

Population based study of risk factors for underdiagnosis of asthma in adolescence: Odense schoolchild study

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Abstract

Objective: To describe factors related to underdiagnosis of asthma in adolescence.

Design: Subgroup analysis in a population based cohort study.

Setting: Odense municipality, Denmark.

Subjects: 495 schoolchildren aged 12 to 15 years were selected from a cohort of 1369 children investigated 3 years earlier. Selection was done by randomisation (n = 292) and by a history indicating allergy or asthma-like symptoms in subject or family (n = 203).

Main outcome measures: Undiagnosed asthma defined as coexistence of asthma-like symptoms and one or more obstructive airway abnormalities (low ratio of forced expiratory volume in 1 second to forced vital capacity, hyperresponsiveness to methacholine or exercise, or peak flow hypervariability) in the absence of physician diagnosed asthma. Risk factors (odds ratios) for underdiagnosis.

Results: Undiagnosed asthma comprised about one third of all asthma identified. Underdiagnosis was independently associated with low physical activity, high body mass, serious family problems, passive smoking, and the absence of rhinitis. Girls were overrepresented among undiagnosed patients with asthma (69%) and underrepresented among diagnosed patients (33%). Among the risk factors identified, low physical activity and problems in the family were independently associated with female sex. The major symptom among those undiagnosed was cough (58%), whereas wheezing (35%) or breathing trouble (50%) was reported less frequently than among those diagnosed. Less than one third of those undiagnosed had reported their symptoms to a doctor.

Conclusions: Asthma, as defined by combined symptoms and test criteria, was seriously underdiagnosed among adolescents. Underdiagnosis was most prevalent among girls and was associated with a low tendency to report symptoms and with several independent risk factors that may help identification of previously undiagnosed asthmatic patients.

Introduction

Epidemiological surveys have shown asthma-like symptoms to be far more prevalent than physician diagnosed asthma,¹ and underdiagnosis of asthma has repeatedly been suspected during the past two decades, especially in children and young adults.^{2,3} Screening studies that used a combination of symptoms and objective indicators of asthma have confirmed this view.⁴⁻⁶ In the present cohort children who reported asthma-like symptoms but not asthma at age 10 had impaired lung function.⁷

Some risk factors for the underdiagnosis of asthma have recently been proposed, including female sex,^{6,8} low socioeconomic status,⁹ or belonging to an ethnic minority,¹⁰ whereas the diagnostic process seems to be facilitated if previous episodes of acute bronchitis or a family history of asthma are reported.⁶

This population based study examined a broad selection of potential risk factors for underdiagnosis of asthma among adolescents with coexisting asthma-like symptoms and obstructive airway abnormalities.

Subjects and methods

The Odense schoolchild study is a prospective multidisciplinary epidemiological study in a community based cohort of 1369 schoolchildren first investigated during their third school year in 1985-6.¹¹ The present analysis is based on data from 495 children aged 12 to 15 years and of Danish origin recruited from the original cohort for an extensive asthma and allergy screening programme. Subjects were selected either at random (n = 292) or on the basis of a history indicating asthma, allergy, or related symptoms or a family history of asthma or allergic rhinitis (n = 203).¹² Subjects completed a comprehensive questionnaire and monitored their peak expiratory flow twice daily for 2 weeks. Laboratory examinations included anthropometric measurements, puberty staging, spirometry, treadmill exercise testing, and provocation with inhaled methacholine. Subjects were asked to stop taking bronchodilators (but not inhaled steroids) before testing. Informed consent was obtained from all children and parents or guardians before participation. The study was approved by the local research ethics committee, the local school board, and the Danish Data Surveillance Authority.

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For the present analysis, currently symptomatic subjects were grouped according to the presence or absence of physician diagnosed asthma and positive test results. The variables analysed are listed in the box. Current asthma-like symptoms (ongoing or within the previous year) were identified by questionnaire as previously reported.¹² Symptoms accepted included non-infectious cough, wheezing, and trouble breathing. Physician diagnosed asthma was identified by an affirmative answer to the question, "Is it your doctor's opinion, that you have asthma?" or the use of prescribed asthma medication, or both. Subjects with no previous diagnosis of asthma but asthma-like symptoms and at least one positive test result (hypervariability in peak expiratory flow, hyperresponsiveness to exercise or inhaled methacholine, or low ratio of forced expiratory volume in 1 second (FEV₁) to forced vital capacity (FVC)) were labelled as having undiagnosed asthma.

