

Health Consequences for Children With Undiagnosed Asthma-like Symptoms

Karin Yeatts, PhD; Carl Shy, MD; Mark Sotir, MPH; Stan Music, MD; Casey Herget, MSW, MPH

Background: A growing body of evidence indicates that there are a substantial number of children who report asthma-like symptoms and are not diagnosed with asthma. However, there is little information on the health consequences of asthma-like symptoms for children with these symptoms and no asthma diagnosis.

Objective: To assess the prevalence and health consequences (school absences, sleep disturbances, activity limitations, physician visits, emergency department visits, and hospitalizations) of asthma-like symptoms among children with and without physician diagnosis.

Study Design: We surveyed 122829 children aged 12 to 14 years in 499 North Carolina public middle schools. A standardized questionnaire (International Study of Asthma and Allergies in Childhood [ISAAC]) containing video scenes of adolescents experiencing asthma-like symptoms was adapted to include questions on health consequences.

Results: Seventeen percent (n=21 184) reported current asthma-like symptoms with no diagnosis of asthma (during the last 12 months.) Eleven percent (n=13 619)

of the children reported physician-diagnosed asthma with current asthma-like symptoms. Of the children with asthma-like symptoms and no diagnosis of asthma, 20% missed a half day or more of school per month because of wheeze, 25% had limited activities because of wheeze once or more per month, and 32% had sleep disturbances because of wheeze in the last 4 weeks. Seven percent of children with current asthma-like symptoms but no diagnosis reported 1 or more emergency department visits for asthma-like symptoms, and 5% reported wheeze-related hospitalizations in the last year. Of children with physician-diagnosed asthma, almost half (47%) reported missing a half day or more of school in the last month. Thirty percent of physician-diagnosed children reported 1 or more emergency department visits in the last year for asthma-like symptoms.

Conclusions: The health consequences of asthma-like symptoms in children with no diagnosis are substantial; these children are essentially untreated. Better detection of this disease group by the medical community has the potential to improve health consequences for these children.

Arch Pediatr Adolesc Med. 2003;157:540-544

From the Department of Epidemiology, School of Public Health, University of North Carolina at Chapel Hill (Drs Yeatts and Shy and Mr Sotir); and Division of Public Health, North Carolina Department of Health and Human Services, Raleigh (Dr Music and Ms Herget). Dr Music is now affiliated with Merck & Co, Inc, West Point, Penn.

THE PREVALENCE of asthma among children has increased in the last 20 years,¹⁻³ and it is now the most common chronic childhood disease in the United States.⁴ Recent evidence, much of it from Europe, suggests that asthma is underdiagnosed and undertreated,⁵⁻¹¹ although to what extent is still debated, as not all asthma-like symptoms warrant asthma diagnosis. The magnitude of health consequences of wheezing symptoms (sleep disturbances, activity limitations, and missed school days) in children with no diagnosis of asthma is generally unknown, and little information has been reported on health care use in these symptomatic groups.^{6,7}

Researchers developed an internationally standardized instrument to as-

sess the prevalence of asthma-like symptoms (International Study of Asthma and Allergies in Childhood [ISAAC]). This instrument was designed to overcome problems in the reporting of asthma-like symptoms because of variations in diagnostic criteria, access, and use of health care, as well as the subject's lack of symptom recognition.¹² The ISAAC questionnaire is a validated survey tool that has been shown to have better sensitivity and specificity than bronchial hyperresponsiveness in measuring asthma prevalence among the population.^{13,14} It is a simple, low-cost, valid,¹⁵ and efficient way to measure the prevalence of asthma-like symptoms and physician-diagnosed asthma.

Given the strengths of the ISAAC questionnaire in obtaining population-based estimates of the prevalence of

asthma-like symptoms and diagnosis, while minimizing diagnostic bias and failure of subjects to recognize symptoms, we adapted the ISAAC methods for this statewide surveillance of asthma and asthma-like symptoms among North Carolina children attending public middle schools.¹⁶ The state health department recognized the need to systematically measure the prevalence of asthma statewide on a school-specific and a county-specific basis and to establish a baseline from which subsequent assessment of the effectiveness of planned and locally designed interventions could be conducted.

In this population-based survey, we measured the prevalence of asthma-like symptoms (wheezing and cough) among children with and without a physician diagnosis of asthma. We compared the functional consequences and health care use of children with current wheezing symptoms with no physician diagnosis with those of 2 groups: (1) children with physician-diagnosed asthma with current asthma-like symptoms and (2) asymptomatic children who reported never having any asthma-like symptoms or diagnosis.

