

## ORIGINAL ARTICLE

## Evaluation of criteria for the diagnosis of asthma using an epidemiological questionnaire\*

Avaliação de critérios para o diagnóstico de asma através de um questionário epidemiológico

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### Abstract

**Objective:** To evaluate criteria for the diagnosis of asthma in an epidemiological survey. **Methods:** Adolescents (13–14 years of age) and legal guardians of schoolchildren (6–7 years of age) in the city of Santo André, Brazil, completed the International Study of Asthma and Allergies in Childhood (ISAAC) standard written questionnaire. Affirmative responses regarding wheezing within the last 12 months, asthma ever, bronchitis ever (question added at the end of the questionnaire), as well as the overall ISAAC score above the predefined cutoff points, were considered indicative of asthma. **Results:** The legal guardians of 2,180 schoolchildren and 3,231 adolescents completed the questionnaires properly. Depending on the criterion adopted, the prevalence of asthma ranged from 4.9% to 26.8% for the schoolchildren and from 8.9% to 27.9% for the adolescents. The criteria with the lowest and highest prevalences were, respectively, physician-diagnosed asthma and physician-diagnosed bronchitis. When compared with other criteria, physician-diagnosed bronchitis showed concordance levels between 71.9% and 79.4%, positive predictive values between 0.16 and 0.63 and poor concordance (kappa: 0.21–0.46). Strong concordance levels were found only between wheezing within the last 12 months and the overall ISAAC score (kappa: 0.82 and 0.98). **Conclusions:** The prevalence of asthma varied significantly, depending on the criterion adopted, and there was poor concordance among the criteria. Wheezing within the last 12 months and the overall ISAAC score are the best criteria for the diagnosis of asthma, whereas the question regarding bronchitis ever did not improve the questionnaire. Modifications in this instrument can make it difficult to draw comparisons and should therefore be carefully evaluated.

**Keywords:** Asthma; Bronchitis; Diagnosis; Epidemiology; Child; Adolescent.

### Resumo

**Objetivo:** Avaliar critérios para o diagnóstico de asma em um estudo epidemiológico. **Métodos:** Adolescentes (13–14 anos) e responsáveis por escolares (6–7 anos) do município de Santo André, São Paulo, responderam o questionário escrito padrão do *International Study of Asthma and Allergies in Childhood* (ISAAC). Respostas afirmativas quanto a ter sibilos nos últimos 12 meses, ter asma ou ter bronquite (pergunta adicionada ao final do questionário), assim como o escore global do ISAAC acima dos pontos de corte pré-definidos, foram consideradas como indicativo de asma. **Resultados:** Os questionários foram adequadamente preenchidos por 2.180 responsáveis por escolares e 3.231 adolescentes. Dependendo do critério empregado, a prevalência de asma variou de 4,9% a 26,8% para os escolares, e de 8,9% a 27,9% para os adolescentes. Os critérios com as menores e maiores prevalências foram, respectivamente, diagnóstico médico de asma e diagnóstico médico de bronquite. A análise comparativa entre o diagnóstico médico de bronquite e os demais critérios mostrou níveis de concordância entre 71,9% e 79,4%, valores preditivos positivos entre 0,16 e 0,63 e concordância fraca (kappa: 0,21–0,46). Índices elevados de concordância foram observados entre sibilos nos últimos 12 meses e o escore global do ISAAC (kappa: 0,82 e 0,98). **Conclusões:** A prevalência de asma variou significativamente, de acordo com o critério diagnóstico adotado, e houve baixa concordância entre os critérios. Sibilos nos últimos 12 meses e o escore global do ISAAC são os critérios mais recomendados para se diagnosticar asma, ao passo que a pergunta “bronquite alguma vez” não demonstrou melhorar o questionário. Modificações nesse instrumento devem ser cuidadosamente avaliadas e podem dificultar comparações.

