

Validation of Questionnaire and Bronchial Hyperresponsiveness against Respiratory Physician Assessment in the Diagnosis of Asthma

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Background. The Tasmanian Asthma Survey (TAS) and the International Study of Asthma and Allergies in Childhood (ISAAC) have used questionnaires to measure the prevalence of asthma in adults and children. We have investigated the validity of these questionnaires by comparing response to questionnaire with a physician assessment of asthma status in the past 12 months.

Methods. Ninety-three adults were given the TAS questionnaire to complete and 361 children were given the ISAAC questionnaire. Ninety-one adults and 168 children completed bronchial challenge with hypertonic saline. A consultation with a respiratory physician blinded to the results of the questionnaire and bronchial challenge was given to all subjects.

Results. In both adults and children, questionnaires showed high agreement with respiratory physician diagnosis with respect to asthma symptoms in the past 12 months. For the TAS questionnaire the positive and negative predictive values (95% confidence limits) for physician diagnosis for adults were 0.89 (0.68–0.98) and 0.94 (0.86–0.98) respectively. The instrument was also sensitive 0.80 (0.58–0.93) and highly specific 0.97 (0.90–0.99). For the ISAAC questionnaire the positive and negative predictive values for physician diagnosis of asthma in children were 0.61 (0.50–0.71) and 0.94 (0.88–0.98) respectively. Sensitivity and specificity were 0.85 (0.73–0.93) and 0.81 (0.76–0.86) respectively. Compared to the physician diagnosis, the sensitivity of bronchial hyperresponsiveness (BHR) for asthma was low for adults 0.39 (0.21–0.61) and children 0.54 (0.48–0.67) as were the positive predictive values: 0.55 (0.31–0.79) for adults and 0.64 (0.49–0.77) for children. A definition of asthma requiring both a positive questionnaire response and BHR was highly specific but not sensitive for adults 0.37 (0.20–0.59) or children 0.47 (0.35–0.60).

Conclusion. Both the TAS and ISAAC questionnaires are valid instruments for the determination of asthma symptoms in the past 12 months.

Keywords: asthma, bronchial hyperresponsiveness, questionnaire, validation, physician diagnosis, Australia

Questionnaires are frequently used in epidemiological studies of asthma, but difficulties arise in assessing their validity because of the variable nature of the disease. Asthma is a common respiratory disease in both adults and children with a prevalence estimated in

Australia between 20% and 40%.^{1,2} It is characterized by an increased responsiveness of the airways to various stimuli and manifested by a widespread narrowing of the airways that changes in severity either spontaneously or as a result of therapy. The main symptoms of asthma are episodes of breathlessness, wheezing (an audible whistling sound from the chest on breathing), and cough, varying from mild and almost undetectable to severe and unremitting.³

Large population-based surveys of asthma often rely on questionnaires as they are relatively economical when compared to examination of each subject. Regrettably, due to the complexities of the wide range of severity,

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triggers, and lack of medical knowledge among the general public, it is impossible to formulate an entirely reliable questionnaire. Questions thought to be most reliable in diagnosing asthma are those that include symptom-based components such as 'wheeze' or 'tightness in the chest'. These types of questions do not rely on lay understanding of asthma and therefore are more sensitive than items only inquiring about 'asthma'. Due to these complexities, there is no gold standard against which to validate asthma questionnaires. Previous attempts at validation have been restricted to studies of repeatability where subjects are retested using the same questionnaire.^{4,5}

In an attempt to increase the accuracy of epidemiological studies, objective measurements of the responsiveness of the airways have been used. One characteristic of asthma is hyperreactivity of the airways which results in constriction in response to non-specific stimuli at levels which usually do not affect non-asthmatics. Agents commonly used in testing for hyperreactivity include pharmacological ones, such as histamine and methacholine, and non-pharmacological ones, such as exercise, cold dry air and more recently hypertonic saline. The more sensitive the airways are, the more they constrict in response to the stimulus, resulting in limiting airflow. Bronchial hyperreactivity (BHR) is defined by the development of a specified decrease in the forced expiratory volume in the first second (FEV1) after exposure to an arbitrary but generally agreed upon dose.

