

Original article

Stabilization of asthma prevalence among adolescents and increase among schoolchildren (ISAAC phases I and III) in Spain*

Background: Most studies show a steep increase in asthma prevalence in the last decades, although few studies had applied the same methodology. Recent reports point out the possibility that the epidemic has come to an end. We have studied the prevalence of asthma in a very large sample of children, repeating the study eight years apart.

Methods: Repeated cross-sectional studies using the International Study of Asthma and Allergies in Childhood (ISAAC) protocol in a sample of Spanish schoolchildren 6–7 (parent-reported) and 13–14 (self-reported) years old in 1994–95 (phase I) and 2002–2003 (phase III). The number of participants was 42 417 in phase I and 42 813 in phase III. The participation rate was over 87% (13–14 years) and 70% (6–7 years).

Results: The prevalence of wheezing in the previous year in children aged 13–14 years was 9.0 and 9.3% for boys and 9.6 and 9.2% for girls for phases I and III, respectively. Children 6–7 years of age showed a substantial increase in wheezing in the previous year (7.0 and 10.7% for boys and 5.3 and 8.2% for girls). Other symptoms and severity indexes followed the same patterns.

Conclusions: In the last 8 years, the prevalence of asthma has not changed in 13–14-year-old Spanish children but has increased substantially in 6–7-year olds.

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Although there has been adequate consensus about the increase of asthma prevalence in children during the past decades (1–11) there are some recent reports, although with some limitations, that point out the possibility of that increase to have come to an end both in adults (12)

and in children (13–15). Still other studies report an increase confined to mild symptoms (16). In the former East Germany, a study reported an increase in allergy but not in asthma between the years 1992 and 1996 (17), although a more recent study in the same population shows an increase of both atopy and asthma between 1993 and 1999 (18). There have been suggestions as to the increase of asthma being only in children with no family history of atopy (19). The number of studies that compare two different time-points using the same methodology are not so numerous (20). Time trends may be influenced not only by the use of a different methodology (20) but also

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by diagnostic changes (classification bias) (20, 21) or by increased awareness of symptoms and the willingness of doctors to diagnose asthma (information bias) (20, 22). Other factors such as the changes in patient care or the inclusion of new drugs in the anti-asthma armamentarium can also affect the trend of asthma prevalence (23). A recent review of studies that included objective measurements in their surveys concludes that only three of 16 studies found a consistent increase of several of those measurements with time (24).

The first worldwide comparison of asthma prevalence in children was published in 1998 by the International Study of Asthma and Allergies in Childhood (ISAAC) (25), when different areas of prevalence were drawn, with English-speaking countries having the highest prevalences and Eastern European countries, China and Indonesia having the lowest. Quite strikingly, most Spanish- and Portuguese-speaking countries of Latin America had much higher prevalences than Spain or Portugal. Except for Greece, in which asthma prevalence was one of the lowest (3.7%), the rest of the Mediterranean countries of western Europe shared a similar and medium prevalence (8.9–13.5%) which was quite comparable with that of other countries of central Europe.

Most of the time-trend comparisons on asthma prevalence are from the countries in the ISAAC upper-prevalence range. To the best of our knowledge, only two studies from the middle-prevalence-range countries have been published to date. In the first study, which used a questionnaire developed in Italy, carried out in Rome, no substantial increase of asthma prevalence was reported from 1992 to 1998 among schoolchildren, 6–14 years of age (14). The only study as yet published comparing ISAAC phase I (1994–95) with phase III (1999–2000) was performed in Münster (Germany) in the same age groups targeted in this study (6–7- and 13–14-year olds). In contrast to the Italian study, a slight increase has been described between the two phases, being higher in girls than in boys (11).

The aim of our study is to provide more information about asthma time-trends in a country with a medium prevalence, comparing ISAAC phase I and III in a very large sample of children and adolescents.

Methods

Population and data collection

The Spanish ISAAC study group included 10 cities in 1994–95 (phase I) and 11 in 2002–2003 (phase III). The results presented in this study are from the eight cities (centres) in which both phase I and III had been performed. Those centres were: Cartagena, Barcelona, Bilbao, Castellón, Madrid, Pamplona, Valencia and Valladolid. Except for Barcelona and Madrid, the rest of the centres included all schools inside the city district which had children of the targeted age range. In Madrid, all schools within the health area of the 'Hospital 12 de Octubre' and in Barcelona, 'Hospital del Mar' were included. According to the ISAAC protocol, the study was

carried out in two groups of children: 13–14- and 6–7-year olds, aiming at 3000 participants per centre in each age group. All eight centres were included in the older age group, whereas only six were included in the younger one (in Valladolid and Barcelona the survey was performed only in the 13–14-year group).

