

# Asthma and Rhinitis in South America: How Different They are From Other Parts of the World

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Asthma and rhinitis epidemiology has wide variations around the world. The aim of this review was to verify the prevalence of asthma and rhinitis in South America and report differences from other regions of the world. We reviewed studies with International Study of Asthma and Allergies in Childhood (ISAAC) methodology in South America, Phases I and III. In South America the ISAAC Phase I ranked four countries among top ten in prevalence of asthma and three countries among top ten in prevalence of rhinoconjunctivitis. ISAAC Phase III showed little changes in asthma and rhinitis prevalence in South American countries. The prevalence increases of asthma and rhinitis in South American centers indicate that the burden of both is continuing to rise, but the differences in prevalence are lessening.

**Key Words:** Asthma; epidemiology; rhinitis

## INTRODUCTION

The occurrence of asthma and allergies, as well as their causes, can be studied at many different levels such as in populations, individuals, organs, tissues or cells. All of these approaches are potentially useful, and individual researchers will focus on different levels of analysis depending on their training, areas of interest, and availability of funding.<sup>1</sup>

Asher and co-workers founded the International Study of Asthma and Allergies in Childhood (ISAAC). The ISAAC is a unique worldwide epidemiological research programme established in 1991 to investigate asthma, rhinitis and eczema in children due to considerable concern that these conditions were increasing in western and developing countries, and that the causes of this increase were unknown.<sup>2</sup>

ISAAC was created from a merging of two multinational collaborative projects each investigating variations in childhood asthma at the population level. These were initiated from Auckland, New Zealand to conduct an international comparative study of asthma severity, and an initiative from Bochum, Germany to conduct an international study to monitor time trends and determinants of the prevalence of asthma and allergies in children.<sup>2</sup>

By the time ISAAC was conceived, in the early 1990s, most previous research had looked at the reasons why some individuals develop asthma and allergic conditions such as allergic

rhinitis and eczema. A major risk factor was a family history of atopic disease, but various environmental factors had been also considered important in the expression of disease. Such studies within populations had shed little light on the reasons why the occurrence of atopic disease varies from population to population.<sup>2</sup>

Factors affecting the prevalence of disease at a population level may be different to those that determine which individuals within a population are at greatest risk. In addition, the relationship between the three atopic conditions may be different among populations. It was therefore considered likely that “ecological” (between-population) analyses might reveal further important determinants of asthma, allergic rhinitis and eczema. There was also widespread concern that these conditions were increasing in both developed and developing countries, but there was a lack of information on the burden of allergic diseases in many parts of the world.<sup>2</sup>

ISAAC Phase One was an international multi-center cross-sectional study involving two age groups of school children, 13-14 year olds (adolescents) and 6-7 year olds (children). Schools

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were randomly selected from a defined geographical area. Written questionnaires on asthma, rhinitis and eczema symptoms (translated from English) were completed by the adolescents at school, and at home by parents of the children. An asthma symptoms video questionnaire for the adolescents was optional.<sup>3</sup>

ISAAC Phase Three, a repetition of Phase One after an interval of at least five years, examined variations in time trends of childhood asthma, rhinoconjunctivitis and eczema around the world, and expanded the world maps of these conditions. Additional questions on risk factors were included in an "environmental questionnaire."<sup>4</sup> ISAAC Phase Three surveyed about 1,200,000 children from 233 centers in 98 countries, involving almost 800,000 children aged 13-14 years and almost 400,000 aged 6-7 years. Of the 54 languages used in Phase Three, English was the most common (21%) followed by Spanish (20%), Portuguese (11%), Arabic (7%), Italian (6%), French (5%) and Chinese (4%). The number of participating centres per Region ranged from 7 in North America to 56 in Latin America.

In more than twenty years, ISAAC involved next to two million children, 306 research centres in 105 countries, in 53 different languages, resulting in more than 500 publications, and of course, claimed a place in the Guinness Book of the World Records.<sup>2</sup>

### ASTHMA IN ISAAC PHASE I AND III

ISAAC Phase One used core questionnaire designed to assess the prevalence and severity of asthma and allergic disease in defined populations. In the 13-14 year age group, 155 centres from 56 countries participated, with a total of 463,801 children. The video questionnaire was completed in 99 collaborating centres in 42 countries, with a total of 304,796 children. For the 6-7 years old there were 91 collaborating centres in 38 countries, with a total of 257,800 participating children.<sup>5-7</sup>

The highest prevalence was about 20 times higher than the lowest prevalence (range 1.6-36.8%), with an eight-fold variation between the 10th and 90th percentiles (3.9-30.6%).<sup>5-7</sup>