METHODS

The target population was enumerated from 1999-2000 enrollment records kept by the North Carolina Department of Public Instruction and included 565 public schools with 192 248 children in the seventh and eighth grades. The University of North Carolina at Chapel Hill School of Public Health Institutional Review Board reviewed and approved the project. In December 1999, questionnaires were mailed to the 565 public school principals. The 30-minute survey was conducted in homerooms, science class, or physical education class. All questionnaires were administered and completed by June 2000. To ensure high-quality data, questionnaires were checked for missing data and skip patterns.

Schools that participated were compared with those that did not with respect to demographic data. These data were obtained from the statistical branch of the North Carolina Department of Public Instruction. Demographic data on ethnicity, sex, and free school lunch program enrollment were compared between the 499 participating schools and the 66 non-participating schools. There were no significant differences among the demographic variables of socioeconomic status (enrollment in the free or reduced school lunch program), ethnicity, or sex for schools that participated and those that did not ($P=.66$, $P=.61$, and $P=.58$, respectively; χ^2 test).

The final response rate was 67% (128 568/192 248) for seventh- and eighth-grade children (aged 12-14 years) enrolled in public school in 1999-2000. Response rates by school (499/565, 88%) and county (99/100, 99%) were substantially higher. Of the 128 568 children who filled out questionnaires, 5739 had missing data on the video symptom and physician diagnosis questions and were excluded from the analyses. Analyses were presented for the remaining 122 829 children.

The questionnaire was adapted from the ISAAC survey.¹⁶⁻¹⁸ Written and video symptom questions from the ISAAC survey were included. The video symptom sequence consisted of 5 symptom scenes being experienced by an adolescent: (1) wheezing at rest during the day, (2) wheezing after exercise, (3) waking at night by wheezing, (4) waking at night by cough, and (5) a severe wheezing attack with intercostal retractions. Children were considered as having asthma-like symptoms if they gave a positive response to any of scenes 1, 2, 3, or 5.

Questions were added regarding physician diagnosis, functional consequences of wheezing or breathing problems, health

Table 1. Prevalence of Asthma-like Symptoms Among 122 829 Children With and Without a Physician Diagnosis of Asthma*

Group	Symptom	No. (%) of Children
Diagnosed asthmatics	Current wheeze	12 174 (9.9)
	Current cough	1445 (1.2)
	No current symptoms	5748 (4.7)
Asthma-like symptoms with no diagnosis	Current wheezers	21 184 (17.2)
	Current cough only	9594 (7.8)
	No current symptoms	8040 (6.5)
Asymptomatic children	No wheezing symptoms ever	64 644 (52.6)

*Percentages do not sum to 100 because of rounding.

care use, and environmental exposures. Functional consequences included wheezing-related sleep disturbances, activity limitations, and missed school days. Health care use questions consisted of wheezing-related physician visits, emergency department visits, and hospitalizations. To standardize the administration of the questionnaire and to aid children with reading difficulties, the entire questionnaire was visually presented on a video screen and read aloud 1 question at a time, with skip patterns emphasized. The students were guided by the videotape through the entire written questionnaire. This method of administration was found to be feasible for statewide surveillance.¹⁶

Functional consequences and health care use variables were presented for the following groups: (1) children reporting current (during the last 12 months) wheezing symptoms (any of 4 ISAAC video wheezing symptoms) and no physician diagnosis of asthma ($n=21\,184$), (2) children reporting current wheezing symptoms (any ISAAC video wheezing symptoms) and physician diagnosis of asthma ($n=12\,174$), and (3) asymptomatic children reporting no wheezing or coughing (none of the ISAAC video symptoms ever) and no physician diagnosis of asthma ($n=64\,644$). No seasonal variations in symptom reporting, functional consequences, or health care use were found in the 2 diseased groups.

Differences in proportions among groups were assessed using χ^2 statistics with respect to functional consequences, health care use, and medication use. Categories for each of the outcome variables of functional consequences, health care use, and medication use were collapsed to none or any.

RESULTS

The study population ($N=122\,829$) was ethnically diverse, with 63% white, 26% African American, 2% Native American, 2% Asian, and 6% of more than 1 race. Nine percent of the children reported Latino ethnicity. Thirty-three percent of the children reported being enrolled in the free or reduced school lunch program. Forty-nine percent of the children were classified as living in rural areas based on county of residence. Fifteen percent of the children reported current smoking (in the last 30 days).

