

Comparison of clinically diagnosed asthma with parental assessment of children's asthma in a questionnaire

Hederos C-A, Hasselgren M, Hedlin G, Bornehag C-G. Comparison of clinically diagnosed asthma with parental assessment of children's asthma in a questionnaire.

Pediatr Allergy Immunol 2006.

© 2006 The Authors

Journal Compilation © 2006 Blackwell Munksgaard

Epidemiological evaluations of the prevalence of asthma are usually based on written questionnaires (WQs) in combination with validation by clinical investigation. In the present investigation, we compared parental assessment of asthma among their preschool children in response to a WQ with the corresponding medical records in the same region. An International Study of Asthma and Allergies in Childhood (ISAAC)-based WQ was answered by 75% of the parents of 6295 children aged 1–6 yr. Clinically diagnosed asthma, recorded in connection with admissions to the hospital or a visit to any of the outpatient clinics in the same region, were analysed in parallel. Finally, a complementary WQ was sent to the parents of children identified as asthmatic by either or both of this approaches. In response to the WQ 5.9% were claimed to suffer from asthma diagnosed by a doctor. According to the medical records, the prevalence of clinically diagnosed asthma was 4.9%. The estimated prevalence among children requiring treatment for their asthma was 4.4%. The sensitivity of the WQ was 77%, the specificity 97.5%. In the 1–2 yr age group the sensitivity was only 22%. This WQ was able to identify 54% of the children with a medical record of asthma. Forty percent of the children claimed by their parents to be asthmatic had no medical record of asthma. An ISAAC-based parentally completed WQ provided an acceptable estimation of the prevalence of asthma in children 2–6 yr of age, although only half of the individual patients identified in this manner are the same as those identified clinically.

Carl-Axel Hederos^{1,3}, Mikael Hasselgren², Gunilla Hedlin³ and Carl-Gustaf Bornehag^{4,5,6}

¹Primary Care Research Unit, Karlstad, ²Section of Family Medicine and Clinical Epidemiology, Department of Public Health and Caring Sciences, Uppsala University, Uppsala, ³Karolinska Institute, Astrid Lindgrens Children's Hospital, Stockholm, ⁴Division for Public Health, Department of Social Sciences, Karlstad University, Karlstad, ⁵Swedish National Testing and Research Institute, Borås, Sweden, ⁶International Centre for Indoor Environment and Energy, Technical University of Denmark, Copenhagen, Denmark

Key words: asthma; medical records; preschool children; prevalence; questionnaires

Carl-Axel Hederos, Primary Care Research Unit, BUM VC Gripen, Box 547, SE 651 12 Karlstad, Sweden
Tel.: +46 54 616645
Fax: +46 54 616619
E-mail: carl-axel.hederos@liv.se

Accepted 14 August 2006

The prevalence of asthma, a major chronic disease around the world, is most often estimated on the basis of responses to written questionnaires (WQs), which indicate an increasing frequency during the past few decades although there are indications of a shift in this trend (1–3). Telephone surveys represent another approach to estimate prevalence of this disease (4). However, certain reports indicate that WQs or other types of parental assessments of asthma do not correlate with the prevalence of symptoms, clinical findings or pulmonary function test results (5–7).

Furthermore, studies of the medical records of adult patients have indicated a prevalence of asthma lower than that suggested by corresponding questionnaires (8). Another approach to determine the prevalence asthma involves analysis of purchases of asthma medication which identifies those in need of asthma treatment (9, 10). Still another indirect way is to analyze the use of healthcare services (11).

Probably the best alternative to establish the prevalence and incidence is to perform prospective studies (12). However, these are

time-consuming and for practical purposes questionnaires will continue to be used.

Although validation of one of these, the International Study of Asthma and Allergies in Childhood (ISAAC) WQ in school children, has been performed employing clinical investigations the use of this same WQ with preschool children has not been validated clinically (13). The reproducibility of answers to similar questions has been evaluated for other WQs designed for this age group (14).