In South America ten centres from five countries studied 27,182 children aged 6-7 years old and 43,362 adolescents aged 13-14 years old from fourteen centres in six countries. The core symptoms of asthma and rhinoconjunctivitis based on the 12-month provided period prevalence (current prevalence) for 6-7 and 13-14 year olds.<sup>8</sup>

There were significant differences in the current prevalence of respiratory symptoms indicative of asthma between countries in the region and also between centers in the same country, with up to twofold and fourfold variation in prevalence of current wheezing in children and adolescents, respectively. There was a trend for asthma prevalence to be lower in centers located at the south latitudes (Punta Arenas, Chile and Buenos Aires, Argentina) with higher rates at tropical latitudes (Lima, Peru and

Recife and Salvador, Brazil); however, these findings were not always consistent. No significant difference for asthma symptoms was found between boys and girls.<sup>8</sup>

The prevalence of respiratory symptoms related to asthma in children from South America was high and quite similar to that reported from industrialized countries. There was significant variability in the prevalence of asthma between participating centers, with a trend toward higher figures in centers with a tropical climate. Factors known to be protective against asthma, such as a higher number of children per family, a higher number of acute viral respiratory infections and gastrointestinal parasites, and poor hygiene, do not seem to play a protective role in this region. Conversely, these factors seem to act as risk factors for asthma and suggest that the socioeconomic status of populations is playing a major role in the high prevalence of asthma symptoms.<sup>8</sup>

Five to 10 years later the survey was repeated as ISAAC Phase III. For children aged 6-7 years there were 91 collaborating centres in 38 countries with a total of 257,800 participating children. Of centres that participated in Phase I, 106 centres in 56 countries completed the Phase III survey and met the requirements for analysis, with a total of 304,679 participating children in the 13-14 year age group (overall response rate 91%); 54 centres in 32 countries (a total of 167,513 children) also completed the video questionnaires in this age group. Sixty-six centres in 37 countries, a total of 193,404 children completed the survey and met the requirements for analysis in the 6-7 year age group. Four of the centres had surveyed children aged 6-7 year: totalling 110 centres (in either age group) in 58 countries. The mean symptom prevalence of current wheeze in the last 12 months changed slightly from 13.2% to 13.7% in the 13-14 year age group (mean increase of 0.06% per year) and from 11.1% to 11.6% in the 6-7 year age group (mean increase of 0.13% per year).<sup>9,10</sup> There was also little change in the mean symptom prevalence of severe asthma or the symptom prevalence with the asthma video questionnaire. However, the time trends in asthma symptom prevalence showed different regional patterns. In Western Europe, current wheeze decreased by 0.07% per year in children aged 13-14 years but increased by 0.20% per year in children aged 6-7 years. The corresponding findings per year for the other regions in children aged 13-14 years and 6-7 years, respectively, were: Oceania (20.39% and 20.21%); Latin America (+0.32% and +0.07%); Northern and Eastern Europe (+0.26% and +0.05%); Africa (+0.16% and +0.10%); North America (+0.12% and +0.32%); Eastern Mediterranean (20.10% and +0.79%); Asia-Pacific (+0.07% and 20.06%); and the Indian subcontinent (+0.02% and +0.06%). There was particularly a marked reduction in current asthma symptom prevalence in English language countries (20.51% and 20.09%). Similar patterns were observed for symptoms of severe asthma. However, the percentage of children reported to have had asthma at some time in their lives increased by 0.28% per year in the 13-14 year age

group and by 0.18% per year in the 6-7 year age group.<sup>9,10</sup>

ISAAC Phase Three in South America was successfully conducted in nine countries. There were 39 registered centers and all provided data for children 13-14 years old (n = 118,351). There was not significant difference in the mean prevalence of asthma symptoms between coastal and inland centers, or tropical and nontropical center locations. Southern latitude centers had significantly higher mean prevalence of current wheezing than northern latitude centers (Table 1).<sup>11</sup>

Correlation between the prevalence of asthma symptoms, socioeconomic status indicators (GNI and percentage of population under the line of poverty) were only possible at country level. Regarding all nine South American countries, no significant correlation was found between country-average prevalence of asthma symptoms and GNI and percentage of population under the line of poverty. In Brazil, in which the proportion of population with African descent was officially available, no significant association was found between the prevalence of current asthma symptoms and proportion of African descent.<sup>11</sup>

