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Original Article

Prevalence and Geographic Variations in Asthma Symptoms in Children and Adolescents in Galicia (Spain)☆

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ABSTRACT

Objectives: To determine the prevalence and geographic variations of the symptoms associated with asthma in Galician children and adolescents.
Population and methods: A cross-sectional epidemiological study following ISAAC (International Study of Asthma and Allergies in Childhood) methodology, and using a written questionnaire distributed in schools. The study sample included 10 371 6-7 year-old children and 10 372 13-14 year-old adolescents, all of them from Galician Health Areas. A logistic regression model was used to analyse geographic variations.
Results: In the 6-7 year-old group, *wheezing in the last 12 months* varied from 11.4% (Santiago) to 15.7% (Vigo) and in the adolescents varied from 8.8% (Ourense) to 18.8% (Vigo). The *distribution by gender* showed a predominant significance in 6-7 year-old males ($P < .001$), and near to be statistically significant in 13-14 year-old females ($P = .08$). The risk (odds ratio [OR]) of wheezing in the last 12 months in the area with highest prevalence in comparison with the area of lowest prevalence was 1.45 (95% Confidence Interval [CI], 1.12-1.88) for children and 2.39 (95% CI, 1.82-3.13) for adolescents. The *estimated prevalence* of asthma in the Autonomous Community of Galicia was 13.6% in younger children and 12.2% in adolescents.
Conclusions: The prevalence of wheezing in the last 12 months in the different areas of Galicia is *considerably higher* than the rest of Spanish ISAAC cities in the 6-7 years group and very similar in the 13-14 years group, except in Vigo where it is considerably higher. We found a clearly defined geographic pattern in the adolescent group, with higher prevalences in coastal areas than in the interior.

Prevalencia de síntomas de asma en los niños y adolescentes de la Comunidad Autónoma de Galicia (España) y sus variaciones geográficas

Palabras clave:
Asma
Prevalencia
Niño
Adolescente

RESUMEN

Objetivos: Determinar la prevalencia y variaciones geográficas de síntomas relacionados con asma en niños y adolescentes gallegos.
Población y métodos: Estudio transversal según la metodología ISAAC *(Internacional Study of Asthma and Allergies in Childhood)* mediante cuestionario escrito distribuido en el medio escolar. Se incluyeron 10.371 niños de 6-7 años y 10.372 adolescentes de 13-14 años de todas las Áreas Sanitarias de Galicia. Se analizaron las variaciones geográficas mediante un modelo de regresión logística.

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Resultados: Las sibilancias en los últimos 12 meses oscilaron en los pequeños, del 11,4 (Santiago) al 15,7% (Vigo) y en los adolescentes del 8,8 (Ourense) al 18,8% (Vigo). Según el género se observó una mayor frecuencia en varones de 6-7 años (p < 0,001) y con tendencia a la significación estadística en las chicas de 13-14 años (p = 0,08). El riesgo (*Odds ratio* [OR]) de sibilancias en los últimos 12 meses, en el área de mayor prevalencia con respecto a la de menor, fue 1,45 (intervalo de confianza [IC] del 95%: 1,12-1,88) en niños y 2,39 (IC 95%: 1,82-3,13) en adolescentes. La prevalencia de asma estimada para Galicia fue de 13,6% en niños y 12,2% en adolescentes.

Conclusiones: La prevalencia de sibilancias en los últimos 12 meses en las diferentes áreas gallegas es sensiblemente superior al resto de ciudades españolas participantes en el ISAAC en los pequeños, siendo muy similar en los adolescentes, salvo en Vigo donde es sensiblemente superior. Encontramos un patrón geográfico muy definido en los adolescentes, siendo mayores las prevalencias en la costa que en el interior.

Introduction

Asthma is the most frequent chronic pediatric disease in developed countries.[1] The study of its epidemiology is important in order to gauge it as a health problem and to know the factors that influence it. There have been many studies in this respect, with varying results. Comparisons amongst them are difficult due to the differences in methodology and populations studied. In this context, the ISAAC study came about in the 90's with the aim of optimizing the epidemiological analysis of asthma, rhinoconjunctivitis and atopic dermatitis.[2] In doing so, it introduced a standardized methodology, which has been validated and utilized in more than 280 centers in more than 100 countries with the objective of obtaining comparable data in multiple centers throughout the world.[3] In the results of ISAAC, major variations have been seen in the prevalence of the diseases studied among countries, regions and even nearby cities,[4,5] therefore the data obtained in one center cannot be extrapolated to the region. For example, in phase 3 in the case of wheezing in the last 12 months, worldwide variations were observed to be between 2.4 and 37.6% in children aged 6-7 and between 0.8 and 32.6% in those aged 13-14. In Spain, in phase 3, results were obtained between 7.1 and 12.9% in the younger children and between 7.1 and 15.3% in the older group. The important differences found, even between genetically-similar groups suggested that the environmental factors are the fundamental basis of these discrepancies.[6]

In Galicia, in northwestern Spain, there are only two studies published on asthma prevalence and both were done in A Coruña. The first, carried out in 1989 in an urban and rural population aged 4 to 18 using an adapted questionnaire from the *National Heart Lung and Blood Institute*, obtained an asthma prevalence of 10.8%.[7] In the second, done in 2003 in an urban population within the ISAAC framework, the prevalence of wheezing in the last 12 months reached 12.9% in children aged 6-7 and 15.2% in those aged 13-14, which are the highest levels in Spain.[4,8] As was mentioned before, these results cannot necessarily be extrapolated to the rest of Galicia, and even more so when taken into account that there are important environmental differences amongst the different areas of the province. The objective of this present study is to determine the prevalence of asthma symptoms in the chosen age groups in all the Health-Care Areas of Galicia that have not been previously studied, following the territorial division made by the health-care administration of our Autonomous Community. With the incorporation of the results recently obtained in A Coruña using the same methodology, we will analyze the differences between the areas and estimate the overall prevalence of asthma in Galicia as a whole. The use of the ISAAC methodology allows for the comparison of the results with those of other ISAAC centers in Spain and in other countries.