The aim of our present investigation was to generally discuss the usefulness of WQs for estimation of the asthma prevalence with the help of a comparison of the results from a modified version of the ISAAC WQ filled out by parents of children 1–6 yr old in a given region of Sweden to the diagnosis of asthma found in the medical records for this same region.

Methods

Three different sets of data were employed in the present study. The primary source of data was questions from the ISAAC WQ used in the first phase of the Dampness in Buildings and Health (DBH) study, while the second source was the medical records for this same region (15). The children included in the medical records and in the WQ were all matched on the basis of their personal identification numbers. This was possible as each individual in Sweden is characterized by an identification number. All outpatient centers in our region have computerized records of their patients and each visit is registered, along with the ICD 10 code, to allow statistical evaluation (not for billing). This code can then be used as a measure of period prevalence in clinical practice.

The respiratory symptoms and frequency of the parent reported doctor-diagnosed asthma reported in response to the WQ were compared with the recorded medical diagnose. As there were discrepancies in the findings obtained using these two approaches we decided also to design and distribute a complementary WQ to the parents of all children with asthma according to either or both of these data sets, the responses to which constituted the third data set.

The DBH WQ

The DBH WQ was sent in March 2000 to the parents of all the 14,077 children in Värmland Sweden, who were 1–6 yr old in 1999. However, in the present investigation, only the responses concerning children living in Karlstad, the

regional capital or surrounding areas were considered. The response rate in this region was 75%; 4749 of the 6295 parents who received the WQ responded, but of these 53 did not answer the specific question, 'Has your child been diagnosed with asthma by a doctor?'. This was the only question modified compared with the original ISAAC WQ.

The medical records

In Sweden, preschool children with asthma receive their main care from pediatricians working in ambulatory clinics. Wheezy children are often identified as asthmatics in these clinics or after admission to a pediatric ward (11). Children with asthma can also be identified and treated by General Practitioners (GPs) but are usually referred to pediatric ambulatory care (16). Therefore, all 70 of the GPs in the study area also made reports concerning asthma diagnosis in this age group.

Using the patient records from the Central Hospital of Karlstad, as well as the records of all the pediatric outpatient clinics in our study area, i.e. five pediatricians, including the sole private pediatrician, we examined the information for 1999 concerning asthma in all children aged 1–6 yr.

In Sweden, the diagnosis of asthma in children of this age group is routinely based on one of the following criteria: (i) three episodes of wheezing prior to 2 yr of age; (ii) a first wheezing episode after the age of 2; or (iii) the first episode of wheezing in a child who also suffers from other atopic diseases.

The complementary WQ

By matching these two data sets and assuming that the medical diagnostic code was correct four groups of patients were identified:

- 1 The false-negative group, who had a clinical diagnosis of asthma, but whose parents denied this in responding to the DBH WQ.
- 2 The false-positive group, who had no clinical record of asthma but whose parents stated the opposite in response to the DBH WQ.
- 3 The congruent group, for whom doctors and parents agreed that the child had asthma.
- 4 The non-responders, who had a recorded clinical diagnosis of asthma and whose parents did not answer the DBH WQ.

In an attempt to explain the discrepancies observed concerning the diagnosis of asthma

the parents of the children in these four groups received a postal complementary WQ during 2003 which could be answered anonymously. The central questions included in this WQ are presented in Table 5. If no answer was received two reminders were sent.

Statistical analysis

Analysis of descriptive statistics was performed employing the statistical package for social sciences, SPSS, version 11.0 (SPSS, Chicago, IL, USA). In connection with tests for two-sided levels of significance, a p -value < 0.05 was considered significant. Prevalence rates are presented together with their 95% CI. This study was approved by the regional ethics committee.

Results

The DBH WQ vs. medical records

As summarized in Table 1, the prevalence pre-school asthma in the DBH WQ was 5.9% (95% CI = 5.2–6.6). The findings based on medical records are presented in Table 2. We received answers from all the centers in the study area, allowing complete documentation of clinically diagnosed asthma. Fifty percent of the asthmatic children were diagnosed by pediatricians in ambulatory clinics, 33% at the outpatient clinic of the hospital and 17% by GPs. The overall prevalence of clinical asthma was 4.9% (95% CI = 4.4–5.4) corresponding to 309 children altogether. This prevalence is different from the WQ prevalence ($p < 0.05$). On the average each child made 2.4 visits to the outpatient clinics per year. Hospital admissions for asthma were frequent during the first 2–3 yr of life.