The survey used the ISAAC questionnaires for phase I and III according to the respective manuals (<http://isaac.auckland.ac.nz>). ISAAC methods have been previously validated (26, 27). Questionnaires were translated into Spanish and back-translated into English according to the instructions of the protocol. As recommended in the protocol, the 13–14-year group also completed a video questionnaire. In the phase I, we used the Caucasian version, whereas in phase III the International version was used. The video contains five different sequences related to asthma symptoms and severity: (i) moderate whistling at rest; (ii) wheezing and shortness of breath after exercise; (iii) nocturnal wheezing; (iv) nocturnal cough; and (v) severe wheezing and shortness of breath at rest. The video questionnaire was completed after the written one and the children answered the questions after each of the scenes. Three of the scenes [no. (ii), (iii) and (v)] were different between the two versions. In no. (ii) and (iii), the wheezing sound was much clearer in the International than in the Caucasian version, whereas no. (v) was very similar in the two versions.

Children 13–14 years of age completed the written and the video questionnaires by themselves while in class, whereas 6–7-year-old children were given only the written questionnaire in order to be completed by their parents and returned to school. The study was approved by the Asturias Ethics Committee.

The participation rate was higher in the 13–14-year age group (88.5 and 87.3% for phases I and III, respectively) than in the 6–7-year age group (70.3 and 71.5% for phases I and III, respectively). The overall number of participants in phase I was 42 417 (23 380 for the 13–14-year group and 19 037 for the 6–7-year group); while the overall number for phase III was 42 813 (24 214 for the 13–14-year group and 18 599 for the 6–7-year group).

Phase I questionnaires were entered manually in the computer using a double-entry method by means of an EPI-INFO V 6.0 program (Centers of Disease Control and Prevention, Atlanta, GA, USA) while phase III questionnaires were scanned once using an optical mark recognition software (Remark Office OMR V5, Paoli, PA, USA).

Data analysis

Of the 85 230 children who participated either in phase I or III, a total of 85 were discarded for missing values for sex, and a total of 85 145 children were included in the analysis. Missing or inconsistent answers were included in the denominator for prevalence calculations while they were excluded from subsequent bivariate analysis according to ISAAC recommendations (28, 29). Prevalence was calculated with a 95% confidence interval. Chi-square tests were performed to check the significance of differences between proportions in the two surveys. Odds ratios (OR) with 95% confidence interval (CI) were also calculated, using phase I as the base. To express the increase of phase III when compared with phase I in a selected number of variables, a relative percentage was calculated as follows: [(phase III prevalence – phase I prevalence)/phase I prevalence] × 100; the significance of this increase was tested using the OR and its 95% CI. Those calculations were carried out only with a selected number of variables: wheezing or whistling of the chest during the past year, having <4, or ≥4 asthma attacks in the previous year, experiencing at least a severe attack in that period, and having an asthma diagnosis at any time of the life. Stata 7.0 software (College Station, TX, USA) was used for statistical calculations.

Table 1. Absolute number, prevalence and their 95% confidence intervals of different asthma symptoms in 13–14-year olds in 1994–95 and 2002–2003 (ISAAC phases I and III)