Population and Methods

Following the ISAAC[9] methodology, we carried out a cross-sectional, descriptive study through a population survey in the school setting in order to determine the prevalence of asthma symptoms in the population of children in the cities of Ferrol, Santiago, Pontevedra, Vigo, Ourense and Lugo. We also studied a representative group of the rural parts of all the Health-Care Areas in Galicia, according to the territorial distribution of the Consellería de Sanidade (Galician Health-Care Administration). For the estimation of the data corresponding to the entire Autonomous Community and for the comparisons between Areas, we also used the data of the city of A Coruña, obtained with an identical methodology.[4,8] The project was approved by the Ethics Committee for Clinical Research of Galicia and from the corresponding authorities.

The target population of the study was all those school children aged 6-7 and 13-14 of each area studied. At these ages, schooling is mandatory by law, thus it can be assumed that the schooling rate is quite close to 100%. Consequently, the data obtained are representative of the entire Galician population at these ages. Each school center was considered a unit of the study, and in each center all the children in the corresponding age groups participated in the analysis. The participating centers were either all those of each study area or, if not, a randomized selection of these centers. The ISAAC questionnaire, translated into Spanish, was used for each age group (Table 1). In the case of the younger children, it was filled out by their parents at home, while the group of older students filled out the survey themselves in the centers themselves.

Following the ISAAC[9] protocol, a minimum sample size of 1000 valid questionnaires was established for each age group and for each area studied in order to obtain the levels of prevalence, and to also detect the possible differences between the areas analyzed. For the rural group, we used a stratified sampling for each Health-Care Area, using proportional assignation in such a way that the number of children included in the sample of the rural area of each Health-Care Area was proportional to its size within the Galician population. In the previous study in A Coruña, there were around 3000 in each age group.

The intention was to obtain the prevalence data for each of the cities and a sample representative of the rural area, thus enabling a final estimation of the prevalence for the entire province. In the cities of Santiago, Vigo, Ourense and Lugo, the sample was limited to the corresponding urban areas in both age groups. In the city of Ferrol, the population in both age groups was insufficient to reach the desired sample size, taking into account the predicted participation according to the data of previous studies. Therefore, we also included the towns of Narón and Fene. Today, both suburbs have undergone recent booms in construction and are practically a prolongation of the city of Ferrol. This same situation was given in the

Table 1
ISAAC Asthma Symptom Questionnaire (6-7 Years/13-14 Years).

1. Has your child ever had wheezing or whistling in the chest at any time in the past?/Have you ever had wheezing or whistling in the chest at any time in the past?			
Yes	No		
2. Has your child had wheezing or whistling in the chest in the past 12 months?/Have you had wheezing or whistling in the chest in the past 12 months?			
Yes	No		
3. How many attacks of wheezing has your child had in the past 12 months?/How many attacks of wheezing have you had in the past 12 months?			
None	1 to 3	4 to 12	More than 12
4. In the past 12 months, how often, on average, has your child's sleep been disturbed due to wheezing?/In the past 12 months, how often, on average, has your sleep been disturbed due to wheezing?			
Never woken with wheezing	Less than one night per week	One or more nights per week	
5. In the past 12 months, has wheezing ever been severe enough to limit your child's speech to only one or two words at a time between breaths?/In the past 12 months, has wheezing ever been severe enough to limit your speech to only one or two words at a time between breaths?			
Yes	No		
6. Has your child ever had asthma?/Have you ever had asthma?			
Yes	No		
7. In the past 12 months, has your child's chest sounded wheezy during or after exercise?/In the past 12 months, has your chest sounded wheezy during or after exercise?			
Yes	No		
8. In the past 12 months, has your child had a dry cough at night, apart from a cough associated with a cold or chest infection?/In the past 12 months, have you had a dry cough at night, apart from a cough associated with a cold or chest infection?			
Yes	No		

case of Pontevedra, where the municipality of Marín was included, but only in the 6-7 year-old group. In the previous study of A Coruña, likewise and only in the younger age group, the towns of Culleredo and Oleiros were added.

In the group representative of the rural area, the entire population not included in the urban areas was considered. We randomized the schools in the rural parts of all the Galician Health-Care Areas, including the rural part of the area of A Coruña, thus completing the study of all the population of Galicia.

The fieldwork was developed in all the areas studied between the months of October 2006 and February 2007 (A Coruña, October – December 2003).

Statistical Analysis

For each age group, we determined the prevalence of asthma symptoms according to the geographic area and sex, together with the 95% confidence interval. The comparison between sexes was done by means of the chi-squared test, the estimation of Odds ratios (OR) and their 95% confidence interval. We adjusted multiple logistic regression models to determine the differences in the prevalence of asthma symptoms according to sex and geographic area for each age group. We took as a reference for the calculation of the OR the area with least prevalence and the female sex.

The prevalence of asthma was estimated in the Autonomous Community of Galicia, taking as a reference the values obtained of wheezing in the last 12 months in each area (parameter that better correlated with the prevalence of the disease in the validation studies[10]) and calculating the results of each area according to the population data of the municipal census of inhabitants as of January 1, 2006, stratifying by age groups and sex. The 95% confidence interval was obtained using the formula corresponding to a stratified sample.