**Descritores:** Asma; Bronquite; Diagnóstico; Epidemiologia; Criança, Adolescente.

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## Introduction

Asthma is one of the principal chronic childhood diseases, presenting increasing mortality rates, responsible for a great number of hospitalizations and resulting in high social costs.<sup>(1)</sup> Until recently, there were few epidemiological data available on asthma in Brazil, which made it difficult to evaluate the impact of this disease, as well as to establish strategies to control it.<sup>(2)</sup> This scenario was changed by the International Study of Asthma and Allergies in Childhood (ISAAC),<sup>(3)</sup> a landmark study in the epidemiology of asthma worldwide and especially in Brazil. At the Brazilian centers that participated in the ISAAC Phase One, the average prevalence of wheezing within the last 12 months, a key question for the diagnosis of asthma today, was 19.5% for adolescents (13-14 years of age) and 23.1% for children (6-7 years of age). However, the reported prevalence of physician-diagnosed asthma, 13.0% for adolescents and 8.7% for children, was considerably lower.<sup>(4)</sup>

Seven years after the ISAAC Phase One had been concluded, the ISAAC Phase Three was carried out in Brazil. In the ISAAC Phase Three, the average prevalence of wheezing within the last 12 months was 19.0% and 24.3%, for adolescents and children, respectively, whereas the prevalence of physician-diagnosed asthma was 13.8% and 10.3%, respectively.<sup>(5)</sup> When analyzed individually, these data indicate minor changes in the prevalence of asthma in Brazil. We must consider, however, that only five centers participated in the ISAAC Phases One and Three, as well as that, at those centers, the actual prevalence of asthma among adolescents decreased (27.7% in Phase One vs. 19.9% in Phase Three;  $p < 0.01$ ), whereas the prevalence of physician-diagnosed asthma did not change (14.9% in Phase One vs. 14.7% in Phase Three).<sup>(6)</sup> These data indicate that the results can differ among populations, even when the same research design is employed.

Because written questionnaires are inexpensive and easily administered, they have been the method of choice for use in population studies on asthma. However, no consensus exists on how to define the diagnosis of asthma in such questionnaires. Characteristic symptoms, such as wheezing in the previous year, and physician-diagnosed asthma have been the general criteria for the assessment of asthma among children<sup>(3)</sup>

and adults.<sup>(7)</sup> The large discrepancy between these two criteria in estimating the prevalence of asthma in Brazil, in both phases of the ISAAC,<sup>(5,8)</sup> illustrates some of the difficulties encountered in the epidemiological assessment of asthma.<sup>(9)</sup> An additional problem in Brazil, and especially in the state of São Paulo, is that asthma is frequently referred to as “bronchitis”, especially when occurring in children. This might be one of the reasons why Brazilians do not know whether or not they have been diagnosed with asthma, which produces an additional bias in epidemiological assessments.

The objective of the present study was to assess the various criteria used for the diagnosis of asthma in children and adolescents. To that end, we conducted an epidemiological study based on the ISAAC protocol and applying the ISAAC written questionnaire.

## Methods

A total of 2,662 children (aged 6-7 years) and 3,423 adolescents (aged 13-14 years) were invited to participate in this study. All of the participants were enrolled in public or private schools in Santo André, Brazil (56 schools in total; 20 schools included) and had been identified in the 2000 school census carried out by the Santo André Second Municipal Office of Education. The participants were recruited on the basis of geographic distribution and proportion of public to private schools.