Details of test procedures have been reported previously.¹² The body mass index (weight (kg)/(height (m)²)) was also calculated. Puberty staging was done according to Tanner and Whitehouse¹³ and corrected for age by sex. Forced expiratory volumes were measured according to European recommendations.¹⁴ For the 6 minute treadmill provocation test results were expressed as the lowest FEV₁ obtained during the first 10 minutes after exercise in percentage of the best value before exercise. Bronchoprovocation with methacholine was performed according to Yan et al¹⁵ and expressed as the methacholine dose response slope.¹⁶ It was ensured that all subjects regained their baseline FEV₁ (within 10%) either spontaneously or aided by inhaled terbutaline (Bricanyl Turbohaler). Peak expiratory flow was recorded twice daily for 14 consecutive days with a Mini-Wright adult type peak flow meter. Variability in peak expiratory flow was expressed as the average of the two lowest values as a percentage of the period mean, after the first three recording days were discarded (the two lowest % mean index).¹⁷ Test results were considered abnormal if they were beyond the value delimiting the 5% "most asthmatic" part of the test distribution in 150 asymptomatic, non-smoking, and non-asthmatic reference subjects from the randomly selected part of the present cohort. The association of a range of medical, environmental, social, school, and activity related factors (see box) with undiagnosed versus diagnosed asthma and with asthma versus asthma-like symptoms only was assessed by logistic regression with SPSS.¹⁸

Variables that seemed to be differently distributed ($P < 0.15$) between the groups compared were included in the logistic regression analysis by using backward selection (final removal criterion $P > 0.05$). Questionnaire information and test results directly related to grouping criteria were not included in the regression models but were analysed separately. The Medstat program (Astra Denmark, Copenhagen) was used to calculate 95% confidence intervals on proportions. Proportions were compared with χ^2 statistics with Yates's correction.

Results

Among 495 subjects investigated, 128 had current asthma-like symptoms. Of these, 15 (12%) were excluded from analysis because of missing data for

Variables analysed

Anthropometric and related measurements

Sex
Puberty stage
Standing height
Sitting height/standing height
Body mass index
Diastolic blood pressure
Systolic blood pressure

Questionnaire information at age 10

Birth weight
Dyspnoea (nights or mornings)
Wheezing or cough on exertion
Bronchitis (explained)
Eczema at elbows or knees (explained)

Questionnaire information at age 13

Family and home environment:
Number of subjects sharing home
Number of children < 15 years
Serious family problems
Living with father/male guardian
Passive smoking (hours/day)
Active smoking
Type of home (house or apartment)
Size of home
Age of building
Pet in bedroom
Carpets in bedroom
Signs of high humidity in home
School environment:
Inner city school
Distance to school
Absence with illness (days)
Happy with school
Bad indoor environment
Activities:
Physical activity (hours per week)
Sitting down more than half of spare time
Given up job due to health problem
Given up sport due to health problem
Biking to school
Allergy: history and test:
Predisposition for asthma, hay fever, or eczema
Colic in first year of life
Frequent diarrhoea in first year of life
Passive smoking in first year of life
Pets at home in first year of life
Breast feeding time (months)
Eye itching
Serial sneezing (≥ 3)
Watery nasal secretion
Eczema ever (explained)
Urticaria (explained)
Diet restrictions (allergy/intolerance)
Frequency of extrapulmonary symptoms:
Headache
General indisposition
Unprovoked articular pain
Stomach ache
Diarrhoea

group allocation. Forty five had physician diagnosed asthma, and 26 were considered as having undiagnosed asthma. The 42 remaining subjects had "symptoms only" (negative test results and not diagnosed with asthma). Despite the "normalising" effect of treatment with inhaled steroids on test results,¹² the sensitivity of the test battery for symptomatic physician diagnosed asthma was high (87%). The proportion of undiagnosed asthmatic sub-

Table 1 Unadjusted associations of selected risk factors with undiagnosed asthma as opposed to asthma diagnosed by doctor