The analysis was done with the SPSS and EPIDAT 3.1 programs for Windows. All the tests were carried out with a bilateral approach, and *P* values <.05 were considered significant.

Results

In the 6-7 year-old group, 284 centers were randomly selected, out of which 253 collaborated with 14 320 students. Of these, 3949 refused to participate, obtaining 10 371 valid questionnaires with a participation rate of 72.4%. In the 13-14 year-old group, 143 schools were randomly selected, out of which 123 collaborated, with a total of 12 289 students. Of these, 1917 children refused to participate, obtaining 10 372 valid questionnaires with a participation rate of 84.4%. Table 2 shows the percentages of participation according to age group and study areas.

The descriptive data about the prevalence of asthma symptoms are reflected in [Table 3] and [Table 4]. In the group of children aged 6-7, between 35.3% (Santiago) and 43.5% (Lugo) of the children presented *wheezing at some time*. Between 11.4% (Santiago) and 15.7% (Vigo) of those surveyed showed *wheezing in the last 12 months*, data that have a greater correlation with the current prevalence of asthma. As for the presence of *asthma at some time* which gives us information of the previous diagnosis of asthma, the positive response oscillated between 8.5% (Santiago) and 17.4% (Lugo). In the group of adolescents aged 13-14, between 16.2% (Ourense) and 31.4% (Vigo) of the children presented *wheezing at some time*. Between 8.8% (Ourense) and 18.8% (Vigo) of those surveyed presented *wheezing in the last 12 months*. Regarding the presence of *asthma at some time*, the positive response ranged between 11.4% (Ourense) and 21.4% (Vigo). The prevalences of *wheezing with exercise in the last 12 months* were higher for the adolescents than for the children. Although wheezing had interfered little with sleep during the previous year, the prevalence of nocturnal cough was high in both age groups, especially in the group of adolescents.

The comparative description according to gender for each of the questions is shown in Table 5 for the two age groups. In the 6-7 year old group, the males, in a statistically significant manner, respond affirmatively to the questions with greater frequency. In contrast, in the 13-14 year-old group, with the exception of the question *asthma at some time*, it is the female adolescents who respond affirmatively to the questions more frequently.

Table 2
Percentage of Participation According to Age Groups and Study Areas.

	Ages 6-7	Ages 13-14
Ferrol	74.8%	82.6%
A Coruña	73.8%	93.6%
Santiago	67.7%	68.5%
Lugo	67.5%	89.3%
Pontevedra	66.2%	81.6%
Vigo	86.4%	88.9%
Ourense	75.3%	91.2%
Rural	69.6%	75.6%
Galicia	72.4%	84.4%

Table 3
Prevalence of Asthma Symptoms in Children Aged 6-7.[a]

	Rural No.=1405 % (95% CI)	A Coruña[4,8] No.=3017 % (95% CI)	Ferrol No.=1131 % (95% CI)	Lugo No.=932 % (95% CI)	Orense No.=936 % (95% CI)	Pontevedra No.=966 % (95% CI)	Santiago No.=1,008 % (95% CI)	Vigo No.=976 % (95% CI)
Wheezing at some time	38.9 (36.3-41.5)	37.1 (35.4-38.7)	41.7 (38.8-44.6)	43.5 (40.2-46.7)	36.9 (33.7-40.0)	39.8 (36.6-42.9)	35.3 (32.3-38.3)	43.4 (40.3-46.6)
Recent wheezing[b]	13.2 (11.4-15.0)	12.9 (11.7-14.1)	15.3 (13.1-17.4)	15.2 (12.9-17.6)	12.7 (10.5-14.9)	12.8 (10.7-15.0)	11.4 (9.4-13.4)	15.7 (13.3-18.0)
Recent attack of wheezing								
From 1 to 3 attacks	10.0 (8.4-11.6)	9.5 (8.5-10.6)	11.0 (9.1-12.8)	11.7 (9.6-13.8)	9.5 (7.6-11.4)	9.6 (7.7-11.5)	9.4 (7.6-11.3)	11.3 (9.2-13.3)
From 4 to 12 attacks	2.3 (1.5-3.1)	2.9 (2.3-3.6)	2.9 (1.9-3.9)	2.4 (1.3-3.4)	2.2 (1.2-3.2)	2.8 (1.7-3.9)	1.5 (0.7-2.3)	3.9 (2.6-5.1)
More than 12 attacks	0.4 (0.1-0.8)	0.4 (0.1-0.6)	0.6 (0.1-1.1)	0.4 (0.1-1.1)	0.4 (0.1-1.1)	0.7 (0.1-1.3)	0.2 (0-0.7)	0.3 (0.1-0.9)
Awoken by recent wheezing								
Less than one night per week	4.7 (3.5-5.8)	5.5 (4.6-6.3)	6.5 (5.0-7.9)	6.1 (4.5-7.7)	5.3 (3.8-6.8)	5.6 (4.1-7.1)	5.2 (3.7-6.6)	6.3 (4.7-7.8)
One or more nights per week	2.3 (1.5-3.1)	1.4 (0.9-1.8)	1.7 (0.9-2.5)	1.8 (0.9-2.7)	1.3 (0.5-2.0)	2.1 (1.1-3.0)	0.9 (0.3-1.5)	2.2 (1.2-3.1)
Recent severe wheezing	1.6 (0.9-2.3)	2.1 (1.5-2.6)	2.2 (1.3-3.1)	2.5 (1.4-3.5)	1.5 (0.7-2.3)	2.6 (1.5-3.6)	1.0 (0.3-1.6)	3.0 (1.8-4.1)
Asthma at some time	10.5 (8.9-12.2)	13.7 (12.5-15.0)	13.6 (11.6-15.6)	17.4 (14.9-19.9)	8.8 (6.9-10.6)	9.3 (7.4-11.2)	8.5 (6.7-10.3)	15.2 (12.9-17.5)
Recent wheezing with exercise	6.3 (5.0-7.6)	6.0 (5.2-6.9)	8.7 (7.0-10.3)	6.9 (5.2-8.5)	5.2 (3.7-6.7)	5.5 (4.0-7.0)	4.9 (3.5-6.2)	7.6 (5.9-9.3)
Recent cough at night	21.9 (19.7-24.1)	23.6 (22.0-25.1)	22.8 (20.3-25.3)	21.8 (19.1-24.5)	20.7 (18.1-23.4)	23.3 (20.6-26.0)	18.9 (16.5-21.4)	23.4 (20.6-26.1)