The prevalence of asthma symptoms in South American children is high and varies largely across the region, with most centers reporting prevalence over 15%. Country average socioeconomic indicators (such as GNI), tropical location, latitude, and altitude were unrelated to asthma symptom prevalence. The high prevalence of asthma symptoms found in children living in areas with low socioeconomic development challenges the protective role against asthma of low hygiene and poverty; on the contrary, in this region they would act as risk factors.<sup>11</sup>

The large variability of asthma symptoms found in South America cannot be explained by current theories that seem feasible in developed areas of the world, suggesting that complex ecological interactions, distinct for each place, are likely to be involved as main determinants for the wide variability of asthma prevalence in South America.<sup>11</sup>

### RHINITIS AND ISAAC PHASE I AND III

The ISAAC protocol was also developed to verify rhinitis and rhinoconjunctivitis epidemiology.<sup>2-4</sup> In the ISAAC Phase one, 12-month prevalences of symptoms demonstrated near 30-fold variation in the rate of allergic-rhinoconjunctivitis symptoms among centres (range 1.4-39.7%), with a four-fold variation seen between the 10th and 90th percentiles (4.9-21%). The grouping of centres with a high prevalence of allergic-rhinoconjunctivitis symptoms into specific regions was less well defined than for asthma; by contrast, the centres with the lowest symptom prevalences of allergic rhinoconjunctivitis were similar to those of asthma symptoms. Several centres with the highest rhinoconjunctivitis symptom prevalences were not represented among the centres with the highest asthma prevalences; therefore, the major risk factors for these related disorders may differ or may involve different latency periods and time trends.<sup>5,7</sup>

**Table 1.** Prevalence of current asthma in children and adolescents at South American centres

Country/Center	6-7-yr ISAAC I (%)	13-14-yr ISAAC I (%)	6-7-yr ISAAC III (%)	13-14-yr ISAAC III (%)
<b>Argentina</b>				
Buenos Aires <sup>8</sup>	15.4	9.9	-	-
Córdoba <sup>2,11</sup>	-	11.2	-	13.6
Neuquén <sup>2,11</sup>	-	-	14.9	10.2
Rosario City <sup>2,8,11</sup>	17.3	11.8	17.9	13.4
Salta <sup>11</sup>	-	-	-	12.5
<b>Bolivia</b>				
Santa Cruz <sup>11</sup>	-	-	-	13.5
<b>Brazil</b>				
Aracaju <sup>11,13</sup>	-	-	16.5	18.7
Belo Horizonte <sup>11,12</sup>	-	-	24.3	17.8
Brasília <sup>11,14</sup>	-	-	-	19.7
Caruaru <sup>11,13</sup>	-	-	-	17.9
Curitiba <sup>8,11-13,15-18</sup>	22.9	18.4	-	18.9
Feira de Santana <sup>11,12</sup>	-	-	20.7	21.5
Itabira <sup>8</sup>	16.1	9.6	-	-
Itajaí <sup>11,12</sup>	-	-	20.6	12.3
Maceió <sup>11-13</sup>	-	-	-	14.8
Manaus <sup>11,12</sup>	-	-	24.4	18.1
Nova Iguaçu <sup>11,12,19,20</sup>	-	-	26.3	11.8
Passo Fundo <sup>11,12,21</sup>	-	-	-	20.5
Porto Alegre <sup>8,11,12,17,18</sup>	23.5	24.7	-	18.2
Recife <sup>8,11-13,17,18,22,23</sup>	27.2	19.7	-	19.1
Rural Santa Maria <sup>11,12</sup>	-	-	-	15.3
Salvador <sup>8,11-13,17,18</sup>	-	27	17.2	24.6
Santa Maria <sup>11,12</sup>	-	-	-	16.7
Santo André <sup>11,12</sup>	-	-	23.9	23.2
São Paulo <sup>8,11,12,17,18,24,25</sup>	21.3	23.3	24.4	18.7
São Paulo West <sup>8,11,12,17,18,24,25</sup>	-	-	31.2	21.9
Uberlândia <sup>8</sup>	20.2	21.1	-	-
Vitória da Conquista <sup>11-13</sup>	-	-	24.3	30.5
<b>Chile</b>				
Calama <sup>11</sup>	-	-	-	11.1
Central Santiago <sup>2</sup>	16.5	11.7	-	-
Chiloe <sup>11</sup>	-	-	-	16.9
Punta Arenas <sup>8,11,26</sup>	17.1	6.8	17.6	13.6
South Santiago <sup>8,11,26</sup>	16.9	11.1	21.4	17
Valdivia <sup>8,11,26</sup>	20.5	11.5	14.7	16
<b>Colombia</b>				
Barranquilla <sup>2,11</sup>	-	-	15.2	13.8
Bogotá <sup>2,11,27</sup>	-	-	10	8.5
Caliz <sup>2,11</sup>	-	-	17.3	13.8
<b>Ecuador</b>				
Guayaquil <sup>11</sup>	-	-	-	15.5
Quito <sup>2,11</sup>	-	-	16.8	17.8
<b>Paraguay</b>				
Asunción <sup>8,11</sup>	-	19.4	-	20.9
<b>Peru</b>				
Lima <sup>8,11</sup>	26	-	-	19.6
<b>Uruguay</b>				
Montevideo <sup>8,11</sup>	18	19	-	17.9
Paysandú <sup>11</sup>	-	-	-	13.7
<b>Venezuela</b>				
Caracas <sup>11</sup>	-	-	20	15.4