The parents of 216 of the 309 children with clinical asthma (70%) answered the DBH WQ in its entirety. Fifty of these 216 parents (23%) who denied or had forgotten that their children had asthma in the WQ constituted the false-negative group (Table 3). Of the 275 children whose

Table 2. The medical records: prevalence of asthma, visits to the outpatient clinic, and hospital admissions in children 1–6 yr of age during 1999

Age (yr)	n	Children with asthma, n (%)	Visits to the outpatient clinic per child	Hospital admissions per 1000 children
1 to <2	1371	46 (3.9)	3.2	11.9
2 to <3	1345	70 (6.1)	2.5	6.9
3 to <4	1246	67 (5.4)	2.1	4.8
4 to <5	1154	73 (5.4)	2.2	4.5
5 to 6	1179	53 (3.9)	2.1	0.7
Total	6295	309 (4.9)	2.4	5.8

Table 3. Comparison of the prevalence of asthma among 1- to 6-yr-old children indicated by their parents' responses to the Dampness in Buildings and Health questionnaire and by the medical records

	Clinical diagnosis		Total number
	Asthmatic	Non-asthmatic	
Children reported by their parents to have asthma	166	109	275
Children reported by their parents not to have asthma	50	4371	4421
Children whose parents did not answer the questionnaire	93	1506	1599
Total number	309	5986	6295

parents reported that they had asthma in the WQ, only 166 had actually received such a diagnosis and thus belonged to the congruent group. Accordingly the false-positive group included the remaining 109 children. In addition, the medical records revealed that 93 children whose parents did not answer the WQ had clinical asthma, indicating a prevalence among the non-responders of 5.8% (95% CI = 4.8–7.2). This prevalence is not different from the responders or from the clinical prevalence. There were no differences in age or gender distribution compared to those who answered the WQ except that the asthma prevalence in the 5–6 yr old was higher (9.2%).

Validation of the respiratory symptoms reported by parents in response to the DBH WQ

Table 1. Prevalence of parent reported symptoms localized to the airways in girls and boys of different ages during 1999 according to 4696 answers to the Dampness in Buildings and Health questionnaire

Symptoms	Prevalence, n (%)							
	Total	Gender		Age (yr)				
		Girls	Boys	1 to <2, n = 896	2 to <3, n = 886	3 to <4, n = 922	4 to <5, n = 984	5 to 6, n = 1008
Wheezing ever	1189 (25.4)	515 (21.7)	674 (29.0)	232 (25.9)	246 (27.8)	236 (25.6)	240 (24.4)	235 (23.3)
Wheezing during the past 12 months	886 (19.1)	396 (16.7)	490 (21.1)	238 (26.6)	198 (22.4)	163 (17.7)	154 (15.7)	133 (13.2)
Doctor-diagnosed asthma	275 (5.9)	105 (4.4)	170 (7.3)	32 (3.6)	59 (6.7)	60 (6.5)	67 (6.8)	57 (5.7)

Table 4. Validation of the respiratory symptoms reported by parents in response to the Dampness in Buildings and Health questionnaire in relationship to clinically diagnosed asthma

	Sensitivity (%)	Specificity (%)	Positive predictive value
Asthma diagnosed by a doctor?	76.9	97.5	0.60
Wheezing during the past 12 months?	86.3	84.1	0.21
Wheezing ever?	94.5	77.8	0.17

against clinically diagnosed asthma is presented in Table 4. Further analysis showed that the age-adjusted sensitivity of the question concerning diagnosis of asthma by a doctor was 22% for children 1–2 yr of age, but for 2- to 3-yr-old children this value was 66% and it rose to 83% in the 5- to 6-yr-old children.

Considering all discrepancies between these two sets of data, including lack of response, it can be concluded that the WQ was able to identify only 54% (166/309) of the children with clinically diagnosed asthma, while yielding 40% (109/275) false-positive diagnoses.