[a] CI: confidence interval
[b] recent: in the last 12 months.

The multivariate logistic regression model of asthma symptoms analyzed the OR for both age groups, by geographical area and sex, taking as a reference the area of less prevalence and the female sex ([Table 6] and [Table 7]). The analysis was done for *wheezing in the last 12 months*, *asthma at some time* and *wheezing in the last 12 months with exercise*. The reference population areas, being those with less prevalence, were Santiago for these three questions in the group of small children, while in adolescents it was Ourense for the first two questions and Santiago for the third. The highest OR adjusted for geographical area for *wheezing in the last 12 months* corresponded with the children of Vigo, Ferrol and Lugo and the adolescents of Vigo, A Coruña, Ferrol and Pontevedra. Analogously,

Table 4
Prevalence of Asthma Symptoms in Adolescents Aged 13-14.[a]

	Rural No.=1238 % (95% CI)	A Coruña[4,8] No.=2981 % (95% CI)	Ferrol No.=1062 % (95% CI)	Lugo No.=999 % (95% CI)	Orense No.=938 % (95% CI)	Pontevedra No.=891 % (95% CI)	Santiago No.=1181 % (95% CI)	Vigo No.=1082 % (95% CI)
Wheezing at some time	20.1 (17.8-22.4)	25.3 (23.7-26.8)	24.4 (21.7-27.0)	18.0 (15.6-20.4)	16.2 (13.8-18.6)	24.8 (21.9-27.7)	20.2 (17.8-22.5)	31.4 (28.6-34.2)
Recent wheezing[b]	11.0 (9.2-12.8)	15.2 (13.9-16.5)	13.7 (11.5-15.8)	9.4 (7.5-11.3)	8.8 (7.0-10.7)	13.6 (11.3-15.9)	11.5 (9.6-13.4)	18.8 (16.4-21.1)
Recent attack of wheezing								
1 to 3	8.0 (6.4-9.5)	10.4 (9.2-11.5)	9.4 (7.6-11.2)	6.0 (4.5-7.5)	5.0 (3.6-6.5)	8.6 (6. 7-10.5)	7.3 (5.7-8.8)	13.5 (11.4-15.6)
4 to 12	1.5 (0.8-2.3)	2.8 (2.2-3.4)	3.2 (2.1-4.3)	1.9 (1.0-2.8)	1.9 (1.0-2.8)	3.7 (2.4-5.0)	2.4 (1.5-3.3)	3.2 (2.1-4.3)
More than 12	0.8 (0.3-1.3)	1.9 (1.4-2.4)	1.0 (0.4-1.7)	1.0 (0.3-1.7)	1.3 (0.5-2.0)	1.0 (0.3-1.7)	1.1 (0.5-1.7)	1.1 (0.4-1.8)
Awoken by recent wheezing								
Less than one night per week	2.7 (1.7-3.6)	3.8 (3.1-4.5)	4.0 (2.7-5.2)	2.1 (1.2-3.0)	2.0 (1.1-3.0)	3.6 (2.3-4.9)	3.1 (2.1-4.2)	5.8 (4.4-7.3)
One or more nights per week	1.2 (0.6-1.9)	1.0 (0.6-1.4)	1.1 (0.4-1.8)	0.1 (0-0.6)	0.5 (0.2-1.2)	1.1 (0.4-1.9)	0.7 (0.2-1.2)	0.9 (0.3-1.5)
Recent severe wheezing	3.0 (2.0-4.0)	3.2 (2.5-3.8)	1.8 (0.9-2.6)	2.3 (1.3-3.3)	2.6 (1.5-3.6)	3.3 (2.0-4.5)	2.3 (1.4-3.2)	4.2 (2.9-5.4)
Asthma at some time	15.3 (13.3-19.8)	18.5 (17.1-19.9)	20.2 (17.8-22.7)	18.8 16.3-21.3	11.4 9.3-13.5	18.1 (15.5-20.6)	14.6 (12.6-16.7)	21.4 (18.9-23.9)
Recent wheezing with exercise	17.7 (15.5-19.8)	21.0 (19.5-22.4)	19.5 (17.1-21.9)	18.0 (15.6-20.4)	18.1 (15.6-20.6)	22.2 (19.4-25.0)	16.3 (14.2-18.5)	25.4 (22.8-28.0)
Recent cough at night	22.7 (20.3-25.1)	28.2 (26.6-29.8)	23.8 (21.2-26.4)	22.7 (20.1-25.4)	25.3 (22.4-28.1)	28.1 (25.0-31.1)	23.7 (21.2-26.2)	27.8 (25.1-30.5)

[a] CI: confidence interval.
[b] recent: in the last 12 months.