Risk factor and categories	Mean* or proportion in subjects with asthma	Odds ratio	P value
Sex (female v male)	33/71	4.50	0.005
Body mass index† (per kg/m ²)	19.9*	1.24	0.03
Systolic blood pressure (per mm Hg)	116*	1.04	0.07
Symptoms on exercise at 10 years (any v none)	22/61	0.12	0.008
Problems in family† (severe v trivial)	6/70	3.82	0.14
Living with father (yes v no)	56/70	0.36	0.09
Passive smoking† (per hours/day)	2.3*	1.46	0.005
Type of home (apartment v house)	11/70	3.68	0.06
Pet in bedroom (yes v no)	30/71	2.11	0.14
Carpets in bedroom (yes v no)	46/71	7.33	0.004
Physical activity† (per hours/week)	9.0*	0.86	0.004
Spare time spent sitting (more v less than half)	18/71	5.57	0.004
Given up sport (yes v no)	21/64	0.39	0.12
Biking to school (yes v no)	53/69	12.4	0.02
Diarrhoea before age 1 (frequent v none)	12/69	0.12	0.05
Itching eyes (yes v no)	39/70	0.25	0.008
Serial sneezing† (yes v no)	33/70	0.14	0.0007
Watery nasal secretion (yes v no)	26/70	0.12	0.002
Diet restrictions (yes v no)	26/70	0.36	0.07
Headache (monthly) (yes v no)	24/71	2.36	0.10
Stomach ache (monthly) (yes v no)	21/71	2.57	0.08

*N=62 for passive smoking, ≥69 for other continuous variables.

†Included in final model (see table 2).

jects among all asthmatic subjects (36.6%) did not differ significantly between subjects selected randomly or by history. The prevalence of any positive test result among 256 non-asthmatic subjects in the random group was 16.0% (not significantly different from the expected value $1 - (0.95)^4 = 18.5\%$ for four independent tests), and the symptom prevalence was 12.1%. Thus, about eight subjects (16% of 12% (1.9%) of 435 subjects with no previous diagnosis of asthma) may have been misclassified as having asthma by chance. After correction for this the proportion of asthmatic patients not previously diagnosed was 29% (18/(18 + 45)).

Undiagnosed versus diagnosed asthma

Individual regression data for the 21 variables selected for logistic regression are shown in table 1. Adjusted odds ratios for independently contributing risk factors are given in table 2. Undiagnosed asthma was independently associated with self reported problems in the family (“we have very stressful problems in our family” (highest of three levels)), daily exposure to environmental tobacco smoke (“for how many hours a day are you usually exposed to indoor tobacco smoking”), low physical activity (“state average number of hours a week spent with physical activities”), high body mass index, and the absence of serial sneezing (“attacks of more than three consecutive sneezes”). No significant interactions between these factors were found.

Among those with diagnosed asthma only 33% (95% confidence interval 20% to 49%) were girls compared with 69% (48% to 86%) among those undiagnosed ($P=0.007$). The sex distribution was about neutral in the “symptoms only” group (52%

(36% to 68%) girls) and in the reference group (45% (37% to 54%) girls). A negative association was found between female sex and physical activity (odds ratio 0.91 (0.84 to 1.00) per hours/week, $\chi^2=4.12$, $df=1$, $P=0.04$, $n=59$), whereas female sex and problems in the family were positively associated (14.8 (1.0 to 220), $\chi^2=3.97$, $df=1$, $P=0.05$, $n=59$).

Cough was equally prevalent among diagnosed (58%) and undiagnosed subjects (58%), but the latter group reported less breathing trouble (50% v 100%, $P<0.001$) and wheezing (35% v 96%, $P<0.001$). Among undiagnosed subjects only 31% had reported any asthma-like symptom to a doctor. Subjects with diagnosed asthma had a significantly higher response to inhaled methacholine than did undiagnosed subjects with asthma (median methacholine dose response slope 12.0 v 4.8 $\mu\text{mol/l}$, $P=0.02$), whereas the results of baseline spirometry, exercise provocation, and peak flow monitoring did not differ between groups. No significant differences in test results were found between those subjects without asthma who had symptoms but negative test results and the reference group.

Undiagnosed asthma versus symptoms only

Among symptomatic subjects not previously diagnosed with asthma, independent risk factors (see box) for having undiagnosed asthma as opposed to asthma-like “symptoms only” were bronchitis at age 10 (odds ratio 7.35 (1.52 to 35.4), $\chi^2=6.2$, $df=1$, $P=0.01$), signs of humidity in home (0.28 (0.08 to 1.00), $\chi^2=3.81$, $df=1$, $P=0.05$), and physical activity (0.89 (0.79 to 1.00), $\chi^2=3.80$, $df=1$, $P=0.05$). The odds ratios stated were adjusted for all contributing variables ($n=66$, two missing). No significant interactions were found between the variables contributing to model.