The parents of only 63% of the children at high risk for persistent asthma (as identified and monitored by pediatricians) responded to the WQ, but the sensitivity with respect to this group was 100%.

The complementary WQ

Our complementary WQ directed to the parents of children who were asthmatic either according to the DBH WQ and/or medical records had a response rate of 76% and is summarized in Table 5. The gender distribution was the same as in the clinical and WQ material. However, there were only half as many children among the false-negative group 5–6 yr old and likewise only half as many in the 1–2 yr old in the false-positive group as expected. In the congruent group there was only one of five of the expected number of children in the 1- to 2-yr-old group.

Discussion

The most interesting findings of our present investigation arose from comparison of the medical records to the responses to the DBH WQ. The overall prevalence indicated by these two sets of data was similar, but the individual patients identified as asthmatic were far from identical.

Our validation of the DBH WQ utilizing clinically diagnosed asthma registered in medical records as the reference point revealed a relatively high and, at least at ages older than 2, constant sensitivity and specificity, but the positive predictive value (PPV) was low (Table 4). Obviously the predictive usefulness of a WQ in 1–6 yr old could be improved if children 1–2 yr old were omitted because of low sensitivity in this age group, probably because of problems to define asthma during these years (17). As clinically diagnosed asthma was as common among non-responders as among responders to the DBH WQ, selection bias cannot explain this discrepancy.

The DBH WQ identified no more than 54% of the children with medical records of asthma and gave simultaneously a 40% false-positive rate of diagnosis. The conclusion to be drawn is that even though WQs may provide a correct estimate of the overall prevalence of asthma, it is not possible to identify individual children with clinically diagnosed asthma simply by asking their parents. These findings are in agreement with those obtained by analyzing the purchase of asthma medication (9). In that study only 35% of those children reported by their parents as being asthmatics were associated with the purchase of asthma medication. On the other hand, 45% of those whose parents had purchased such medication were not described as having asthma. Accordingly, these investigators conclude that relying on parental reports may lead to underestimation of the prevalence of serious asthma. This is in agreement with our present results

Table 5. Responses of parents of children who were asthmatics in 1999 (according either to their parents and/or doctors) to the complementary questionnaire (%)

Children with the following characteristics	False-negative group (n = 50)	False-positive group (n = 109)	Congruent group (n = 166)	No response group (n = 93)
Wheezing prior to 1999	32 (64)	85 (78)	152 (92)	82 (88)
Wheezing during 1999	28 (56)	68 (62)	142 (86)	74 (79)
Asthma prior to 1999	15 (29)	63 (58)	106 (64)	41 (44)
Asthma during 1999	12 (24)	39 (36)	111 (67)	54 (58)
Visit to a doctor because of asthma during 1999	15 (29)	29 (27)	105 (63)	61 (65)
Use of short-acting beta-2 agonists during 1999	34 (67)	53 (49)	151 (91)	84 (90)
Use of inhaled corticosteroids during 1999	17 (33)	35 (32)	137 (83)	70 (75)
Asthma in 2003	9 (18)	29 (27)	103 (62)	45 (48)

where only two of three of the parents of the children at high risk for persistent asthma answered the DBH questionnaire and reflects the major important drawback that the parents of such children are often involved in other studies and tends not to answer questionnaires.

As shown in Table 4, the sensitivity of the occurrence of wheezing during the past 12 months as an identifier of asthma was 86%. Thus, for screening a population for asthma, a symptom-related question seems to be more reliable than questions concerning diagnosis which was also the conclusion drawn in another recent report (18). This is, however, not in agreement with the results of earlier studies (19).

In the phase II of the DBH study a nested case-control validation was carried out where WQ alleged doctor diagnosed asthma was compared with a diagnosis of asthma made by an examination with a sensitivity of 70.0%, a specificity of 97.8% and a PPV of 0.93 (M. Hasselgren, personal communication). These values are similar to those obtained by other clinical validations of WQs (4, 20). The discrepancies between these results and the findings we document here can presumably be explained by selection biases. To be included in the phase II of the DBH study children had to exhibit at least two allergic symptoms and the investigations performed on them were extensive. Parents who are willing to let their children participate in this type of validation represent a select group that differs from the general population. Factors associated with participating were a high socio-economic status of the family, more health problem in the case families, and health-related lifestyle factors, such as non-smoking parents (21).