Distribution of the questionnaire followed the ISAAC protocol: the questionnaire was completed by the legal guardians of the children, whereas the adolescents completed it themselves, in classrooms.<sup>(3)</sup> In addition to the

**Table 1** – Prevalence of asthma by age group according to the various diagnostic criteria.

Diagnostic criteria	Age group, in years	
	6-7 (n = 2,180)	13-14 (n = 3,231)
Wheezing in the last 12 months <sup>(a)</sup>	23.8%	23.2%
Asthma ever <sup>(b)</sup>	4.9%	8.9%
Bronchitis ever <sup>(c)</sup>	26.8%	27.9%
Overall symptom score <sup>(d)</sup>	24.5%	21.8%

<sup>(b)</sup> < <sup>(a),(c)</sup> and <sup>(d)</sup> for both age groups; <sup>(c)</sup> > <sup>(a)</sup> for the 6-7-year-old age group; and <sup>(c)</sup> > <sup>(a)</sup> and <sup>(d)</sup> for the 13-14-year-old age group.

eight questions that compose the core questionnaire for asthma,<sup>(3)</sup> the following question was added at the end of the questionnaire: "Have you or your child ever had bronchitis?" After the questionnaires had been checked for missing data and incomplete responses, the data collected were transcribed into a database (Epi Info 6.0), provided by the international coordinators of the ISAAC, and then transferred to a Microsoft Excel 1997 spreadsheet.

A diagnosis of asthma was established based on four criteria: a) an affirmative response regarding wheezing within the last 12 months (question 2); b) an affirmative response regarding physician-diagnosed asthma (question 6); c) an affirmative response regarding physician-diagnosed "bronchitis" (additional question); and d) the overall ISAAC score, which was obtained by summing the points for each question of the ISAAC questionnaire, with a cut-off point of six for adolescents and five for children.<sup>(10)</sup> The ISAAC questionnaire and the points used to determine the overall score are shown in Appendix 1.

For the statistical analysis, considering the nature of the variables assessed, we employed the Student's t-test and the kappa statistic (to determine concordance). Sensitivity, specificity, the positive predictive value, the negative predictive value and the Youden index were also calculated. The responses to the question regarding "bronchitis ever" were compared with the other diagnostic criteria. The level of significance required in order to reject the null hypothesis was set at 5% ( $p < 0.05$ ) in all tests.

This study design was submitted to and approved by the Ethics in Research Committee of the Federal University of São Paulo and the ABC School of Medicine.

## Results

Of the 2,662 questionnaires distributed among the children, 2,180 (81.9%) were properly completed and returned, compared with 3,231 (94.4%) of the 3,423 distributed among the adolescents.

When the diagnosis was based on the overall ISAAC score, wheezing within the last 12 months and physician-diagnosed "bronchitis", the prevalence of asthma was higher than 20% in both age groups. In both age groups, a significantly greater number of subjects with asthma were identified based on the question regarding "bronchitis ever" than on that regarding wheezing within the last 12 months. Among the adolescents, the prevalence of asthma based on the question regarding "bronchitis ever" was significantly higher than was that based on the overall ISAAC score. However, when the criterion "asthma ever" (physician-diagnosed asthma) was applied, the prevalence of asthma was significantly lower in both age groups (4.9% for children and 8.9% for adolescents) than when any of the other criteria were applied (Table 1).

The comparative analysis between the responses to the question regarding "bronchitis ever" and the other diagnostic criteria showed concordance ranging from 71.9% to 79.4%, with a tendency toward greater concordance for children (Table 2). However, sensitivity, specificity, the positive predictive value, the negative predictive value, the Youden index and the kappa statistic were all found to be low (Table 2).

Table 3 shows the kappa statistic for each diagnostic criterion and for both age groups. For both age groups, wheezing within the last 12 months presented excellent concordance

**Table 2** – Comparative analysis between the question regarding "bronchitis ever" and the other criteria habitually used (wheezing in the last 12 months, "asthma ever" and overall score) for the diagnosis of asthma.