Table 5
Prevalence of Asthma Symptoms in Children Aged 6-7 and Adolescents Aged 13-14, According to Sex.[a]

	Ages 6-7						Ages 13-14					
	Male		Female			OR (95% CI)	Male		Female			OR (95% CI)
	No.=5204		No.=5167				No.=5204		No.=5167			
	%	95% CI	%	95% CI	p		%	95% CI	%	95% CI	*P*	
Wheezing at some time	43.0	43.0-44.4	35.1	33.8-36.4	<.001	1.4 (1.3-1.5)	22.8	21.6-23.9	23.4	22.2-24.5	.480	1.03 (0.94-1.13)
Recent wheezing[b]	15.5	14.5-16.5	11.5	10.6-12.3	<.001	1.4 (13-1.6)	12.6	11.7-13.6	13.8	12.8-14.7	.089	1.10 (0.98-1.24)
Recent attack of wheezing					<.001						.086	
None						1						1
1 to 3	11.6	10.7-12.5	8.6	7.8-9.4		1.4 (1.2-1.6)	8.5	7.7-9.2	9.3	8.5-10.1		0.89 (0.78-1.02)
4 to 12	3.1	2.6-3.6	2.2	1.8-2.6		1.4 (1.1-1.8)	2.3	1.9-2.7	2.9	2.4-3.3		0.79 (0.62-1.01)
More than 12	0.6	0.4-0.8	0.2	0.1-0.4		2.7 (1.4-5.2)	1.4	1.0-1.7	1.2	0.9-1.5		1.13 (0.80-1.59)
Awoken by recent wheezing					<.001						.546	
Never						1						1
Less than one night per week	6.7	6.0-7.4	4.5	3.9-5.0		1.5 (1.3-1.8)	3.4	2.9-3.9	3.6	3.1-4.1		0.94 (0.76-1.16)
One or more nights per week	1.9	1.5-2.3	1.4	1.1-1.8		1.3 (1.0-1.8)	0.8	0.5-1.0	1.0	0.7-1.2		0.81 (0.54-1.23)
Recent severe wheezing	2.4	2.0-2.9	1.6	1.3-2.0	0.003	1.5 (1.1-2.0)	2.4	2.0-2.8	3.3	2.8-3.8	.004	1.41 (1.12-1.78)
Asthma at some time	15.1	14.1-16.1	9.7	8.8-10.5	<.001	1.7 (1.5-1.9)	19.8	18.7-20.9	15.2	14.3-16.2	<.001	0.73 (0.66-0.81)
Recent wheezing with exercise	7.2	6.5-7.9	5.5	4.8-6.1	<.001	1.3 (1.1-1.6)	17.1	16.1-18.2	22.7	21.5-23.8	<.001	1.42 (1.29-1.56)
Recent cough at night	23.7	22.6-24.9	21.0	19.8-22.1	.001	1.2 (1.1-1.3)	23.7	22.5-24.8	27.8	26.5-29.0	<.001	1.24 (1.13-1.35)

[a] CI: confidence interval.
[b] recent: in the last 12 months; OR: odds ratio.

the highest adjusted OR for *asthma at some time* was found in the children of Lugo, Vigo, A Coruña and Ferrol and the adolescents of Vigo, Ferrol and Lugo. Lastly, the highest adjusted OR for *wheezing with exercise in the last 12 months* corresponded with the children of Ferrol and Vigo and the adolescents of Vigo and Pontevedra. The OR adjusted for sex showed that being male is a greater risk for *wheezing in the last 12 months* in the group of children, but not in adolescents. Likewise, being male carries a greater risk for *asthma at some time* in both age groups.

Discussion

The ISAAC study was designed in order to try to know the prevalence of allergic diseases in children and adolescents.[5] The participating centers emerged throughout the world on their own initiative, not having been randomly selected. This limits the use of the data obtained in the different centers as representative of a region or country. For the first time, our study presents the asthma symptom prevalence data for all the Health-Care Areas in Galicia which have not been previously studied (6 urban areas and the rural areas). With the incorporation of the previous data from A Coruña,[4] the map of Galicia is complete for the prevalence of recent wheezing, and for the first time in Spain we have estimated the overall asthma prevalence for an entire province for the referred age ranges.

In order to be able to compare our results with those of other ISAAC centers, it is important to obtain similar participation rates, as an important difference could imply bias by the non-participants.

Table 6
Logistic Regression Model: Estimation of the Odds Ratio (OR) for Recent Wheezing, Asthma at Some Time and Recent Wheezing With Exercise by Geographical Area and Sex, Using as a Reference the Geographical Area With Less Prevalence and the Female Sex. Group of 6-7 Year Olds.[a]

	Recent Wheezing[b]			Asthma at Some Time			Recent Wheezing With Exercise		
	P	OR	95% CI	*P*	OR	95% CI	*P*	OR	95% CI
Sex	<.001			<.001			<.001		
Female		1.00			1.00			1.00	
Male	<.001	1.42	1.27-1.59	<.001	1.67	1.48-1.89	<.001	1.34	1.14-1.57
Geographical area	.036			<.001			.005		
Santiago		1.00			1.00			1.00	
A Coruña[4,8]	.189	1.16	0.93-1.45	<.001	1.73	1.36-2.21	.153	1.27	0.92-1.75
Ferrol	.008	1.41	1.09-1.82	<.001	1.71	1.29-2.26	.001	1.86	1.31-2.66
Lugo	.013	1.40	1.07-1.82	<.001	2.27	1.72-3.01	.060	1.44	0.98-2.12
Orense	.366	1.13	0.86-1.49	.839	1.03	0.75-1.42	.699	1.08	0.72-1.63
Pontevedra	.325	1.15	0.87-1.50	.530	1.10	0.81-1.51	.526	1.14	0.76-1.70
Vigo	.005	1.45	1.12-1.88	<.001	1.93	1.45-2.56	.012	1.61	1.11-2.33
Rural area	.171	1.19	0.93-1.52	.094	1.27	0.96-1.68	.121	1.33	0.93-1.90

[a] CI: confidence interval.
[b] recent: in the last 12 months.