Discussion

Few studies have investigated the characteristics of previously undiagnosed asthmatic patients, probably in part because of the lack of an accepted definition of this condition and the need for objective measurements to confirm the diagnosis to avoid overestimation.¹⁹ For epidemiology a pragmatic definition of asthma as the coexistence of recent wheeze and methacholine hyperresponsiveness has been proposed.²⁰ Cough, however, may be the sole expression of asthma,²¹ and various tests of airway responsiveness may identify different types of abnormalities of the airways.¹² Therefore, we extended our definition of asthma to comprise non-infectious cough or any breathing trouble, or both, in combination with any test result confirming abnormal variations in airway calibre

Table 2 Associations of independent risk factors with undiagnosed asthma as opposed to asthma diagnosed by doctor

Risk factor and categories	No of subjects	Odds ratio (95% CI)*	χ^2 (df=1)	P value
Body mass index (per kg/m ²)	59	3.01 (1.16 to 7.83)	5.12	0.02
Problems in family (serious v trivial)	59	846 (2.22 to ∞)	4.94	0.03
Passive smoking (per hours/day)	59	2.39 (1.16 to 4.92)	5.59	0.02
Physical activity (per hours/week)	59	0.60 (0.41 to 0.87)	7.24	0.01
Serial sneezing (any v none)	59	0.005 (0.00 to 0.34)	5.99	0.01

*Adjusted for all factors included in model.

Key messages

- One third of young people with asthma are not diagnosed; most are girls
- Undiagnosed asthma is associated with low physical activity, high body mass index, serious family problems, passive smoking, and the absence of symptoms of rhinitis
- Cough is the most common symptom among those with undiagnosed asthma
- Two thirds of those with undiagnosed asthma do not report their symptoms to a doctor, suggesting a need for targeted asthma campaigns

including monitoring of peak expiratory flow, airway responsiveness to methacholine or exercise, and resting spirometry. By this definition subjects with previously undiagnosed asthma made up about one third of all asthmatic patients identified. True asthmatic patients were unlikely to hide in the “symptoms only” group because test results did not differ between those with symptoms but negative test results and reference subjects without symptoms.

Undiagnosed versus diagnosed asthma

Independent risk factors for undiagnosed as opposed to previously diagnosed asthma were serious family problems, low physical activity, high body mass index, high exposure to environmental tobacco smoke, and no history of serial sneezing, a characteristic symptom of allergic rhinitis. The first two of these risk factors were significantly associated with female sex, which, in accordance with previous reports,^{6, 8} comprised two thirds of the undiagnosed but only one third of the diagnosed patients with asthma.

The logistic regression analysis was based on a relatively large number of potential risk factors ($n = 51$) compared with the number of asthmatic subjects identified ($n = 71$). Thus, mass significance could not be excluded. The relevance of the five independent risk factors, however, was supported by the presence of several associated factors competing for entry in the final model (see table 1).

Why is asthma overlooked?

The presence of one or more of the five independent risk factors could in several ways lead to misinterpretation or neglect of asthma-like symptoms by patients, parents, or medical professionals. A low level of physical activity is relatively unlikely to provoke symptoms of asthma induced by exercise and may serve as a means of self “treatment” in childhood asthma. Furthermore, low activity promotes weight gain (high body mass index) which in turn may lead to misinterpretation of asthma symptoms as due to lack of physical fitness. Social status, previously associated with underdiagnosis of asthma,⁹ was not directly measured but may be related to parents’ smoking habits as well as problems in the family. Family problems may reduce focus on a child’s symptoms, and parents who smoke may be disinclined to get a doctor’s advice regarding symptoms related to smoking in the family. Environmental tobacco smoke has previously been shown to be a risk factor for childhood wheeze²² and is

likely to be strongly advised against and thus probably reduced when a child is diagnosed with asthma.

In accordance with previous reports,⁶ symptoms were rarely reported to a physician by undiagnosed subjects with asthma, who thereby effectively avoided getting diagnosed and properly treated. Cough seemed to be particularly overlooked as an expression of asthma. Even though the more severely affected patients with asthma (in terms of airway responsiveness and symptoms) were also the most likely to get diagnosed, several moderately to severely affected subjects were first identified as a result of the present study.

The role of atopy as a risk factor for asthma has been established by population based studies with physician independent markers of asthma such as lung function impairment, bronchial responsiveness to methacholine, or typical asthma symptoms.^{23–25} We speculate, however, that the traditional emphasis on two associated risk factors²⁶ for asthma—namely, atopy and male sex—may have led to the underrecognition of non-atopic girls with asthma suggested by our data. It seems likely that allergy affecting nose or eyes facilitates a diagnosis of asthma, both by promoting contact with a doctor and by increasing the doctor’s awareness towards this diagnosis.