Table 1 illustrates the prevalence of asthma-like symptoms with and without physician diagnosis among the 122 829 children. More than half (53%) of the children reported never having had wheezing, coughing, or breathing difficulties in their life. The prevalence of ever physician-diagnosed asthma was 16%, 10% had current

Table 2. Prevalence of Health Consequences by Disease Group

Consequence	Undiagnosed Wheezers* (n = 21 184)		Diagnosed Current Asthmatics (n = 12 174)		Asymptomatic† (n = 64 644)	
	% of Children	95% CI	% of Children	95% CI	% of Children	95% CI
Any sleep disturbances at night because of wheezing in last 4 wk	31.52	30.89-32.15	49.72	48.83-50.61	2.41	2.29-2.53
Limited activities because of wheezing ≥1 times per month in last 12 mo	24.81	24.23-25.39	51.51	50.62-52.40	1.56	1.46-1.66
≥½ School day per month missed because of wheezing in last 12 mo	20.28	19.74-20.82	46.25	45.36-47.14	2.29	2.17-2.41
≥1 Physician visits because of wheezing in last 12 mo	27.59	26.99-28.19	71.12	70.31-71.93	4.48	4.32-4.64
≥1 Emergency department visits because of wheezing in last 12 mo	6.97	6.63-7.32	30.09	29.27-30.91	0.67	0.61-0.73
≥1 Hospitalizations because of wheezing in last 12 mo	5.76	5.45-6.07	23.11	22.36-23.86	0.48	0.43-0.53
Used an inhaler ≥1 times per month in last 12 mo	9.22	8.83-9.61	78.29	77.55-79.03	0.87	0.80-0.94

Abbreviation: CI, confidence interval.

*Children with current wheezing symptoms and no diagnosis of asthma.

†Children reporting no asthma-like symptoms or asthma diagnosis ever.

(in the last 12 months) wheezing symptoms, 1% had current cough, and 5% had no current symptoms. Combining diagnosed asthmatics with current symptoms (11%), diagnosed asthmatics without current symptoms (5%), and children with undiagnosed current wheezing (17%) gives a population-based prevalence of 33% for ever having asthma or asthma-like symptoms. More than one quarter (28%) of the children reported current asthma-like symptoms or asthma.

One half of the diagnosed asthmatics with current wheezing and one third of the children with undiagnosed current wheezing reported frequent symptoms, defined as wheezing 1 or more times per month (data not shown). There were no differences between urban and rural counties in the prevalence of physician-diagnosed asthma or wheezing with no diagnosis.

Functional consequences and health care use related to asthma-like symptoms for the 3 groups of interest are presented in **Table 2**. All χ^2 statistics calculated to evaluate differences among groups with respect to functional consequences, health care use, and inhaler use were statistically significant at $P < .001$, with the 95% confidence intervals not overlapping for any of the variables or groups. As expected, diagnosed asthmatics with current symptoms experienced a high frequency of functional consequences (47%, 52%, and 49% reporting missed school days, activity limitations, and sleep disturbances, respectively) because of wheezing or problems in the last year or 4 weeks. However, children with undiagnosed wheezing also reported substantial amounts of missed school days, activity limitations, and sleep disturbances because of wheezing (20%, 25%, and 32%, respectively).

Table 2 also presents data on the health care use in children with asthma-like symptoms. Children with current wheezing and no asthma diagnosis were essentially untreated in terms of inhaler use (only 9% reported use ≥1 times per month in the last year) but had a considerably higher frequency of clinic (28%) and emergency department visits (7%) for wheezing or breathing difficulties than children with no symptoms and no diagnosis. Although 71% of diagnosed asthmatics reported vis-

iting a physician for wheezing difficulties 1 or more times in the last year and 78% reported using an inhaler in the last year, a high percentage (30%) reported visiting the emergency department 1 or more times in the last year, and 23% reported 1 or more hospitalizations related to wheezing or breathing difficulties.

COMMENT

To our knowledge, this is the first population-based study of this magnitude that has used an internationally validated and standardized survey tool to measure the prevalence of asthma-like symptoms with and without a physician diagnosis and the related health consequences. Although the ISAAC survey has been conducted in 56 countries with 463 801 children,^{17,18} the association of asthma-like symptoms with health consequences has not been previously examined.