Both clinical⁶ and population-based studies⁷⁻¹⁰ have shown that subjects with asthma are more likely to exhibit BHR than subjects without asthma. Indeed, BHR has been considered such an important factor by some researchers as to require its presence for the diagnosis of asthma.¹¹ Unfortunately, however, BHR is not highly sensitive, nor specific for the clinical diagnosis of asthma, as a proportion of asthmatics do not react to the stimulants used and a proportion of those who do not have asthma do exhibit BHR. In a study of 2053 New Zealand school children, Pattermore *et al.* found that 41% of those with BHR to histamine had no current asthma symptoms and 42% of those with current asthma symptoms did not have BHR.¹² The authors concluded that BHR cannot reliably or precisely separate asthmatics from non-asthmatics in the general community. A Canadian study of adult workers found similar difficulties in identifying subjects with asthma and concluded that priority should be placed upon designing and validating an asthma questionnaire.¹³ In a study of 29 asthmatic patients with a history of exercise induced asthma, Makker and Holgate¹⁴ found hypertonic saline responsiveness bears a closer relationship to the severity of exercise induced

asthma symptoms than BHR to histamine or methacholine. The diagnosis of asthma cannot be made solely on the results of laboratory tests of bronchial responsiveness. Asthma remains a clinical diagnosis, dependent upon the presence of certain features, obtained from the history, which may be influenced by the results of objective measures. The demonstration of objective bronchial hyperreactivity, together with a history of asthma symptoms, may identify those individuals whose asthma is more severe.

In practice, the physician assessment of current asthma may be the nearest to a gold standard¹⁵ among available measures. A diagnosis of asthma is made from the history, as physical diagnosis and lung function tests may be normal during asymptomatic intervals, as seen in intermittent episodic asthma. Tests of bronchial responsiveness are rarely useful in the diagnosis, nor in the management of asthma. We have attempted to define a standard clinical diagnosis of asthma, and use this for the physician diagnosis of asthma (see Methods).

We have recently concluded two studies examining prevalence and risk factors of current asthma (asthma symptoms in the past 12 months). These are: (i) the Tasmanian Asthma Survey (TAS), a population-based longitudinal survey of 1494 adults originally studied as children in 1968, and followed up between 1991 and 1993,¹⁶ and (ii) the International Study of Asthma and Allergies in Childhood (ISAAC), a population-based survey of 2836 school children aged 13 and 14 years in greater Melbourne conducted in 1993.¹⁷ The aim of this study was to validate the questionnaires used in both these studies with respect to diagnosis by a respiratory physician. The relationship between asthma diagnosis and BHR to hypertonic saline was also examined.

METHODS

Subjects

Adults. Between 1991 and 1993, the Tasmanian Long Term Health Survey (TLTHS)¹⁶ surveyed, by questionnaire, a random sample of 1494 subjects aged 30-32, as a follow-up of the 1968 Tasmanian Asthma Survey (TAS) in which 8585 subjects were surveyed at age 7 years.^{16,18,19} The subjects followed up in the 1991-1993 survey were selected as a stratified random sample, 50% from the sub-population that had a parent-reported history of asthma or wheezy breathing at age 7 years (16.2% of all subjects) and 50% from those without such a reported history (83.2% of all subjects).

All subjects of the TAS who had completed the TLTHS, and who were living in Victoria, a state of Australia, in 1994, were invited, with their spouses, to take part in a validation study. In total, 138 adult

subjects were approached and 93 (43% male) completed the study giving a response rate of 67.4%. Average age of subjects was 32.9 years ranging from 28 to 44 years (77.5% of subjects were aged 32 or 33 years). Forty subjects (43.6%) were from the 1991–1993 stratified sample who were reported to have asthma or wheezy breathing by age 7 years and the remaining 53 subjects (57.0%) from those with no symptoms by age 7 years.

Subjects were studied in the respiratory laboratory of the Department of Thoracic Medicine at the Royal Children's Hospital, Melbourne, Victoria, where they, in the following order, completed the Tasmanian Long Term Health Survey questionnaire, underwent a consultation with a respiratory physician to establish a diagnosis of current asthma, were given a skin prick test to common allergens, and given a bronchial challenge to hypertonic saline. The results of the skin prick tests are not included in this paper. All tests took place between March and July 1994.

Children. The children were taking part in an epidemiological study of the role of bronchial challenge in screening for asthma.^{17,20} In phase one, all of the 2845 children aged 13–14 years attending 25 randomly selected schools in greater Melbourne were invited to complete a written questionnaire about respiratory and atopic symptoms, and a video questionnaire about respiratory symptoms. The response rate was 97%. As part of phase two of the ISAAC study the 361 children from three representative schools were invited to complete the ISAAC screening questionnaire. Of the 345 children who completed the screening questionnaire (response rate 95%), all 123 who had wheezed during the past year, all 40 who had wheezed in the past (but not during the preceding year), and 123 controls selected randomly from the 182 children who had never wheezed, were invited to take part in lung function testing and bronchial challenge. A total of 206 children participated in lung function testing and successfully completed bronchial challenge, the refusal rate for participating in lung function testing being similar across all three symptom groups. Of these, 168 children (132 boys and 36 girls) were interviewed by a paediatric respiratory physician, in order to establish a physician diagnosis of 'current asthma'.