Undiagnosed asthma versus symptoms only

Undiagnosed patients with asthma also differed from those with symptoms but with no evidence of asthma. In this context, previously undiagnosed asthma at age 13 was positively associated with symptoms of bronchitis—that is, periodic cough for many days or weeks—at age 10, confirming earlier reports on misclassification of asthma as bronchitis⁴ and suggesting that the asthma had been unrecognised for several years. The negative association between undiagnosed asthma and the level of physical activity suggests that exercise induced symptoms limit the activity level in undiagnosed subjects more than in subjects with respiratory symptoms unrelated to asthma. The independent association of indicators of high humidity in the home with non-asthmatic respiratory symptoms was unexpected but may be related to indoor microbial factors.²⁷

Summary

Substantial underdiagnosis of asthma in the adolescent population was confirmed by combined subjective and objective criteria. Underdiagnosis was independently associated with low physical activity, high body mass, serious family problems, passive smoking, and the absence of rhinitis symptoms. Girls were overrepresented among subjects with undiagnosed asthma and equally underrepresented among those with diagnosed asthma, indicating sex bias in the diagnostic process. Most patients with undiagnosed asthma had not reported their symptoms to a physician, suggesting a need for targeted asthma campaigns in the community.

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Contributors: NH initiated the Odense schoolchild study together with HSH, who carried out the background study. HCS designed the protocol for the present follow up study together with NH and HSH. HCS carried out data collection and quality control in cooperation with the technicians acknowledged

above, had the original idea for the present analysis, and wrote the manuscript. HCS also carried out the statistical analysis after thorough discussion with JB and GM. All coauthors made valuable comments to the manuscript and approved the final version. HCS is the guarantor for the study.

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- Sears MR. Epidemiological trends in bronchial asthma. In: Kaliner MA, Barnes PJ, Persson CGA, eds. *Asthma: its pathology and treatment*. New York: Marcel Dekker, 1991.
- Speight AN. Is childhood asthma being underdiagnosed and undertreated? *BMJ* 1978;29:331-2.
- Nish WA, Schwietz LA. Underdiagnosis of asthma in young adults presenting for USAF basic training. *Ann Allergy* 1992;69:239-42.
- Speight AN, Lee DA, Hey EN. Underdiagnosis and undertreatment of asthma in childhood. *BMJ* 1983;286:1253-6.
- Cuijpers C, Wesseling GJ, Swaen GMH, Sturmans F, Wouters EFM. Asthma-related symptoms and lung function in primary school children. *J Asthma* 1994;31:301-12.
- Kolnaar BGM, Beissel E, van den Bosch WJHM, Folgering H, van den Hoogen HJM, van Weel C. Asthma in adolescents and young adults: screening outcome versus diagnosis in general practice. *Fam Pract* 1994;11:133-40.
- Mostgaard G, Siersted HC, Hansen HS, Hyldebrandt N, Oxhøj H. Reduced forced expiratory flow in schoolchildren with respiratory symptoms: the Odense schoolchild study. *Respir Med* 1997;91:443-8.
- Kuhni CE, Sennhauser FH. The Yentl syndrome in childhood asthma: risk factors for undertreatment in Swiss children. *Pediatr Pulmonol* 1995;19:156-60.
- Baumann A, Young L, Peat JK, Hunt J, Larkin P. Asthma under-recognition and undertreatment in an Australian community. *Aust NZ J Med* 1992;22:36-40.
- Duran-Tauleria E, Rona RJ, Chinn S, Burney P. Influence of ethnic group on asthma treatment in children in 1990-1: national cross sectional study. *BMJ* 1996;313:148-52.
- Hansen HS, Hyldebrandt N, Nielsen JR, Froberg K. Blood pressure distribution in a school-age population aged 8-10 years: the Odense schoolchild study. *J Hypertens* 1990;8:641-6.
- Siersted HC, Mostgaard G, Hyldebrandt N, Hansen HS, Boldsen J, Oxhøj H. Interrelationships between diagnosed asthma, asthma-like symptoms,

and abnormal airway behaviour in adolescence: the Odense schoolchild study. *Thorax* 1996;51:503-9.