	Boys				Girls			
	Phase I (<i>n</i> = 12 030)		Phase III (<i>n</i> = 12 508)		Phase I (<i>n</i> = 11 349)		Phase III (<i>n</i> = 11 669)	
	<i>n</i>	% (95% CI)	<i>n</i>	% (95% CI)	<i>n</i>	% (95% CI)	<i>n</i>	% (95% CI)
Previous year prevalence								
Wheezing	1091	9.0 (8.6–9.6)	1166	9.3 (8.8–9.8)	1095	9.6 (9.1–10.2)	1070	9.2 (8.6–9.7)
Exercise-induced wheezing	1623	13.5 (12.9–14.1)	1641	13.1 (12.5–13.7)	1890	16.7 (16.0–17.4)	1953	16.7 (16.0–17.4)
Night cough	2388	19.8 (19.1–20.6)	2428	19.4 (18.7–20.1)	2581	22.7 (22.0–23.5)	2860	24.5 (23.7–25.3)
Number of wheezing attacks								
1–3	714	5.9 (5.5–6.4)	799	6.4 (6.0–6.8)	745	6.6 (6.1–7.0)	751	6.4 (6.0–6.9)
4–12	216	1.8 (1.6–2.0)	259	2.1 (1.8–2.3)	196	1.7 (1.5–2.0)	217	1.9 (1.6–2.1)
>12	89	0.7 (0.6–0.9)	103	0.8 (0.7–1.0)	75	0.7 (0.5–0.8)	89	0.8 (0.6–0.9)
Sleep disturbance because of wheeze								
<1 night/week	290	2.4 (2.1–2.7)	363	2.9 (2.6–3.2)	286	2.5 (2.2–2.8)	351	3.0 (2.7–3.3)
≥1 night/week	94	0.8 (0.6–1.0)	103	0.8 (0.7–1.0)	129	1.1 (0.9–1.3)	108	0.9 (0.8–1.1)
Speech-limiting wheezing	236	2.0 (1.7–2.2)	247	2.0 (1.7–2.2)	255	2.2 (2.0–2.5)	229	2.0 (1.7–2.2)
Lifetime prevalence								
Wheezing	2224	18.5 (17.8–19.2)	2214	17.7 (17.0–18.4)	1990	17.5 (16.8–18.2)	2100	18.0 (17.3–18.7)
Asthma diagnosis	1414	11.7 (11.2–12.3)	1731	13.8 (13.2–14.5)	1023	9.0 (8.5–9.6)	1374	11.8 (11.2–12.4)

Results

The prevalence of different symptoms and severity for boys and girls are depicted in Table 1 (13–14 years group) and Table 2 (6–7 years group). No difference of prevalence between the two surveys could be detected in the older group either in boys or in girls in any of the variables studied but for asthma diagnosis and night disturbance of <1/week, they were significantly more prevalent in 2002–2003 than in 1994–95. In contrast, among 6–7-year olds, all variables increased significantly from 1994–95 to 2002–2003 (Table 3). The amount of the increase was quite uniform for all symptoms measured and severity.

Among 13–14-year olds, the OR of having an asthma diagnosis in boys when compared with girls in phase I was 1.5 (95% CI: 1.4–1.6), whereas in phase III it was 1.2 (95% CI: 1.1–1.3). The corresponding figures for the 6–7-year group were 1.6 (95% CI: 1.4–1.8) and 1.5 (95% CI: 1.4–1.7), respectively.

The results of the video-questionnaire are shown in Table 4. In the two common scenes of phases I and III, there were no significant increases of the previous year prevalence for each sex. Curiously a significantly higher proportion of girls when compared with boys answered positively to the scene of sleep disturbance caused by cough (OR 1.7; 95% CI: 1.6–1.8). In scenes of wheezing accompanied with exercise and sleep disturbance caused by

Table 2. Absolute number, prevalence and their 95% confidence intervals of different asthma symptoms in 6–7-year olds in 1994–95 and 2002–2003 (ISAAC phases I and III)

	Boys				Girls			
	Phase I (<i>n</i> = 9749)		Phase III (<i>n</i> = 9276)		Phase I (<i>n</i> = 9278)		Phase III (<i>n</i> = 9286)	
	<i>n</i>	% (95% CI)	<i>n</i>	% (95% CI)	<i>n</i>	% (95% CI)	<i>n</i>	% (95% CI)
Previous year prevalence								
Wheezing	684	7.0 (6.5–7.5)	993	10.7 (10.1–11.4)	492	5.3 (4.9–5.8)	757	8.2 (7.6–8.7)
Exercise-induced wheezing	331	3.4 (3.0–3.8)	485	5.2 (4.8–5.7)	219	2.4 (2.1–2.7)	363	3.9 (3.5–4.3)
Night cough	1280	13.1 (12.5–13.8)	1840	19.8 (19.0–20.7)	1124	12.1 (11.5–12.8)	1565	16.8 (16.1–17.6)
Number of wheezing attacks								
1–3	488	5.0 (4.6–5.5)	792	8.5 (8.0–9.1)	370	4.0 (3.6–4.4)	577	6.2 (5.7–6.7)
4–12	116	1.2 (1.0–1.4)	156	1.7 (1.4–2.0)	77	0.8 (0.6–1.0)	143	1.5 (1.3–1.8)
>12	27	0.3 (0.2–0.4)	42	0.5 (0.3–0.6)	14	0.2 (0.1–0.3)	33	0.4 (0.2–0.5)
Sleep disturbance caused by wheezing								
<1 night/week	251	2.6 (2.3–2.9)	399	4.3 (4.0–4.7)	179	1.9 (1.7–2.2)	295	3.2 (2.8–3.6)
≥1 night/week	75	0.8 (0.6–1.0)	134	1.4 (1.2–1.7)	55	0.6 (0.4–0.8)	122	1.3 (1.1–1.6)
Speech-limiting wheezing	118	1.2 (1.0–1.4)	176	1.9 (1.6–2.2)	73	0.8 (0.6–1.0)	127	1.4 (1.1–1.6)
Lifetime prevalence								
Wheezing	2045	21.0 (20.2–21.8)	3052	32.9 (31.9–33.9)	1651	17.8 (17.0–18.6)	2431	26.2 (25.3–27.1)
Asthma diagnosis	750	7.7 (7.2–8.2)	1198	12.9 (12.2–13.6)	453	4.9 (4.5–5.3)	832	9.0 (8.4–9.6)