The prevalence of asthma observed in the WQ is lower than that reported from English-speaking countries (1, 14, 22), but in agreement with the prevalence of asthmatic symptoms documented in a recent study in Sweden employing the same questions with children aged 6–7 yr (23). The prevalence of asthma was relatively constant between 2 and 6 yr of age and all symptoms were more frequent among boys, in accordance with earlier studies (9).

The prevalence found in the medical records can be compared with the 5% reported in the 1998 study from this same geographic area (11). A prospective birth cohort investigation from Sweden found an asthma prevalence of 7% at 4 yr of age (24). An Italian study based on the computerized medical records of 0- to 5-yr-old children from 1997 to 1998 reported an asthma prevalence of 6.3% among males and 4% among females (25).

An investigation on the primary health care of Swedish adults revealed only a 2.1% prevalence of asthma in the medical records in comparison with the 5.5% prevalence found by a WQ in the same region (8). These authors concluded that underdiagnosis of asthma among GPs is substantial. Some of the factors that may contribute to this situation are the GPs' neglecting to use the recommended diagnostic codes and/or the fact that patients do not seek care for their asthmatic symptoms or are treated by other caregivers (26).

With respect to preschool children, the problem of underdiagnosis is less extensive, as only 6% of children with probable asthma were not referred to a pediatrician in our region (11). However, even if pediatricians adhere to guidelines concerning diagnosis of these children it is still difficult to predict whether a child will have persistent asthma (27). The rate of remission in this age group is high, which may to some extent explain the discrepancies observed here (28). A WQ may identify previous asthma, as well as asthma which have not yet been detected clinically; whereas medical records might more closely reflect ongoing asthma. Children who were diagnosed during the first months of 2000 were not covered in our study of the medical records which is a weakness with this investigation.

The frequency of visits to outpatient clinics is relatively constant throughout the preschool years, probably reflecting the unchanging prevalence of asthma in children 2 yr of age and older, documented in both the DBH WQ and in medical records study (Tables 1 and 2). In contrast the rate of hospital admissions is very high during the first years of life and practically reduced to none by 6 yr of age, in agreement with other studies (14, 29). This latter pattern can probably be explained by the more widespread use of inhaled corticosteroids (ICS) (30).

The response rate to the complementary WQ sent to the parents of all children who were asthmatic 1999 according to either their parents' and/or medical records was acceptable. Recall bias is, of course, a problem with this type of retrospective study. However, this problem should have been the same in all of the groups, so that we felt justified in comparing the proportion of positive answers in the different groups in attempt to obtain clues as to why the parents had answered the DBH WQ as they did (Table 5).

Obviously, the parents of the children in the false-negative group thought that their children exhibited very mild respiratory problems in 1999 and were not aware that their doctor had diagnosed their children as asthmatics. In the

case of the false-positive group another mechanism seems to have been operating. The question posed in the DBH WQ did not specify whether the diagnosis was presently valid or made previously. These children had probably been prescribed asthma medication earlier, which their parents continued to give them as required during 1999, without consulting a doctor. The fact that many patients can treat themselves with medications prescribed earlier (or even to brothers or sisters) is one important reason for underdiagnosis of asthma in connection with analysis of medical records.

In addition, the doctors apparently failed to make the correct diagnosis in some cases, as one of four of the false-positive group had been diagnosed as asthmatics by 2003. With regard to the group in which the parent-assessed and clinical diagnoses concurred, as well as non-responders, the majority of these children were treated with short-acting beta-2 agonists (SABA) and ICS and obviously had asthma.