- Tanner JM, Whitehouse RH. Clinical longitudinal standards for height, weight, height velocity, weight velocity, and stages of puberty. *Arch Dis Childhood* 1976;51:170-9.
- Quanjer PhH, ed. Standardized lung function testing. Report of the working party on standardization of lung function tests, European Community for Coal and Steel. *Bull Europ Physiopath Respir* 1983;19 (suppl 5):1-95.
- Yan K, Salome C, Woolcock AJ. Rapid method for measurement of bronchial responsiveness. *Thorax* 1983;38:760-5.
- O'Connor G, Sparrow D, Taylor D, Segal M, Weiss S. Analysis of dose-response curves to methacholine. An approach suitable for population studies. *Am Rev Respir Dis* 1987;136:1412-7.
- Siersted HC, Hansen HS, Hansen N-CG, Hyldebrandt N, Mostgaard G, Oxhøj H. Evaluation of peak expiratory flow variability in an adolescent population sample. The Odense schoolchild study. *Am J Respir Crit Care Med* 1994;149:598-603.
- Norusis MJ. *SPSS/PC+ advanced statistics version 4.0*. Chicago: SPSS, 1990.
- Joyce DP, Chapman KR, Kesten S. Prior diagnosis and treatment of patients with normal results of methacholine challenge and unexplained respiratory symptoms. *Chest* 1996;109:697-701.
- Toelle BG, Peat JK, Salome CM, Mellis CM, Woolcock AJ. Toward a definition of asthma for epidemiology. *Am Rev Respir Dis* 1992;146:633-7.
- Hannaway PJ, Hopper GD. Cough variant asthma in children. *JAMA* 1982;247:206-8.
- Cunningham J, O'Connor GT, Dockery DW, Speizer FE. Environmental tobacco smoke, wheezing, and asthma in children in 24 communities. *Am J Respir Crit Care Med* 1996;153:218-24.
- Peat JK, Britton WJ, Salome CM, Woolcock AJ. Bronchial hyperresponsiveness in two populations of Australian schoolchildren. II. Relative importance of associated factors. *Clin Allergy* 1987;17:283-90.
- Clough JB, Williams JD, Holgate ST. Effect of atopy on the natural history of symptoms, peak expiratory flow, and bronchial responsiveness in 7- and 8-year-old children with cough and wheeze. *Am Rev Respir Dis* 1991;143:755-60.
- Sears MR, Burrows B, Herbison GP, Flannery EM, Holdaway MD. Atopy in childhood. III. Relationship with pulmonary function and airway responsiveness. *Clin Exp Allergy* 1993;23:957-63.
- Sears MR, Burrows B, Flannery EM, Herbison GP, Holdaway MD. Atopy in childhood. I. Gender and allergen related risks for development of hay fever and asthma. *Clin Exp Allergy* 1993;23:941-8.
- Husman T. Health effects of indoor-air microorganisms. *Scand J Work Environ Health* 1996;22:5-13.

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Commentary: Risk factors for underdiagnosis of asthma in adolescence

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The Odense schoolchild study of asthma symptoms has provided previous data on this same group of children.¹ The results in adolescents with diagnosed asthma showed that different objective tests (spirometry, responsiveness to methacholine or exercise, variability in peak flow at home) may pick up different subsets of airway pathophysiology. In the current study they have shown that around a third of children who have asthma-like symptoms and one positive test result have not been given a diagnosis of asthma. They suggest that this may be a reason to go out and search for these cases in the community.

Firstly, we need to know whether this underdiagnosis of asthma matters. Possible reasons for such a search might be that these children have current problems such as persistent symptoms which could be relieved by appropriate treatment, have restricted activity because of respiratory symptoms on exercise, or are at risk of severe asthma attacks because of the absence of diagnosis and treatment. Alternatively, there might be longer term risks of more troublesome asthma symptoms in the future or the development of irreversible airway damage which could have been prevented by treatment.

Only 31% of the undiagnosed group had presented an asthma-like symptom to a doctor. In a

few cases this might have been reticence related to an anxiety about the doctor's response to parental smoking. The association found between undiagnosed asthma and limited activity or a higher body mass index suggests that a healthier life style might have brought symptoms to light or that symptoms might have been related inappropriately to weight or lack of fitness.

Overall, the symptoms in the undiagnosed group were milder; breathlessness was less common than in the diagnosed group and methacholine responsiveness was lower. In some cases, however, the findings were less reassuring as "several moderately to severely affected subjects were first identified as a result of the present study." Some of these subjects in the undiagnosed group may have been poor perceivers of their asthma,² a group of patients who need particular care and who may be particularly susceptible to future acute problems.³

These might be legitimate reasons to search for such cases or, at least, to be ready to suspect the diagnosis with few symptoms and the associations shown here. Any argument that the longer term clinical course of asthma might be favourably changed by early diagnosis and treatment of these cases with

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mild symptoms is more difficult to sustain on the present evidence. There is a suggestion that persistent inflammation may cause remodelling of the airways, leaving them less able to reverse back to their full calibre.⁴ Early intervention with corticosteroids is known to control symptoms, reduce inflammation,⁵ and improve bronchial responsiveness. There are suggestions that such treatment might even prevent irreversible change,⁶ but the evidence is not strong enough to recommend this approach in all of the undiagnosed group with minimal symptoms.