We observed a high proportion (28%) of children with current asthma-like symptoms. More than 60% (21 184 divided by [13 619 + 21 184]) of these symptomatic children had no diagnosis of asthma. The effect of asthma-like symptoms on the lives of children with no diagnosis is considerable: 20% missed a half day or more of school per month because of wheezing, 25% had limited activities because of wheeze once or more per month, 32% had sleep disturbances because of wheezing in the last 4 weeks, 7% visited the emergency department for wheezing, and 5% were hospitalized for wheezing or breathing difficulties, all of which are considerably in excess of the experiences reported by asymptomatic or "healthy" children.

Sleep disturbances because of wheezing are one example of the major problems these children face. The long-term clinical implications include chronic sleep deprivation and the related reduced immune function, increased susceptibility to respiratory infections, reduced cognitive function, and decreased learning ability.

Most of the children with asthma-like symptoms and no diagnosis may have a mild form of the disease, given the low use of health care in this group. However, the finding that a considerable proportion of children re-

ported functional consequences (Table 2) supports including these children in the prevalence estimate for asthmatic disease. Children with a lower frequency of wheezing may be below the clinical threshold for a firm diagnosis of asthma, but the health consequences (school absences, activity limitations, and sleep disturbances associated with asthma-like symptoms) make this group similar to the diagnosed asthmatics and distinctly different from asymptomatic children. The term *asthma* unifies what may be a heterogeneous group of disorders or different disease subtypes that produce similar clinical features with various levels of severity.¹²

Our findings that the prevalence of physician-diagnosed asthma is substantially lower than the prevalence of asthma-like symptoms among the community support results of previous studies.^{5-11,19,20} Among children with asthma-like symptoms, 13% to 85% have a physician diagnosis according to various studies,^{5,6,8,10,20} with many estimates being approximately 66%. In our study, using all asthma-like symptoms reported in the last 12 months as the denominator, we estimate 39% of children with asthma-like symptoms being diagnosed as asthmatic, a figure somewhat lower than other estimates. A more conservative estimate would be to include only children with frequent wheezing (≥ 1 times per month) rather than all children with wheezing in the denominator. With the more conservative assumption, we estimate that 65% of children with current asthma-like symptoms are diagnosed as asthmatic. In this estimate, the other 35% are children with asthma-like symptoms but no diagnosis of asthma.

The wide variations in estimates of asthma prevalence around the world are affected by the sampling frame, temporal and country variation in diagnostic patterns, health care delivery system, and parental and clinician recognition of symptoms. Our estimates of wheezing prevalence based on 122829 children agree well with the estimates reported in the worldwide ISAAC survey from other industrialized countries.^{17,18} Our estimates of wheezing during the day at rest in the last 12 months were 23% (written questionnaire) and 13% (video questionnaire), which are similar to the estimates reported in the worldwide study of 20% to 25% (written) and approximately 13% (video) for the US ISAAC sites.¹⁸ Our estimate of 11% of children in the population with physician-diagnosed current asthma is comparable to but somewhat higher than the most recent Third National Health and Nutrition Examination Survey estimate of 6.7% with physician-diagnosed asthma in children aged 2 to 16 years.²¹ The National Health Interview Survey on Child Health reports an asthma estimate considerably lower (4.9%) for children aged 6 to 18 years.²²

Functional consequences and health care use among physician-diagnosed asthmatics have been previously documented by others.^{6,7,21-28} Although there are variations in terms used for *health consequences* (effect, disability, or illness activity), they often include school absences, activity limitations, and sleep disturbances. Many of the studies are based on National Health Interview Survey on Child Health data²²⁻²⁵ and Third National Health and Nutrition Examination Survey data,²¹ both of which use parental reporting of asthma. Other studies include

What This Study Adds

The health consequences of diagnosed asthma in US children have been documented in the literature. However, little information exists concerning the health consequences of asthma-like symptoms in children with no diagnosis of asthma. This study provides evidence indicating that the health consequences of asthma-like symptoms in children with no diagnosis are substantial. These children are essentially untreated and require more recognition from primary care physicians. Better detection of this disease group by the medical community has the potential to improve health consequences and reduce medical care costs. Direct and indirect cost estimates of the effect of asthma in the United States should include this group of children.

children enrolled in managed care organizations²⁷ or school-based surveys.²⁶ Little information exists with regard to the health consequences of wheezing in children with no diagnosis of asthma.