Table 7
Logistic Regression Model: Estimation of the Odds Ratio (OR) for Recent Wheezing, Asthma at Some Time and Recent Wheezing With Exercise by Geographical Area and Sex, Using as a Reference the Geographical Area of Less Prevalence and the Female Sex. Group of 13-14 Year Olds.[a]

	Recent Wheezing[b]			Asthma at Some Time			Recent Wheezing With Exercise		
	P	OR	95% CI	*P*	OR	95% CI	*P*	OR	95% CI
Sex	.058			<.001			<.001		
Female		1.00			1.00			1.00	
Male	.058	0.89	0.80-1.00	<.001	1.37	1.24-1.52	<.001	0.70	0.64-0.77
Geographical area	<.001			<.001			<.001		
Orense		1.00			1.00		.309	1.12	0.90-1.41
Santiago	.044	1.34	1.01-1.79	.033	1.32	1.02-1.71		1.00	
A Coruña[4,8]	<.001	1.86	1.45-2.38	<.001	1.73	1.39-2.16	<.001	1.38	1.15-1.64
Ferrol	.001	1.64	1.23-2.18	<.001	1.95	1.51-2.50	.043	1.25	1.01-1.55
Lugo	.668	1.07	0.78-1.46	<.001	1.80	1.39-2.33	.331	1.12	0.89-1.40
Pontevedra	.001	1.62	1.21-2.18	<.001	1.71	1.31-2.22	.001	1.46	1.17-1.82
Vigo	<.001	2.39	1.82-3.13	<.001	2.11	1.64-2.70	<.001	1.75	1.42-2.15
Rural area	.093	1.28	0.96-1.70	.012	1.39	1.07-1.79	.325	1.11	0.90-1.38

[a] CI: confidence interval.
[b] recent: in the last 12 months.

Our study obtained variable response rates in both age groups (from 68 to 89% in the small children and 72 to 94% in the older ones), a range similar to the rest of Spanish studies carried out with the same methodology.[4] As in other studies, there was greater participation in the group of adolescents, probably because they had filled out the questionnaires themselves while at school.[5]

Questions 1, 2, 6, 7, and 8 of the questionnaire used analyze the prevalence of asthma symptoms, while questions 3, 4, and 5 refer to severe symptoms of the disease. Depending on the expected prevalence for each response, the ISAAC manual[9] recommends a sample size for the analysis of the differences among centers. The most demanding recommendation is for the questions of severity (3, 4, and 5), with 3000 subjects, being sufficient a number of 1000 for the questions of symptom prevalence (1, 2, 6, 7, and 8). In order to ensure the viability of the Project, we limited the sample size to 1,000 subjects in each area studied, which was sufficient to analyze the differences in the questions about asthma symptom prevalence. Thus, in addition to describing/reporting the results of all the questions, in the discussion we will focus on those related to prevalence, meaning those where the power of our data is most adequate in order to be able to analyze the differences among centers.

Question 1 (*wheezing at some time*), which is related with the accumulated prevalence of asthma,[11] was included in order to detect those children who do not have acute crises but have persistent symptoms of the disease. However, this question presents low specificity for the identification of children with asthma in validation studies.[10] The difficulties entailed in the "recall effect" of answering historical questions, as well as the possible positive response of children who have had processes similar to asthma, and even more so in early ages when there are different phenotypes that are very difficult to diferentiate,[12] probably explain this low specificity.

Question 2 (*wheezing in the last 12 months*) tries to reduce the errors in recall, and it is the question that has presented a greater correlation with the current prevalence of asthma in validation studies.[10] In our study, as in the Spanish ISAAC centers,[4] there was great variability in the results in both age groups: 11.4 to 15.7% in the younger children and 8.8 to 18.8% in the older ones. The data in phase 3 of the ISAAC[4,13] on this question show for Spain between 7.1 to 12.9% of children and 7.1 to 15.3% of adolescents with a positive response. The data of the 6-7 year-old group in A Coruña included in our study were nearly the highest in this phase 3 ISAAC,[4,13] only surpassed by the results of a study in the Canary Island population (18.4%)[14] carried out with the same methodology. Four of our study Areas (Vigo, Ferrol, Lugo and the rural area) surpass the data from A Coruña in children aged 6-7. Ourense and Pontevedra offer similar values and those of Santiago are somewhat lower. Therefore, all our study areas would be situated in high ranges compared with the rest of Spanish cities, except Santiago which would be in a mid-high range. According to these data, and adjusting them for sex and geographical area, the children of Vigo would have had almost 50% more possibilities of having wheezing in the last 12 months than the children of Santiago, an area of less prevalence. In this age group, as in the results of phase 3 ISAAC in Spain, we have not identified a clear geographical pattern.