Table 3. Prevalence odds ratios between 1994–95 (base) and 2002–2003 in boys and girls for the two age groups

	13–14-year old		6–7-year old	
	Boys	Girls	Boys	Girls
Last year prevalence				
Wheezing	1.1 (0.9–1.2)	0.9 (0.8–1.0)	1.6 (1.4–1.8)	1.6 (1.4–1.8)
Exercise-induced wheezing	1.0 (0.9–1.0)	1.0 (0.9–1.1)	1.6 (1.4–1.8)	1.7 (1.4–2.0)
Night cough	1.0 (0.9–1.0)	1.1 (1.0–1.2)	1.6 (1.5–1.8)	1.5 (1.4–1.6)
Number of wheezing attacks				
1–3	1.1 (0.9–1.2)	1.0 (0.9–1.1)	1.8 (1.6–2.0)	1.6 (1.4–1.8)
4–12	1.1 (0.9–1.4)	1.1 (0.9–1.3)	1.4 (1.1–1.8)	1.9 (1.4–2.5)
>12	1.1 (0.8–1.5)	1.1 (0.8–1.6)	1.6 (1.0–2.8)	2.4 (1.2–4.8)
Sleep disturbance because of wheezing				
<1 night/week	1.2 (1.0–1.4)	1.2 (1.0–1.4)	1.7 (1.4–2.0)	1.7 (1.4–2.0)
≥1 night/week	1.0 (0.8–1.4)	0.8 (0.6–1.0)	1.9 (1.4–2.5)	2.2 (1.6–3.1)
Speech-limiting wheezing	1.0 (0.8–1.2)	0.9 (0.7–1.0)	1.6 (1.2–2.0)	1.7 (1.3–2.4)
Lifetime prevalence				
Wheezing	0.9 (0.8–1.0)	1.0 (0.9–1.1)	1.8 (1.7–2.0)	1.6 (1.5–1.8)
Asthma diagnosis	1.2 (1.1–1.3)	1.3 (1.2–1.5)	1.8 (1.6–2.0)	1.9 (1.7–2.2)

Table 4. Prevalence of past year positive answers to the five video scenes of the video-questionnaire in 1994–95 (phase I) and 2002–2003 (phase III). Scenes (ii), (iii) and (v) were different between the two surveys

	Boys				Girls			
	Phase I (n = 12 030)		Phase III (n = 12 508)		Phase I (n = 11 349)		Phase III (n = 11 669)	
	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)
Scene (i): Wheezing at rest	963	8.0 (7.5–8.5)	908	7.3 (6.8–7.7)	776	6.8 (6.4–7.3)	834	7.1 (6.7–7.6)
Scene (ii): Wheezing with exercise	2443	20.3 (19.6–21.0)	1400	11.2 (10.6–11.8)	3379	29.8 (28.9–30.6)	1448	12.4 (11.8–13.0)
Scene (iii): Sleep disturbance because of wheezing	509	4.2 (3.9–4.6)	298	2.4 (2.1–2.7)	509	4.5 (4.1–4.9)	301	2.6 (2.3–2.9)
Scene (iv): Sleep disturbance caused by cough	1502	12.5 (11.9–13.1)	1587	12.7 (12.1–13.3)	2221	19.6 (18.8–20.3)	2394	20.5 (19.8–21.3)
Scene (v): Severe wheezing	421	3.5 (3.2–3.8)	481	3.8 (3.5–4.2)	434	3.8 (3.5–4.2)	554	4.7 (4.4–5.1)

wheezing, there was a steep decrease from phase I to phase III: from 24.9 to 11.8% ($P < 0.001$) and from 4.4 to 2.5% ($P < 0.001$), respectively, for the whole group. The results of the fifth scene, the one that shows a severe asthma attack, was quite uniform between surveys, although there was a certain increase that was mainly because of the increase seen in girls (from 3.8 to 4.7%; $P < 0.001$).