A potential limitation of this study is that the data are self-reported by the adolescents. Clinicians have rigorously validated the ISAAC.^{13,15,29} Self-reported symptoms using the ISAAC questionnaire were found to be more reliable than bronchial hyperresponsiveness, compared with physician diagnosis of asthma as a gold standard.^{13,30} The validity of adolescents' reporting of asthma-like symptoms in the ISAAC video questionnaire was high, with a specificity of 0.87 and sensitivity of 0.75, vs a physician diagnosis of clinically active asthma as a gold standard.¹⁵ In a validation study of the ISAAC questionnaire, Renzoni et al²⁹ evaluated the agreement between parents' and adolescents' reporting of physician-diagnosed asthma. They found that 97.3% of adolescents agreed with their parents that they did not have asthma. Research has shown that parents underestimate the presence of wheezing in their adolescent children and suggests that obtaining direct information from adolescents may be essential for a correct evaluation of respiratory symptoms.^{29,31} In our study, a small percentage of asymptomatic adolescents with no reported wheezing symptoms reported functional consequences ($\leq 2\%$) and health care use ($\leq 4\%$). The question asked was phrased as to whether the functional consequences and health care use were because of "wheezing, dry cough, or breathing difficulties not due to a cold or chest infection." It would have been optimal to validate questionnaire responses with medical records in a subset of students; however, the public health budget and confidentiality limitations precluded such activities.

Strengths of the study include (1) a population-based sample rather than a clinic-based sample, the latter of which includes only those children with access to care or parents who seek care for their children, (2) an internationally standardized and validated measurement tool, and (3) a large diverse study sample with a high response rate.

The results of this large, population-based survey using an internationally standardized measurement tool indicate that among adolescents there is a high preva-

lence of asthma-like symptoms with and without physician diagnosis and that both groups experience substantial functional consequences. However, children with asthma-like symptoms and no physician diagnosis are essentially untreated.

Accepted for publication January 16, 2003.

This study was funded by grant 15301013 from the Children and Youth Branch, Women's and Children's Health Section, Division of Public Health, North Carolina Department of Health and Human Services.

Corresponding author and reprints: Karin Yeatts, PhD, Department of Epidemiology, School of Public Health, University of North Carolina at Chapel Hill, Campus Box 7435, McGavran Greenberg Hall, Chapel Hill, NC 27599-7435 (e-mail: Karin_Yeatts@unc.edu).