In the group of adolescents aged 13-14 in phase 3 of the ISAAC in Spain, A Coruña was, after Asturias, the center with the most positive responses on question 2.[4,13] In a study carried out in Cantabria[15] with the same methodology, high prevalences were also obtained (16.7%). The data obtained in our study areas are situated in ranges very similar to the Spanish centers, and only the data from Vigo were somewhat higher. Adjusting for sex and geographical area, the adolescents from Vigo would have had more than double the possibilities of having wheezing in the last 12 months than those from Ourense (area of lesser prevalence). In the Galician teenagers, as in ISAAC Spain, the variability between areas is greater than in the younger children and there seems to exist a very clear geographical pattern. The coastal cities present a higher prevalence, especially those located on the Atlantic Coast. In our case, this fact is confirmed quite clearly when comparing the higher levels of Vigo, A Coruña, Ferrol and Pontevedra (coast), the low levels of Ourense and Lugo (interior), and intermediate levels in rural areas (with schools in both coastal and interior areas) and Santiago (interior). In previous studies, it was interpreted that this could be due to environmental factors. The differences in prevalence between populations can be due to genetic factors, different proportion of immigrant population, different environmental factors (geography, climate, food, habits or customs, etc.),[6,16] organization (health-care system, accessibility to health care, diagnostic means, concepts and knowledge of the disease) or even linguistics.[13,17] The population of the Areas analyzed in this study belong to the same Autonomous Community, with very few expected genetic differences, few immigrants (1.4% in the year 2006),[18] with similar eating habits and customs, identical health-care system and management, and similar language. Thus, the differences found between such homogenous populations suggest even more strongly that the differences can be due to specific environmental factors, the most important of which are probably the climates in general and the humidity in particular, as seen in the differences found between the coastal and interior areas. The greater level of humidity in the coastal cities and the mild climate of Galicia could affect the level of exposure to perennial allergens (mites), which could favor higher

prevalences of symptoms of the disease. This fact could be of greater importance in the group of adolescents where the allergens are a more important triggering factor of the disease symptoms than in small children, where the infectious agents play a primordial role. This could explain why in the adolescent group the geographic pattern is clear and in the group of younger children it is less so. The finding of lower prevalences in the populations of Lugo and Ourense, with more rural, less industrialized settings than the other areas, could lead us to consider the protective effect of allergic pathologies, with regard to the exposure to endotoxins and a rural setting as suggested by previous studies, which has come to be known as "hygiene hypothesis".[19] Nevertheless, when we observe in the group representing the rural population prevalences in intermediate values of our study, the hypothesis of hygiene cannot be defended in our population. It is also striking that A Coruña and Vigo (cities that are 3 - 4 times greater in population) have prevalences higher than the other coastal cities (Ferrol and Pontevedra). This could be due to some added climate factor, depending on the size of the cities, as well as for instance the traffic.[20]

Although the prevalences are high compared with the Spanish population in the group of younger children, and are more similar in the adolescent group, these levels in both age groups are much lower than those observed in other studies that followed the ISAAC methodology in Anglo-Saxon and Latin American countries. Our results are found within the intermediate range of the world-wide panorama.[5,21]

Comparing the two age groups, a greater frequency of symptoms can be observed in the younger children. This concurs with the expected evolution of the asthma symptoms, progressively dropping from childhood until adolescence.[22] We also cannot rule out a certain effect due to the fact that in one age group the respondents are the children themselves and in another the respondents are their parents, a fact which has also been demonstrated to influence the type of response obtained.[23]

When making a comparison by sex, we observe clearly higher prevalences in males in the younger group, while in the adolescents the levels become more equal, even becoming a bit higher in the females. The boys aged 6-7 have almost 50% higher risk for having wheezing in the last 12 months than did the girls, while in the male adolescents the risk is slightly less than in the girls. This concurs with the expected values, given the known evolution of asthma, with a predominance of males at younger ages, and an inverted ratio in the periadolescent phase.[24] Different factors (differences in the caliber of the airway at specific ages[25] and hormonal stages[26]) seem to contribute to the inversion of the gender effect depending on age and the different expressivity or perception of the sintoms.[27]

Question 6 (*asthma at some time*) questions about diagnosed asthma, as occasionally asthma may be diagnosed in absence of wheezing. Some authors report that presenting a higher prevalence of wheezing in the last 12 months than having ever had asthma can indicate underdiagnosis of this disease. In this study, in contrast with what was observed in the Canary Island population aged 6-7,[14] it seems that the asthma would be acceptably diagnosed in this age group, although there is an important variability among areas, while in most there could be a certain degree of overdiagnosis. However, in our opinion these interpretations have an important limitation: question 2 is limited to what has occurred in the last 12 months, while *asthma at some time* is historical. Thus, in addition to referring to different lifetime periods with the consequent "recall factor", there is the added difficulty of diagnosing the disease at early ages, with patients presenting different phenotypes that are difficult to differentiate, some of which have nothing to do with asthma in its later evolution. In any case, the relationship should be established with question 1, which is also historical, and in this case the data obtained in both is quite disparate. Curiously enough, in this question, related with the diagnosis of the disease, there is a predominance of positive responses amongst males in both age ranges, something that we could come to expect in the younger boys in whom the prevalence of the disease is greater, but which is surprising in the older boys, an age at which the prevalence of the disease is similar or even slightly higher in the girls. This same observation has been made in the Spanish cities of phase 3 ISAAC.[4,13]

Question 7 (*wheezing with exercise in the last 12 months*), which intends to increase the sensitivity of the questionnaire by detecting patients with symptoms only under such circumstances, highlights the high rate of positive responses in adolescents. These data reported in the studies carried out in other Spanish cities[4] suggest doubts about how the respondents interpret this question. On the other hand, what stands out is the low percentage of children aged 6-7 who respond positively to this question, possibly related with the difficulty of the parents to perceive wheezing. In the older group, despite having a similar prevalence in both sexes according to question 2 ("*wheezing in the last 12 months*"), the girls present a higher rate of positive responses to this question. This fact, as described previously, could be influenced because girls at this age generally have less physical preparation, or even due to cultural factors due to which girls at this age tend to more easily admit less effort tolerance than do boys.[28]

In the last question about *cough at night in the last 12 months*, the differences in the results between the areas of our study present an inexistent correlation with question 2 (*wheezing in the last 12 months*), as was observed in the rest of the Spanish cities.