All tests were carried out in the schools by the staff of the respiratory laboratory of the Department of Thoracic Medicine, Royal Children's Hospital, Melbourne, Victoria, between July and September 1993.

Questionnaire

Adults. The Tasmanian Long Term Health Survey questionnaire includes the questions: 'Have you at any

time in your life suffered from attacks of asthma or wheezy breathing?' and 'How long is it since the last attack?'. If the response to the first question was 'yes' and the response to the second question was 'less than 12 months ago' then the subject was classified as having current wheeze.

Children. The ISAAC questionnaire includes the questions 'Have you ever had wheezing or whistling in the chest at any time in the past?' and 'Have you had wheezing or whistling in the chest in the last 12 months?' Current wheeze was defined as a positive response to both questions.

Diagnosis of Current Asthma by a Respiratory Physician

Each subject was interviewed by a paediatric respiratory physician (JRC or CFR), who was blinded to the responses of the Tasmanian Long Term Health Survey, the ISAAC questionnaires and the tests of BHR. Subjects were asked if they had ever experienced any wheezing described as 'whistling in the chest'. The subjects were then asked to explain the word 'wheeze', and an explanation was given according to the subject's response, rather than there being a standard definition, as in the clinical situation. If necessary the physician did demonstrate wheezing. Subjects were then asked about the circumstances in which wheeze occurred, whether it occurred at any particular time of the day, or after any trigger factors, such as exercise. The presence of nocturnal cough, sputum production, and smoking habits were noted. Details of any associated atopic diseases, such as hay fever and eczema, were obtained. The subjects who reported wheezing were asked about any treatment they had received, and their response to therapy. A physician diagnosis of 'current asthma' was defined as a history of wheeze suggestive of a clinical diagnosis of asthma within the past 12 months.

Hypertonic Saline Challenge

Subjects were asked to withhold the following asthma medications prior to the challenge test: antihistamines for 48 hours, theophyllines for 24 hours, inhaled anticholinergics, beta agonists and cromoglycate for 8 hours. Baseline FEV1 measurements were performed using a spirometer (Flowmate, Jaeger, Germany) until two successive FEV1 readings did not differ by more than 5%. Bronchial challenge was precluded if baseline FEV1 was 65% of predicted.

The hypertonic saline (HS) challenge tests were carried out according to the protocol developed by Smith and Anderson,²¹ with some minor modifications, as described by Riedler.²²

Subjects were defined as responsive to HS if they experienced a fall in FEV1 of 15% or more from their baseline values during the challenge, and as non-responsive if after a cumulative inhalation time of 15.5 minutes, FEV1 was still within 15% of their baseline value.

Statistical Methods

Validity of the questionnaires was determined by agreement between the questionnaire responses and respiratory physician diagnosis. We also assessed agreement between the response to the hypertonic saline challenge and the physician diagnosis, and between a diagnosis requiring both a positive response on the questionnaire and a positive challenge test and the physician diagnosis. Agreement was measured as positive and negative predictive values, sensitivity, specificity and also Youden's index, $Y = \text{sensitivity} + \text{specificity} - 1$.²³ Youden's index is of particular interest when considering the value of a screening test in estimating population prevalence, since if the true prevalences of a disease in two populations are p_1 and p_2 respectively, then the expected difference in prevalence, as measured by the screening test, is $Y(p_1 - p_2)$: in other words Y measures the extent to which the difference is attenuated by the imperfection of the test.

For both the adult and child data, not all information was obtained from groups sampled randomly from the population, and the analysis has been adjusted appropriately. Essentially, in both cases a form of stratified sampling was used, so that sensitivity, specificity and predictive values were calculated separately in each stratum and then combined using appropriate weighting to adjust for the representativeness of the stratified sample in the population.

For the TAS the sample was stratified by the reported asthma status of the child proband in the original 1968 survey. Taking the calculation of sensitivity as an example, the appropriate estimate is obtained as a weighted combination, $w p_{se}^A + (1 - w) p_{se}^B$, of the sensitivities estimated in each stratum, which we denote p_{se}^A for the stratum ('A') where the child had a childhood report of asthma and p_{se}^B for the other stratum ('B'), respectively. The weight w estimates the conditional probability that a subject is in stratum A given that they are positive according to the physician diagnosis, and may be estimated using Bayes' rule as

$$w = \frac{p_A p_+^A}{p_A p_+^A + p_B p_+^B}$$

where $p_{A[B]}$ is the population proportion for stratum A [B], that is, 0.162 [0.838] in this study, and $p_+^{A[B]}$ is the proportion that is positive according to physician

diagnosis in stratum A [B]. Similar formulae are used to obtain specificity, positive/negative predictive values, and Youden's index was calculated directly from the sensitivity and specificity.