From a clinical point of view it is obviously important to identify these individuals requiring treatment for asthma. Those requiring treatment with ICS constitute a core group of asthmatic children. Although there is probably a certain amount of over-treatment with SABA, most children receiving these drugs (and especially those who had seen a doctor for wheezing) could be labeled as asthmatics. On the basis of the results in Table 5, we suggest that at least 40% of the false-negative and the false-positive groups and 80% of the congruent group and the non-responders were actually asthmatics requiring treatment. This adds up to 271 children altogether, or 4.4% (95% CI = 3.9–4.9) of the total study population. Forty-four of these (16%) children were not identified in the medical records and this group compensate in part for the 50 children in the false-negative group, explaining why assessment of the prevalence of asthma based on the DBH WQ appears to be adequate. In addition, among the 1599 children whose parents did not answer the WQ there were probably a number receiving anti-asthmatic treatment who had not visited a doctor during 1999.

In summary, this calculation indicates that in 1999 the prevalence of asthma requiring treatment among Swedish children 1–6 yr of age was at least 4.4%. This value is in agreement with the 4.9% prevalence arrived at on the basis of medical records. The prevalence of 5.9% indicated by the responses to the DBH WQ is similar to that found in the medical records. If children younger than 2 yr old are omitted the prevalence

increases. Nearly half of the individual patients identified using these two approaches differed. A clinical validation of the applicability of the ISAAC WQ to preschool children would be of value for future studies.

Acknowledgments

This study was supported financially by grants from the Värmland County Council. The authors wish to thank all the GPs and pediatricians in the region who provided us with information.

References

1. The ISAAC Steering Committee. Worldwide variations in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis and atopic eczema: the International Study of Asthma and Allergies in Childhood. *Lancet* 1998; 351: 1225–32.
2. SOTO-QUIROS ME, SOTO-MARTINEZ M, HANSON LA. Epidemiological studies of the very high prevalence of asthma and related symptoms among school children in Costa Rica from 1989 to 1998. *Pediatr Allergy Immunol* 2002; 13: 342–9.
3. VAN SCHAYCH CP, SMIT HA. The prevalence of asthma in children. *Eur Respir J* 2005; 26: 647–50.
4. ARIF A, BORDERS T, PATTERSON P, ROHRER J, XU K. Prevalence and correlates of paediatric asthma and wheezing in a largely rural USA population. *J Paediatr Child Health* 2004; 40: 189–94.
5. CUNNINGHAM J, DOCKERY DW, SPEIZER FE. Race, asthma, and persistent wheeze in Philadelphia school-children. *Am J Public Health* 1996; 86: 1406–9.
6. ROBERTS EM. Racial and ethnic disparities in childhood asthma diagnosis: the role of clinical findings. *J Natl Med Assoc* 2002; 94: 215–23.
7. COULTAS DB, MAPEL D, GAGNON R, LYDICK E. The health impact of undiagnosed air flow obstruction in a national sample of United States adults. *Am J Respir Crit Care Med* 2001; 164: 372–7.
8. MONTNÉMERY P, HANSSON L, LANKE J, et al. Accuracy of first diagnosis of asthma in primary health care. *Fam Pract* 2002; 4: 365–8.
9. ROBERTS EM. Does your child have asthma? Parent reports and medication use for pediatric asthma. *Arch Pediatr Adolesc Med* 2003; 157: 449–55.
10. MAZIAK W, VON MUTIUS E, BEIMFOHR C, et al. The management of childhood asthma in the community. *Eur Resp J* 2002; 20: 1476–82.
11. HEDEROS C-A, JANSON S, BORNEHAG C-G, HEDLIN G. The burden of asthma as reflected by the prevalence defined by doctor's diagnosis and the use of healthcare services by preschool children in a Swedish region. *Acta Paediatr* 2002; 91: 1246–50.
12. WICKMAN M, KULL I, PERSHAGEN G, NORDVALL SL. The BAMSE project: presentation of a prospective longitudinal birth cohort study. *Pediatr Allergy Immunol* 2002; 13: 11–3.
13. ASHER MI, KEIL U, ANDERSON HR, et al. International study of asthma and allergens in childhood. (ISAAC): rationale and methods. *Eur Respir J* 1995; 8: 483–91.
14. HABY M, PEAT JK, MARKS GB, WOOLCOCK AJ, LEEDER SR. Asthma in preschool children: prevalence and risk factors. *Thorax* 2001; 56: 589–95.