As we had data available for all the Health-Care Areas of Galicia, including the rural parts, the overall asthma prevalence for the Autonomous Community of Galicia was estimated depending on the prevalences of each area and their population importance. The data of overall prevalence is of evident medical interest as it gauges childhood asthma as a health problem for the administrators responsible for the health-care system, which in Spain is managed by the respective Autonomous Communities.

Limitations of the Study

This is a cross-sectional study of the school-age population at the time the study was carried out, without taking into account the time of residence in our area, so the results may be influenced by modifications in the population due to migratory movements or with different periods of exposure to environmental factors.

In this study, as in the phases 1 and 3 of the ISAAC, objective measurements of the disease are not available; therefore the evaluation depends on the opinion of the children or of their parents. The questionnaire is a tool that compiles information from the perspective of the subject. It therefore presents some problems, given the variability in the perception of symptoms, the inevitable bias of self-selection and recall, as well as the differences in the diagnostic practices.[29] Given the lower sensitivity and specificity of the questionnaires when compared with the objective tests, this could lead to errors in the classification of the diseases by confusing the symptoms of other patologies.[29] However, the use of the questionnaires is simple as they are easily administered, they do not require special equipment, and they are independent of circumstances such as seasonality, respiratory infections or treatments. Their validity is reasonably demonstrated when compared with the studies that include objective measurements, and their utility is manifested in the prevalence studies in large populations, as is the present case.[30]

In the overall prevalence estimations for the entire Autonomous Community and in the comparisons between Areas, we used data of the ISAAC done in A Coruña in 2003. Although it is another study, as it was done with an identical standardized methodology, it is

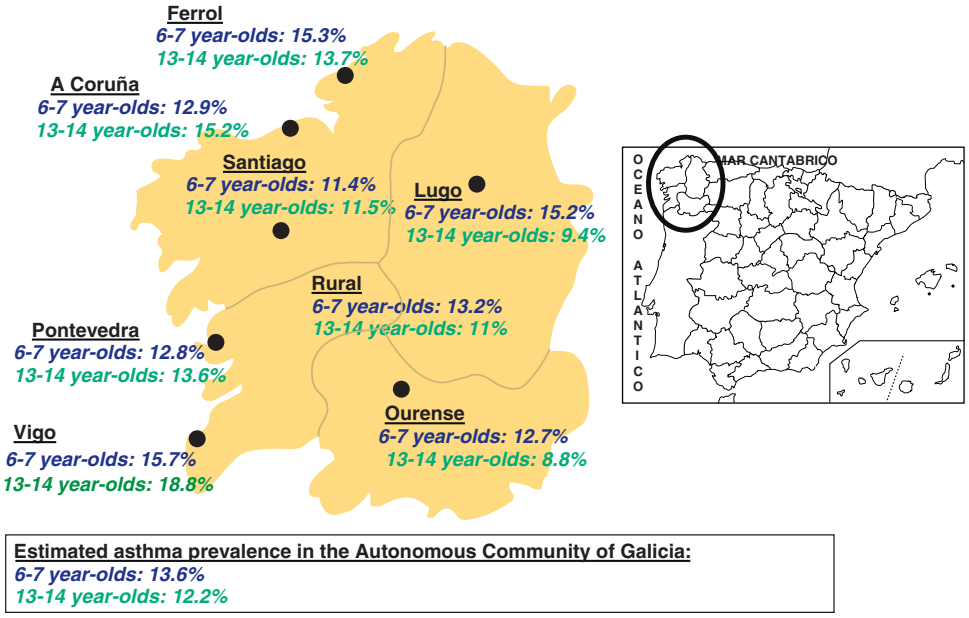

Fig. 1. Prevalence of wheezing in the last 12 months in the Autonomous Community of Galicia, Spain, according to age groups and study areas. Estimation of the overall asthma prevalence in the Autonomous Community of Galicia, Spain, according to age groups.

quite improbable that there could be bias in this overall analysis. According to the analysis of the temporary variations in prevalence between phases 1 and 3 of the ISAAC in Spain, there is a slight increase in the younger subjects (mean increase 0.4% per year, approximately), while in the adolescents there would be a stabilization of the prevalence.[13] We believe that the difference of 3 years between the development of the study of A Coruña and the rest of the studied areas could have a limited influence on the group of small children in the comparisons between areas and in the overall prevalence calculation for the entire province. This would not happen amongst the adolescents.

The rural area groups together all the health care areas of the Autonomous Community of Galicia and, therefore, it is not possible to analyze the influence of the geographic factor in the rural setting.

In conclusion, we present for the first time data on the prevalence of childhood asthma symptoms of 7 previously-unstudied areas of Galicia, and we estimate the overall prevalence of asthma of a Spanish Autonomous Community with the ISAAC methodology. The prevalence of wheezing in the last 12 months in the different parts of Galicia is sensitively higher than the rest of the Spanish cities participating in the ISAAC in the 6-7 year-old group, and it is very similar in the 13-14 year-old group, except in Vigo, which is sensitively higher. As in the rest of Spain we found a well-defined geographic pattern in the group of older children, with higher prevalences on the coast than in the interior. In Galicia, asthma is an important health problem in pediatric ages.With the data obtained in our study, and with the previously published results for A Coruña in the ISAAC, we have constructed a map of prevalences for wheezing in the last 12 months for Galicia in both age groups (Fig. 1). For the group of geographical areas studied in Galicia, the estimation of asthma prevalence was 13.6% in children aged 6-7 and 12.2% in the adolescents aged 13-14.

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