The relative percentage of increase or decrease between phases I and III of a selected group of variables is shown in Fig. 1. This figure illustrates and summarizes that what is shown in the tables: a stable prevalence of asthma symptoms and severity between phases I and III among children 13–14 years old and a considerable increase ($> 50\%$) in all indexes of asthma among younger children, 6–7 years old.

Discussion

This study uses ISAAC methodology and compares data from several centres between two time points. Similar time spans as the one in our study (8 years) have detected substantial increases. Very recently, the study by Maziak et al. (11), in the first study comparing ISAAC phase I

and III data in Münster found an increase of asthma and allergies in children of the same age groups in which our own study was made (6–7 and 13–14 years). The 12-month prevalence of wheezing had an absolute increase of 2.3% (boys) and 4.4% (girls) in the older group and 1.6% (boys) and 5.2% in the younger group. Lifetime diagnosis of asthma did not increase significantly in boys of any age but it did in girls, especially in the older group (1.9 and 0.9% of absolute increase for the older and for the younger group, respectively). The first survey was carried out in 1994–95 and the second in 1999–2000, thus a difference of 5 years. The data from our study clearly contrasts with these, as we really do not have a substantial increase of wheezing in the previous year in the 13–14-year group but have a very steep increase in the 6–7-year group. Our first survey was also performed in 1994–95, although our second was in 2002–2003, thus having a larger time period between the two surveys than the German study. This would have allowed us to detect a lower time-trend increase. In the first survey, the 12-month prevalence of wheezing in our study was somewhat lower than the one found in the German study in the two age groups: 9.0% (boys) and 9.6% (girls) for the 13–14-year group and 7.0% (boys) and 5.3% (girls) for

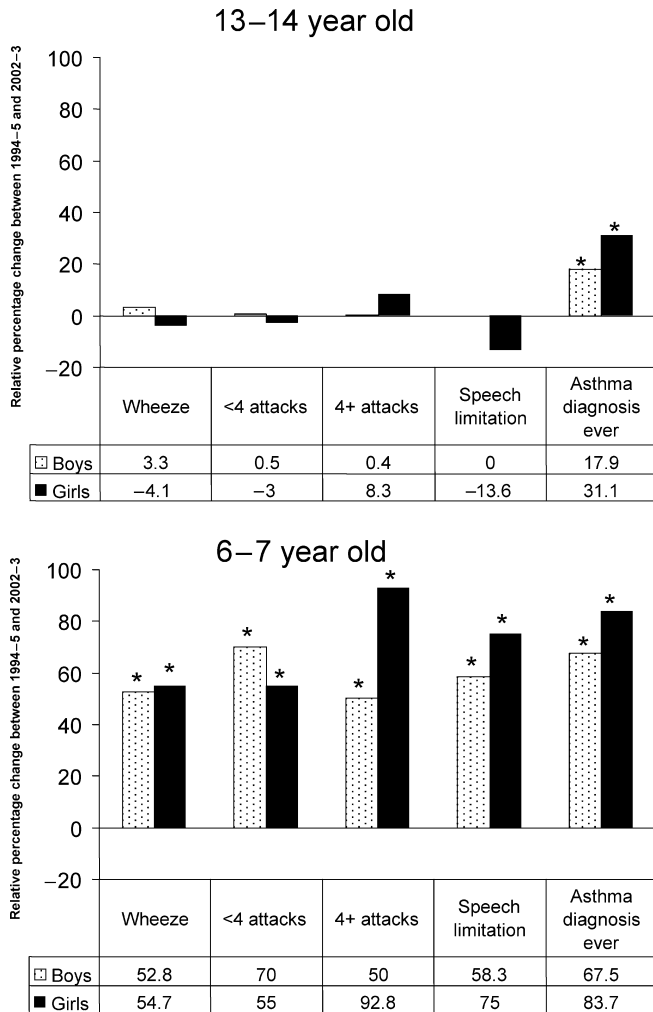


Figure 1. Relative percentage change in the prevalence of selected previous year symptoms and of asthma diagnosis for boys and girls of both age groups. *Significant change between phase I and III, $P < 0.05$.

the 6–7-year group. The absolute increase for the boys of the 13–14-year group was only 0.3%, whereas in girls of this group, we found a decrease of 0.4%. In contrast, within the 6–7-year olds there was an absolute increase of 3.7% (boys) and 2.9% (girls).