Evaluation parameters	Wheezing in the last 12 months		Asthma ever		Overall score	
	6-7 years	13-14 years	6-7 years	13-14 years	6-7 years	13-14 years
Concordance, %	79.1	71.9	77.1	75.4	79.4	73.7
Sensitivity	0.56	0.41	0.90	0.68	0.57	0.40
Specificity	0.88	0.84	0.74	0.76	0.88	0.87
Positive predictive value	0.62	0.50	0.16	0.22	0.63	0.54
Negative predictive value	0.84	0.79	0.99	0.96	0.85	0.80
Youden index	0.44	0.25	0.64	0.44	0.45	0.27
Kappa statistic	0.45	0.26	0.21	0.23	0.46	0.29

**Table 3** – Kappa statistic for the various criteria used for the diagnosis of asthma for both age groups.

Criterion	13-14 years			
	Wheezing in the last 12 months	Asthma ever	Bronchitis ever	Overall score
6-7 years Wheezing in the last 12 months	-	0.22*	0.26*	0.82*
Asthma ever	0.21	-	0.23*	0.28*
Bronchitis ever	0.45	0.21	-	0.29*
Overall score	0.98	0.25	0.46	-

\*coefficients for adolescents.

with the overall ISAAC score. Poor concordance was observed in all other comparisons.

## Discussion

The definition of asthma in epidemiological studies remains controversial, and there is no consensus as to what is the most rapid, inexpensive and practical method of investigation. In written questionnaires, the diagnosis of asthma can be made in different manners: by directly inquiring about physician-diagnosed asthma; by inquiring about its principal symptom (wheezing); or by combining responses to different questions (overall score).<sup>(10)</sup> Each of these criteria has advantages and disadvantages. The criterion physician-diagnosed asthma depends on a previous medical appointment, on the number of doctors the patient has visited, on patient awareness of having been diagnosed with asthma, on patient understanding/recollection of the diagnosis and on the use of the term “asthma” by the physician. In a study conducted to validate the use of the ISAAC written questionnaire after its translation into Brazilian Portuguese, it was observed that only half of the adolescents with asthma monitored at a specialized clinic identified themselves as having asthma.<sup>(10)</sup>

Direct investigation of the symptoms (wheezing) depends less on the level of access to or the quality of health care than on the report of physician-diagnosed asthma. However, it can be less specific and depend on the understanding of the symptom by the patient. In most cases, this question covers a limited period of time in order to minimize memory errors. Various authors consider that, in epidemiological questionnaires, the diagnosis of asthma based on the combination of questions about different aspects of the disease yields more realistic results,<sup>(8,11-14)</sup> which is why overall scores are commonly employed.

Underdiagnosis and undertreatment of asthma, alone or in combination with other factors, are undoubtedly responsible for the majority of pediatric hospitalizations for asthma.<sup>(15)</sup> The delay in establishing a diagnosis of asthma in children results in the worsening of symptoms, tension among family members and greater treatment costs. It has been reported that the interval between the first visit to the doctor due to respiratory symptoms and the diagnosis of asthma can be as long as three years (16 appointments).<sup>(16,17)</sup>

When treating a child with recurrent wheezing, general practitioners and pediatricians are reluctant to use the word “asthma”, more often using the word “infection”. The term “bronchitis” is more closely related to asthma symptoms and is usually easily accepted by the parents, since bronchitis is not viewed as a chronic, incurable disease. A diagnosis of “wheezy bronchitis” would represent a less severe disease than asthma, requiring less investigation and simpler treatment. In addition, many physicians consider it difficult to make a diagnosis of asthma in young children, due to the lack of a sensitive, specific marker, as well as to the existence of other diseases that present similar symptoms.

Various authors believe that clinical history (symptom progression) is most in accordance with the new concept of diagnosing asthma. Therefore, they defend the use of a combination of questions, rather than individual questions in isolation, for the diagnosis of asthma. A study of the construct validity of the ISAAC written questionnaire regarding bronchial hyperresponsiveness demonstrated that the question regarding wheezing within the last 12 months had the highest sensitivity, specificity, positive predictive value and negative predictive value,

underscoring the idea that this is the key question for the diagnosis of asthma in Brazil.<sup>(18)</sup>

