atopic eczema in the international study of asthma and allergies in childhood. *J Allergy Clin Immunol* 1999;103:125–38.
23. Ellwood P, Asher MI, Beasley R, *et al.* The International Study of Asthma and Allergies in Childhood (ISAAC): Phase Three rationale and methods. *Int J Tuberc Lung Dis* 2005;9:10–16.
24. Solé D, Vanna AT, Yamada E, *et al.* International Study of Asthma and Allergies in Childhood (ISAAC) written questionnaire: validation of the asthma component among Brazilian children. *J Invest Allergol Clin Immunol* 1998;8:376–82.
25. Vanna AT, Yamada E, Arruda LK, *et al.* International Study of Asthma and Allergies in Childhood: validation of the rhinitis symptom questionnaire and prevalence of rhinitis in schoolchildren in São Paulo, Brazil. *Pediatr Allergy Immunol* 2001;12:95–101.
26. Yamada E, Vanna AT, Naspitz CK, *et al.* International Study of Asthma and Allergies in Childhood (ISAAC): validation of the written questionnaire (eczema component) and prevalence of atopic eczema among Brazilian children. *J Invest Allergol Clin Immunol* 2002;12:34–41.
27. Selnes A, Nystad W, Bolle R, *et al.* Diverging prevalence trends of atopic disorders in Norwegian children. Results from three cross-sectional studies. *Allergy* 2005;60:894–9.
28. Garcia-Marcos L, Quiros AB, Hernandez GG, *et al.* Stabilization of asthma prevalence among adolescents and increase among schoolchildren (ISAAC phases I and III) in Spain. *Allergy* 2004;59:1301–7.
29. Wong GW, Leung TF, Ko FW, *et al.* Declining asthma prevalence in Hong Kong Chinese schoolchildren. *Clin Exp Allergy* 2004;34:1550–5.
30. Quah BS, Wan-Pauzi I, Ariffin N, *et al.* Prevalence of asthma, eczema and allergic rhinitis: two surveys, 6 years apart, in Kota Bharu, Malaysia. *Respirology* 2005;10:244–9.