15. BORNEHAG C-G, SUNDELL J, SIGSGAARD T. Dampness in Buildings and Health (DBH). Report from an on-going epidemiological investigation on the association between indoor environmental factors and health effects among children in Sweden. *Indoor Air* 2004; 14 (Suppl. 7): 59–66.
16. HASSELGREN M, GUSTAFSSON D, STÄLLBERG B, LISSPERS K, JOHANSSON G. Management, asthma control and quality of life in Swedish adolescents with asthma. *Acta Paediatr* 2005; 94: 682–8.
17. KOOPMAN L, BRUNEKREEFF B, DE JONGSTE JC, NEIJENS HJ. Definition of respiratory symptoms and disease in early childhood in large prospective birth cohort studies that predict the development of asthma. *Pediatr Allergy Immunol* 2001; 12: 118–24.
18. YU ITS, WONG TW, LI W. Using child reported respiratory symptoms to diagnose asthma in the community. *Arch Dis Child* 2004; 89: 544–8.
19. KILPELÄINEN M, TERHO EO, HELENIUS H, KOSKENVUO M. Validation of a new questionnaire on asthma, allergic rhinitis, and conjunctivitis in young adults. *Allergy* 2001; 56: 377–84.
20. RÖNMARK E, LUNDBÄCK B, JÖNSSON E, PLATTS-MILLS T. Asthma, type-1-allergy and related conditions in 7- and 8-year old children in northern Sweden: prevalence rates and risk factor pattern. *Respir Med* 1998; 92: 316–24.
21. BORNEHAG C-G, SUNDELL J, SIGSGAARD T, JANSON S. Potential self-selection bias in a nested case-control study on indoor environmental factors and their association with asthma and allergic symptoms among pre-school children. *Scand J Public Health* 2006; 34: 534–43.
22. KUEHNI CE, DAVIS A, BROOKE AM, SILVERMAN M. Are all wheezing disorders in very young (pre-school) children increasing in prevalence? *Lancet* 2001; 357: 1821–5.
23. BJÖRKSTEN B, DUMITRASCU D, FOUCARD T, et al. Prevalence of childhood asthma, rhinitis and eczema in Scandinavia and Eastern Europe. *Eur Respir J* 1998; 12: 432–7.
24. KULL I, ALMQUIST C, LILJA G, PERSHAGEN G, WICKMAN M. Breast-feeding reduces risk of asthma during the first 4 years of life. *J Allergy Clin Immunol* 2004; 114: 755–60.
25. BARBATO A, PANIZZOLO C, CANTARUTTI L, et al. Peditanet Family Pediatricians Asthma Study Group (F-PASG). Asthma prevalence and drug prescription in asthmatic children. *Allerg Immunol (Paris)* 2003; 35: 47–51.
26. HASSELGREN M, ARNE M, LINDAHL A, JANSON S, LUNDBÄCK B. Estimated prevalences of respiratory symptoms, asthma and chronic obstructive disease related to detection rate in primary health care. *Scand J Prim Health Care* 2001; 9: 54–7.
27. TRINDADE JC. The importance of diagnosis of allergy in early wheezing. *Paediatr Allergy Immunol* 1998; 9 (Suppl. 11): 23–9.
28. MARTINEZ FD, WRIGHT AL, TAUSSIG LM, HOLBERG CJ, HALONEN M, MORGAN WJ. Group Health Medical Associates. Asthma and wheezing in the first six years of life. *N Engl J Med* 1995; 332: 133–8.
29. JONASSON G, CARLSEN LÖDRUP KC, LEEGAARD J, CARLSEN KH, MOWINCKEL P, HALVORSSSEN KS. Trends in hospital admissions for childhood asthma in Oslo, Norway, 1980–95. *Allergy* 2000; 55: 232–9.
30. HOMER CJ, SZALIGYI P, RODEWALD L, et al. Does quality of care affect rates of hospitalisation for childhood asthma? *Pediatrics* 1996; 98: 18–23.