REFERENCES

- Weitzman M, Gortmaker SL, Sobol AM, Perrin JM. Recent trends in the prevalence and severity of childhood asthma. *JAMA*. 1992;268:2673-2677.
- Mannino D, Homa D, Pertowski C, et al. Surveillance for asthma—United States, 1960-1995. *MMWR Morb Mortal Wkly Rep*. 1998;47(SS-1):1-11.
- Gergen PJ, Mullally DI, Evans R. National survey of prevalence of asthma among children in the United States, 1976 to 1980. *Pediatrics*. 1988;81:1-7.
- Adams PF, Marano MA. *Current Estimates From the National Health Interview Survey 1994: Vital and Health Statistics*. Washington, DC: Dept of Health and Human Services; 1995. DHHS publication PHS 96-1521. Series 10, No. 193.
- Siersted HC, Boldsen J, Hansen HS, Mostgaard G, Hyldebrandt N. Population based study of risk factors for underdiagnosis of asthma in adolescence: Odense schoolchild study. *BMJ*. 1998;316:651-656.
- Crain EF, Weiss KB, Bijur PE, Hersh M, Westbrook L, Stein RE. An estimate of the prevalence of asthma and wheezing among inner-city children. *Pediatrics*. 1994;94:356-362.
- Silver E, Crain E, Weiss K. Burden of wheezing illness among US children reported by parents not to have asthma. *J Asthma*. 1998;35:437-443.
- Speight AN. Is childhood asthma being underdiagnosed and undertreated? *BMJ*. 1978;2:331-332.
- Speight AN, Lee DA, Hey EN. Underdiagnosis and undertreatment of asthma in childhood. *BMJ*. 1983;286:1253-1256.
- Kaur B, Anderson HR, Austin J, et al. Prevalence of asthma symptoms, diagnosis, and treatment in 12-14 year old children across Great Britain (International Study of Asthma and Allergies in Childhood, ISAAC UK). *BMJ*. 1998;316:118-124.
- Pearce N, Douwes J, Beasley R. The rise and rise of asthma: a new paradigm for the new millennium? *J Epidemiol Biostat*. 2000;5:5-16.
- Beasley R, Lai CK, Crane J, Pearce N. The video questionnaire: one approach to the identification of the asthmatic phenotype. *Clin Exp Allergy*. 1998;28(suppl 1):8-12.
- Jenkins MA, Clarke JR, Carlin JB, et al. Validation of questionnaire and bronchial hyperresponsiveness against respiratory physician assessment in the diagnosis of asthma. *Int J Epidemiol*. 1996;25:609-616.
- Pearce N, Pekkanen J, Beasley R. Role of bronchial responsiveness testing in asthma prevalence surveys. *Thorax*. 2000;55:352-354.
- Fuso L, De Rosa M, Corbo GM, et al. Repeatability of the ISAAC video questionnaire and its accuracy against a clinical diagnosis of asthma. *Respir Med*. 2000;94:397-403.
- Yeatts K, Shy CM, Wiley J, Music S. Statewide adolescent asthma surveillance. *J Asthma*. 2000;37:425-434.
- ISAAC Steering Committee. Worldwide variations in the prevalence of asthma symptoms: the International Study of Asthma and Allergies in Childhood (ISAAC). *Eur Respir J*. 1998;12:315-335.
- ISAAC Steering Committee. Worldwide variation in prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema: ISAAC: the International Study of Asthma and Allergies in Childhood. *Lancet*. 1998;351:1225-1232.
- Lee DA, Winslow NR, Speight AP, Hey EN. Prevalence and spectrum of asthma in childhood. *BMJ*. 1983;286:1256-1258.
- Strachan DP, Anderson HR, Limb ES, O'Neil A, Wells N. A national survey of asthma prevalence, severity, and treatment in Great Britain. *Arch Dis Child*. 1994;70:174-178.
- Rodriguez MA, Winkleby MA, Ahn D, Sundquist J, Kraemer HC. Identification of population subgroups of children and adolescents with high asthma prevalence: findings from the Third National Health and Nutrition Examination Survey. *Arch Pediatr Adolesc Med*. 2002;156:269-275.
- Fowler MG, Davenport MG, Garg R. School functioning of US children with asthma. *Pediatrics*. 1992;90:939-944.
- Taylor WR, Newacheck PW. Impact of childhood asthma on health. *Pediatrics*. 1992;90:657-662.
- Halfon N, Newacheck PW. Childhood asthma and poverty: differential impacts and utilization of health services. *Pediatrics*. 1993;91:56-61.
- Newacheck PW, Halfon N. Prevalence, impact, and trends in childhood disability due to asthma. *Arch Pediatr Adolesc Med*. 2000;154:287-293.
- Forrest CB, Starfield B, Riley AW, Kang M. The impact of asthma on the health status of adolescents. *Pediatrics* [serial online]. 1997;99:e1. Available at: <http://www.pediatrics.org/cgi/content/full/99/2/e1>. Accessed December 6, 2002.
- Diette GB, Markson L, Skinner EA, Nguyen TT, Algatt-Bergstrom P, Wu AW. Nocturnal asthma in children affects school attendance, school performance, and parents' work attendance. *Arch Pediatr Adolesc Med*. 2000;154:923-928.
- Doull I, Williams A, Freezer N, Holgate S. Descriptive study of cough, wheeze and school absence in childhood. *Thorax*. 1996;51:630-631.
- Renzoni E, Forastiere F, Biggeri A, et al, for the SIDRIA Collaborative Group. Differences in parental- and self-report of asthma, rhinitis and eczema among Italian adolescents: Studi Italiani sui Disordini Respiratori dell' Infanzia e l'Ambiente. *Eur Respir J*. 1999;14:597-604.
- Pekkanen J, Pearce N. Defining asthma in epidemiological studies. *Eur Respir J*. 1999;14:951-957.
- Braun-Fahrlander CH, Gassner M, Grize L, et al, for the SCARPOL-Team. Comparison of responses to an asthma symptom questionnaire (ISAAC core questions) completed by adolescents and their parents: Swiss Study on Childhood Allergy and Respiratory Symptoms With Respect to Air Pollution. *Pediatr Pulmonol*. 1998;25:159-166.