So where does this leave us? It does not provide the evidence for screening in the community until we know that this is beneficial on quality of life or long term outlook. It does show that there are still people with asthma with significant problems who remain undiagnosed and untreated because they or their doctors fail to appreciate the importance of their symptoms. This paper shows some associated features such as physical inactivity, high body mass index, and lower socioeconomic class, which should raise suspicions that the diagnosis is being missed where

symptoms are mild. An exercise test, peak flow at home, methacholine challenge, or a combination should be used to confirm the diagnosis. The advantage of the first two tests is that they can be performed easily by primary care physicians who see most of these children. A positive diagnosis or a high degree of suspicion with significant symptoms should prompt a trial of treatment.

- 1 Siersted HC, Mostgaard G, Hyldebrandt N, Hansen HS, Boldsen J, Oxhøj H. Interrelationships between diagnosed asthma, asthma-like symptoms, and abnormal airway behaviour in adolescence: the Odense schoolchild study. *Thorax* 1996;51:503-9.
- 2 Rubinfield AR, Pain MCF. Perception of asthma. *Lancet* 1976;i:882-4.
- 3 Kikochi Y, Okabe S, Tamura G, Hida W, Homma M, Shirato K, et al. Chemosensitivity and perception of dyspnea in patients with a history of near-fatal asthma. *N Engl J Med* 1994;330:1329-34.
- 4 Laitinen LA, Laitinen A, Altraja A, Virtanen I, Kampe M, Simonsson BG, et al. Bronchial biopsy findings in intermittent or "early" asthma. *J All Clin Immunol* 1996;98:35-6.
- 5 Trigg CJ, Manolitsas ND, Wang J, Calderon MA, McAulay A, Jordan SE, et al. Placebo controlled immunopathologic study of four months of inhaled corticosteroids in asthma. *Am J Respir Crit Care Med* 1994;150:17-22.
- 6 Haahela MJ, Jarvinen M, Kava T, Kiviranta K, Koskinen S, Lehtonen K, et al. Effects of reducing or discontinuing inhaled budesonide in patients with mild asthma. *N Engl J Med* 1994;331:700-5.

Commentary: Identifying the correct risks in diagnosis

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This is a study of young people selected in two ways: firstly, a simple random sample of 292 (21%) children from 1369 in an epidemiological study, and, secondly, a 100% sample (203) of those with personal or family history of asthmatic-like symptoms. (The consequences for analysis of this method of sample selection have been ignored but probably hardly affect the conclusions.) These children were classified into three groups: firstly, those who described themselves as having physician diagnosed asthma; secondly, those with asthma-like symptoms and a positive test result but without a doctor's diagnosis—undiagnosed asthma; and, thirdly, those non-smokers with no symptoms or diagnosis of asthma—the reference group (smokers with no symptoms were excluded).

Logistic regression is a statistical technique that may be used to combine factors that discriminate between two groups. It requires a "gold standard" diagnostic test (which may be invasive or expensive or one for which the result can be obtained only retrospectively) and putative features to be used for discrimination to be measured on all those classified by the gold standard. Generally the groups studied are those with and without disease. Logistic regression can be used to estimate a probability, from the measured features, that a particular individual has the disease.

This study uses the technique to examine features that might be used in those children with asthma to discriminate between those who are diagnosed and those who are not diagnosed. Is this discrimination of value? It may be of marginal interest in theory but does not seem to help practitioners. When a doctor is faced with a patient, the problem is to discriminate between those who have and those who do not have asthma, so that he or she can give appropriate treatment. If they

have already made a diagnosis then distinctions between those with and those without such a diagnosis are no longer of interest.

The fact that being a girl is a "risk factor" for being undiagnosed does not necessarily help unless it also distinguishes between having symptoms only and being undiagnosed. It does suggest that boys are more likely to be diagnosed, but there may be more girls in the non-asthmatic group as a whole. The tables and most of the text of the paper do not contribute to the useful distinction. The results for the discrimination between "symptoms only" and "undiagnosed asthma" are neither very significant (only bronchitis at age 10 is conventionally significant) nor are they the same set of variables for distinguishing between diagnosed and undiagnosed asthma. Physical activity shows a similar trend but is not very helpful in making the clinical decisions with which a doctor is faced in the clinic or general practice.

The message of this paper is that statistical techniques can serve to produce analyses which, while arithmetically correct, are irrelevant. It is an error of the third kind: "Finding the right answer to the wrong question."