It could be inferred then that—in contrast with Münster—there is a different time trend for the 13–14- and for the 6–7-year olds in Spain. The study by Ronchetti et al. (14) had three different surveys carried out in 1974, 1992 and 1998. Although the questionnaire (filled by parents) used by those authors is not the ISAAC questionnaire, two of the questions are equivalent: those that referred to wheezing in the chest and to asthma diagnosis. The findings from this study allow us to conclude that there is a stabilization of asthma prevalence between 1992 and 1998 both for the 6–9.9- and the 10–14-year age groups. Very interestingly, the authors underline the unexpected finding of the prevalence in the younger group being higher than in the older one in

1974 and 1992. In the phase III of our study, the prevalence of wheezing in the previous year in 6–7-year olds is similar to that in 13–14-year olds both in boys (10.7% vs 9.3%) and in girls (8.2 vs 9.2%). Still, one must be very cautious when comparing self-reported symptoms (13–14 years) with parent-reported symptoms (6–7 years). Differently with the Italian study, where an asthma prevalence stabilization is found in children 6–9.9 years of age, our findings show a substantial increase in this age group (52.8% boys and 54.7% girls in wheezing in the previous year).

The study by Senthilshelvan (13) relied on asthma diagnosis extracted from clinical records of the Saskatchewan (Canada) registry. For the 5–14-year group, they found an increase from approximately 6% in 1991 to approximately 8% in 1995 and a subsequent decrease to approximately 7% in 1998. The authors did not find any particular reason for this decline, but argued that self or parental management and new medications could play a role. If stabilization has really occurred in our 13–14-year-old population, we do not think those are important reasons as the questions of the ISAAC survey are addressed to children who should know about their symptoms—especially if they are using anti-asthma medication. The only new drug class marketed in Spain between 1994–95 and 2002–2003 has been the leukotriene antagonists. It does not seem likely that the launching of those drugs have had any effect on the reports of wheezing in the 13–14-year group but not in the 6–7-year group. The fact that in the older group, the prevalence is self-reported and in the younger one parent-reported warrants some caution when comparing the time trends between the two age groups. In Spain, asthma is now considered less as a stigmatizing disease than it was 8 years ago, so the word ‘asthma’ is more readily accepted and used both by doctors and patients. This is reflected in the fact that self-reported asthma diagnosis is the only variable that increased significantly in the 13–14-year group in this period (from 11.7 to 13.8% in boys and from 9.0 to 11.8% in girls) and suffered the highest increase in the 6–7-year group (from 7.7 to 12.9% in boys and from 4.9 to 9.0% in girls). A cohort effect could be an additional explanation, although we are not aware of any major health or environmental change in Spain during the past years that could have had an effect around the time of the birth of the children 6–7 years old who were surveyed in 2002–2003. Considering that at 6–7 years two main different asthma phenotypes still coexist (30), it is possible that only one is provoking the increase. If this was the transient wheeze, which is mainly due to viral infections, one might speculate that virus-related events occurring in the previous 6 or 7 years could play a role. A new survey performed in some years time would add some light on the cohort effect.

As for the video-questionnaire of our study, only two questions were exactly maintained in the 1994–95 and 2002–2003 surveys: wheezing at rest and disturbance caused by cough at night. The figures remain quite stable from one survey to the other, with a slight decrease in boys reporting wheezing at rest. The changes of the rest of

the scenes have provoked dramatic differences. It is noteworthy that the scene of exercise-induced wheezing which was quite confusing in the phase I video, has been reduced to half when the more clear scene of phase III was used. It happens similarly with the third scene which showed a mixture of cough and wheeze in the 1994–95 video and was changed to an ‘only wheeze’ scene in 2002–2003. The fifth scene, although with a different child, was quite similar within the two phases, and so are the proportions of positive responses.

In summary, we have shown in a very large sample of Spanish school children 6–7 and 13–14 years of age that the time trend prevalence is different for each age group. More studies, including objective measurements, are still needed in order to clarify the real trends of asthma prevalence in the new millennium. The future publication of ISAAC phase II data (which includes objective measurements) as a base for future replication of that protocol will clarify the situation worldwide.

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