"-" represents missing data or unpublished.

ISAAC, International Study of Asthma and Allergies in Childhood.

In the Phase I, the prevalence of rhinoconjunctivitis symptoms in South American centres varied from 10% in Chile to 35% in Paraguay, with three countries in the top 10 list of most prevalent worldwide.<sup>5</sup>

In Phase III of the 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-years apart in two age groups comprising 498,083 children. In the 13- to 14-year age group 106 centres in 56 countries participated, and in the 6- to 7-year age group 66 centres participated in 37 countries. A slight worldwide increase in rhinoconjunctivitis prevalence was observed, but the variation was 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 rhinoconjunctivitis prevalence of similar magnitude was only seen in four centres. The changes were less pronounced in the 6- to 7-year-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.<sup>9,28,29</sup> The prevalence of asthma in junior high school children increased over 5 years in Korea. However, in elementary school children, the prevalence of asthma symptoms decreased. The reasons for the different changes in prevalence in different geographical regions, including Korea, remain unclear, although different environmental factors might be involved in each region at a different time justifying new studies to evaluate the trends over time.<sup>30</sup>

In the Phase III of ISAAC, twenty centres involved 53,027 children and forty centres from nine countries evolved 118,351 adolescents, respectively. As observed previously in ISAAC Phase I, the prevalence of current rhinoconjunctivitis symptoms among South American children in Phase III remained high (18.5% for the adolescents and 12.7% for the 6-7-year-old children) and varied widely between centers in different countries and also within a same country. These rates were among the highest in the world. The prevalence of current rhinoconjunctivitis in adolescents varied 5-fold (from 8.9% in São Paulo West [Brazil] to 45.1% in Asuncion [Paraguay]) and 3.7-fold for the 6-7-year-old children (from 5.5% in Rosario City [Argentina] to 20.4% in Caracas [Venezuela]) (Table 2).<sup>31</sup>

Comparing these results to those obtained in Phase I, centers with higher prevalence of current rhinoconjunctivitis still maintained it high in Phase III, and Asuncion (Paraguay) was the center with the highest prevalence rate in both ISAAC's phases.