In the present study, the prevalence of asthma determined based on the physician-diagnosed asthma criterion was significantly lower than that obtained with the other criteria. This is in agreement with the findings of other authors.<sup>(5,8,10)</sup> This demonstrates that few patients diagnosed with asthma are aware of the fact, probably because doctors rarely actually use the term "asthma". Physician-diagnosed "bronchitis" was a highly sensitive criterion in the population studied, presenting the highest prevalence for both age groups. When physician-diagnosed "bronchitis" was compared with the other criteria, we observed that, despite its acceptable degree of concordance, this criterion presented low positive predictive values, Youden indices and kappa statistics, as shown in Table 2. These findings indicate that the inclusion of the question regarding "bronchitis ever" in the ISAAC questionnaire provides no benefit in the epidemiological investigation of asthma.

Various authors have modified the ISAAC written questionnaire, in order to make it more understandable, by changing the question regarding physician-diagnosed asthma to include one of the synonyms generally used by doctors and parents, e.g., "bronchitis".<sup>(14,19,20)</sup> Although the results of the present study are very different from those observed in studies employing the standard method, they are similar to those obtained in studies applying the question regarding wheezing in the last 12 months.<sup>(18,19)</sup> These differences underscore the need for the use of standard instruments in epidemiological studies conducted at the national or international level, without changing their basic structure and therefore producing invalid results. In addition, new questions should be introduced only at the end of the questionnaire, as was done in the present study.

Another noteworthy finding of the present study was the confirmation that it is difficult to obtain a simple criterion for the diagnosis of asthma in a written questionnaire. The degree of concordance between the different criteria assessed was, in general, quite low (Table 3). This lack of consistency was evidenced by the great difference between the question regarding "asthma ever" and the other criteria in terms of the prevalence of asthma obtained. This same

inconsistency was observed between criteria with similar prevalence, such as the questions regarding "bronchitis ever" and wheezing in the last 12 months. For both age groups, a high degree of concordance was observed only between the overall score and the question regarding wheezing in the last 12 months (Table 3), which supports the recommendation that these criteria be used for the diagnosis of asthma. It is of note that the question regarding wheezing in the last 12 months is already included in the ISAAC questionnaire, and greater concordance between this question and the overall score was therefore expected. However, the question regarding wheezing in the last 12 months does not necessarily indicate a positive or a negative overall score. This question accounts for only one third (or two fifths) of the overall score. The overall score allows the diagnosis of asthma in children with more uncommon presentations, in which wheezing is not so evident or easily identified.

In conclusion, the ISAAC written questionnaire for asthma is a valid and effective instrument for identifying patients with asthma in epidemiologic studies. The question regarding wheezing in the last 12 months and the overall ISAAC score are the best criteria for the diagnosis of asthma. Modifications in this instrument can make it difficult to draw comparisons and should be carefully evaluated.

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**Appendix 1** – Core questionnaire for asthma of the International Study of Asthma and Allergies in Childhood and scores used to calculate the overall score (in parentheses).

1. Has your child ever had wheezing or whistling in the chest at any time in the past?  
( 2 ) Yes ( 0 ) No  
If you have answered “no” please skip to question 6.
2. Has your child had wheezing or whistling in the chest in the last 12 months?  
( 2 ) Yes ( 0 ) No
3. How many attacks of wheezing has your child had in the last 12 months?  
None ( 0 ) 1 to 3 ( 1 )  
4 to 12 ( 2 ) More than 12 ( 2 )
4. In the last 12 months, how often, on average, has your child’s sleep been disturbed due to wheezing?  
Never ( 0 )  
Less than one night per week ( 1 )  
One or more nights per week ( 2 )
5. In the last 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?  
( 1 ) Yes ( 0 ) No
6. Has your child ever had asthma?  
( 1 ) Yes ( 0 ) No
7. In the last 12 months, has your child’s chest sounded wheezy during or after exercise?  
( 2 ) Yes ( 0 ) No
8. In the last 12 months, has your child had a dry cough at night, apart from a cough associated with a cold or respiratory infection?  
( 2 ) Yes ( 0 ) No