Correction

Systematic overview of co-proxamol to assess analgesic effects of addition of dextropropoxyphene to paracetamol

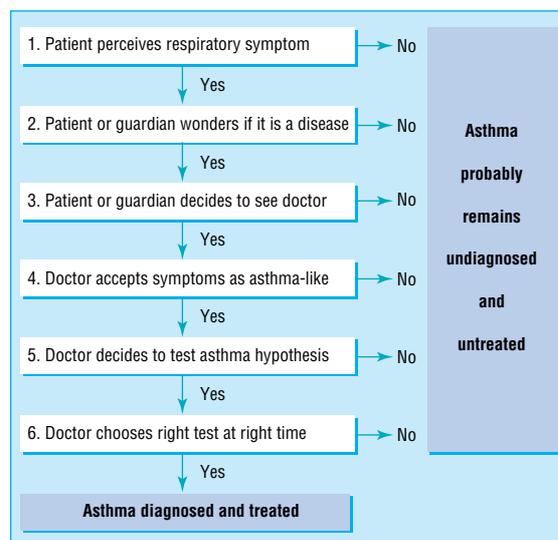
An editorial error occurred in this paper by Li Wan Po and Zhang (13 December, pp 1565-71). In figure 2 the mean rate ratios (95% confidence intervals) for moderate to excellent pain relief between treatments should have been given as numbers [not as percentages, as published].

Commentary: Improving the diagnostic rate in asthma: a community issue

Hans C Siersted

Our definition of asthma—the coexistence of asthma-like symptoms and obstructive airway abnormality—is widely accepted. The test battery and the diagnostic algorithm are routinely used in specialist clinics, and similar principles are applied by general practitioners. Thus we believe that asthma diagnosed in our community based study would also be diagnosed as such if the children visited an observant general practitioner. Our study shows, however, that in many patients asthma is not properly diagnosed.

Most importantly, most of these patients with undiagnosed asthma did not even report their symptoms to a doctor. Therefore we asked ourselves the question: can characteristics of these children with undiagnosed asthma be identified to help to increase awareness about the possibility of asthma in children with respiratory symptoms that are not obviously abnormal to parents, guardians, and school teachers? We believe that knowledge of the risk factors identified for not having asthma diagnosed could certainly promote the diagnostic decision process, especially at the community level (figure), leading new candidates for asthma evaluation to the doctor's waiting room. If then the doctor, considering also risk factors for underdiagnosis, agrees that a patient's symptoms could possibly be asthma, it is not the right time to wonder if more risk factors could help differentiate between asthma and "symptoms only." Instead, it is the time for tests such as peak flow monitoring



Stepwise path for diagnosing asthma in patients with respiratory symptoms

and (if these are negative) challenge with methacholine or exercise.

Thus, knowledge of pitfalls (risk factors for underdiagnosis)—for example, explaining cough alone as a natural response to passive smoking and exercise dyspnoea as simply the result of obesity—may be helpful at all stages of the diagnostic path towards the right answer to the asthma question.

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Numbers of deaths related to intrapartum asphyxia and timing of birth in all Wales perinatal survey, 1993-5

Jane H Stewart, Joan Andrews, Patrick H T Cartledge

Abstract

Objectives: To investigate the relation between the timing of birth and the occurrence of death related to an intrapartum event.

Design: Analysis of 107 206 births to Welsh residents in 1993-5, including 608 cases of stillbirth and 407 of neonatal death identified in the all Wales perinatal survey, the cause of death classified with the clinicopathological system.

Subjects: 79 normally formed babies stillborn or who died in the neonatal period, birth weight > 1499 g, for whom cause of death was related to an intrapartum event.

Main outcome measures: Relative risk of death due to an intrapartum event according to the hour, day, and month of birth.

Results: Mortality was higher in babies born between 9 00 pm and 8 59 am than in those born between 9 00 am and 8 59 pm; relative risk (95% confidence interval) 2.18 (1.37 to 3.47). July and August births also had a higher death rate than births in other months; relative risk 1.99 (1.23 to 3.23). Weekend births had a higher death rate but it was not significant.

Conclusions: The excess of deaths at night and during months when annual leave is popular may indicate an overreliance on inexperienced staff at these times. Errors of judgment may also be related to physical and mental fatigue, demanding a more disciplined systematic approach at night. Mistakes may be ameliorated by increasing shiftwork, but shifts should be carefully designed to avoid undue disruption of circadian rhythms. In addition, greater supervision by senior staff may be required at night and during summer months.

Editorial by Spencer

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