**Table 2.** Prevalence of current rhinoconjunctivitis in children and adolescents at South American centres

Country/Center	6-7-yr ISAAC I (%)	13-14-yr ISAAC I (%)	6-7-yr ISAAC III (%)	13-14-yr ISAAC III (%)
<b>Argentina</b>				
Buenos Aires <sup>2</sup>	9.9	21	-	-
Córdoba <sup>2</sup>	-	17.4	-	16.9
Neuquén <sup>28-30</sup>	-	-	8.9	14.8
Rosario City <sup>9,28-30</sup>	10.5	24.6	5.5	11.3
Salta <sup>9,28-30</sup>	-	-	-	20.9
<b>Bolivia</b>				
Santa Cruz <sup>9,28-30</sup>	-	-	-	22.4
<b>Brazil</b>				
Aracaju <sup>28-30,32</sup>	-	-	9.3	12.3
Belo Horizonte <sup>28-30,32</sup>	-	-	-	11.4
Brasília <sup>14,28-30,32</sup>	-	-	-	12.3
Caruaru <sup>28-30,32</sup>	-	-	-	12.3
Curitiba <sup>16,18,28-32</sup>	-	14.1	-	17
Feira de Santana <sup>28-30</sup>	-	-	-	13.9
Itabira <sup>28-31</sup>	-	-	-	-
Itajaí <sup>28-30</sup>	-	-	9.4	10.6
Maceió <sup>28-30</sup>	-	-	10.8	13.6
Manaus <sup>28-30</sup>	-	-	10.5	12.5
Nova Iguaçu <sup>28-30</sup>	-	-	11.6	12.1
Passo Fundo <sup>21,28-30,32</sup>	-	-	-	15.8
Porto Alegre <sup>2,18,28-32</sup>	10.6	17.6	-	14.2
Recife <sup>2,18,28-32</sup>	10.3	11.3	-	14.2
Rural Santa Maria <sup>28-30,32</sup>	-	-	-	7.8
Salvador <sup>2,18,28-32</sup>	-	25	16.7	21.1
Santa Maria <sup>28-30,32</sup>	-	-	-	10
Santo André <sup>28-30,32</sup>	-	-	13.2	13.8
São Paulo <sup>2,18,25,28-32</sup>	12.5	12.6	12	15.6
São Paulo West <sup>28-30</sup>	-	-	13.3	8.8
Uberlândia	-	-	-	-
Vitória da Conquista <sup>28-30</sup>	-	-	-	19.8
<b>Chile</b>				
Calama <sup>2,28-30</sup>	-	-	-	22.9
Central Santiago <sup>2,18,28-30</sup>	11.2	15.7	-	-
Chiloé <sup>2,28-30</sup>	-	-	-	19.1
Punta Arenas <sup>2,9,28-30</sup>	8.8	8.4	11.2	14.1
South Santiago <sup>2,9,28-30</sup>	11.2	15.7	13.7	26.3
Valdivia <sup>2,9,28-30</sup>	8	9.8	11.9	26.3
<b>Colombia</b>				
Barranquilla <sup>9,28-30</sup>	-	-	15.4	30
Bogotá <sup>9,28-30</sup>	-	-	15.6	22.3
Calí <sup>9,28-30</sup>	-	-	16.7	23.3
<b>Ecuador</b>				
Guayaquil <sup>9,28-30</sup>	-	-	-	23.9
Quito <sup>9,28-30</sup>	-	-	14.6	23.1
<b>Paraguay</b>				
Asunción <sup>2,9,28-30</sup>	-	34.5	-	45.1
<b>Peru</b>				
Lima <sup>2,9,28-30</sup>	-	19.3	-	18.7
<b>Uruguay</b>				
Montevideo <sup>2,9,28-30</sup>	6.6	16	-	10.6
Paysandú <sup>9,28-30</sup>	-	-	6.7	10.2
<b>Venezuela</b>				
Caracas <sup>9,28-30</sup>	-	-	20.4	24.9

"-" represents missing data or unpublished.

ISAAC, International Study of Asthma and Allergies in Childhood.

No correlation was observed for rhinitis symptoms prevalence with respect to latitude, altitude, humid/dry climate or other geographical aspects, suggesting that meteorological and geographic factors, individually, would not be able to explain the large variability of rhinitis prevalence found by both ISAAC phases in South America. Thus, centers located over 2,000 m altitude such as Bogota, Quito and Calama did not have consistently higher or lower prevalence rates when compared to centers located at the sea level. The same occurred for centers with equatorial humid climate (as Guayaquil, Ecuador and Manaus, Brazil) or with cold humid climate (Chiloe, Chile), both with quite similar prevalence rates of current rhinoconjunctivitis symptoms.<sup>31,32</sup>

Comparison of most important markers of country development (GNP, infant mortality rate, annual proportion of registered deaths under 5 years of age due to infectious diseases, percentage of children younger than 1 year of age immunized against: poliomyelitis; measles; diphtheria, tetanus, and pertussis; and tuberculosis, percentage of population with potable drinkable water service, percentage of population with sewage disposal services) and the prevalence of rhinitis-related symptoms did not show any significant correlation.<sup>31</sup>

The ethnic differences, which might be invoked to explain the variability of rhinitis symptoms prevalence in South America, are also unlikely to be a reasonable explanation. The prevalence of current rhinoconjunctivitis symptoms in some locations with a well-known high African genetic ancestry, some cities in Brazil was lower, where the most of the African South American ancestors live.<sup>32</sup>

## CONCLUSION

The current prevalence of asthma and rhinoconjunctivitis in South America was high, different from Korea for example, where the prevalence was lower.<sup>31,33</sup> The Hygiene Hypothesis fail to explain the considerably higher prevalence of allergic diseases in many South American countries as compared to rest of the world, and the difference seems to be more consistent with changes in environmental exposures other than hygiene. Specific environmental factors may be undoubtedly critical in explaining the different prevalence of allergic diseases but the exact nature of risk factors for allergic diseases and its symptoms has not been fully explored.<sup>30,31</sup>

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