For the children's study, different rates of sampling (for administration of the 'gold standard') were used within strata determined by the outcome of the screening questionnaire. The data provide direct estimates of the predictive value within each of these strata, but sensitivity and specificity were estimated by applying Bayes' rule (to obtain estimated probabilities of screening status conditional on disease status). Agreement coefficients for comparing hypertonic saline challenge and saline challenge plus questionnaire with physician diagnosis were calculated using extensions of the same logic as used in the previous paragraph.

For both adult and child data, confidence intervals were obtained using a Bayesian method.²⁴ This method is based on assuming non-informative prior distributions for the parameters of the multinomial distributions appearing in each stratum, and simulating values from the appropriate posterior distributions for the derived parameters of interest (sensitivity, specificity, Youden's index, and predictive values).

Approval to conduct the studies was obtained from the Royal Children's Hospital Ethics in Human Research Committee, and for the children's study approval was also obtained from the Directorate of School Education, Victoria, and from the principals of the schools involved. Written consent was obtained from the parents of the children and from the adult subjects.

RESULTS

Tables 1 and 2 show the number of adults and children respectively, reporting asthma according to questionnaire, by the number of subjects with BHR and by their asthma status according to the diagnosis of the respiratory physician. For questionnaire and BHR combined, 'Yes' indicates subjects who reported asthma in the questionnaire and who had BHR. Subjects are subdivided into the strata from which they were selected for this study. For adults the strata were defined by their parent-reported asthma status in the 1968 TAS. For children the strata were defined by their current asthma status according to self-report on the ISAAC questionnaire.

Table 3 shows the estimated specificity, sensitivity, positive and negative predictive values, and Youden's index (after adjusting for stratification) of the questionnaires and BHR for physician diagnosed asthma. There were no significant differences between males and females for any of these measures.

TABLE 1 Number of adults (stratified by asthma status recorded in the 1968 Tasmanian Asthma Survey) reporting asthma or wheeze in last 12 months by questionnaire in the Tasmanian Long Term Health Survey (TLTHS) and having bronchial hyperresponsiveness (BHR) to hypertonic saline, by the diagnosis of the respiratory physician for current asthma

Asthma status in 1968	TLTHS questionnaire	Physician diagnosis current asthma	Physician diagnosis current asthma	
			Yes	No
Stratum A asthma in 1968	current asthma	Yes	12	1
	or wheeze	No	3	24
Stratum B no asthma in 1968	current asthma	Yes	9	1
	or wheeze	No	2	41
Stratum A asthma in 1968	BHR to hypertonic saline	Yes	10	2
		No	4	23
Stratum B no asthma in 1968	BHR to hypertonic saline	Yes	3	4
		No	8	37
Stratum A asthma in 1968	current asthma or wheeze plus BHR to hypertonic saline	Yes	9	0
		No	5	25
Stratum B no asthma in 1968	current asthma or wheeze plus BHR to hypertonic saline	Yes	3	0
		No	8	41

Two of the 93 adults failed to complete hypertonic saline challenge; challenge was precluded in one female with reduced baseline FEV1 at only 61% predicted, and the other subject, in whom FEV1 had not changed, found the procedure very unpleasant and gave up

TABLE 2 Number of children reporting wheeze in the International Study of Asthma and Allergies in Childhood (ISAAC) by their bronchial hyperresponsiveness (BHR) status to hypertonic saline by the diagnosis of the respiratory physician for current asthma

ISAAC questionnaire	Physician diagnosis current asthma	Physician diagnosis current asthma		
		Yes	No	
Stratum A wheeze last 12 months	BHR to hypertonic saline	Yes	28	10
		No	22	22
Stratum B past history of wheeze	BHR to hypertonic saline	Yes	2	1
		No	2	17
Stratum C no history of wheeze	BHR to hypertonic saline	Yes	0	3
		No	1	60

during the challenge. Amongst the children there were 20 who only had exercise-induced symptoms, in which dyspnoea could not be distinguished from wheezing. These subjects had no symptoms at any other time, or any associated features of asthma. Because of the difficulty in distinguishing wheeze from exercise-induced dyspnoea in this group, they were classified as not having 'current asthma'.

DISCUSSION

This study has shown that current asthma defined by questionnaire response to questions of 'wheeze' in the past 12 months, in the TAS and ISAAC questionnaires,

TABLE 3 Parameter estimates (and 95% confidence intervals^a) of sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and Youden's index between response to questionnaires, bronchial hyperresponsiveness (BHR) to hypertonic saline and physician diagnosis of current asthma

	Sensitivity	Specificity	PPV	NPV	Youden's index
Adults:					
questionnaire vs. diagnosis	0.80 (0.58,0.93)	0.97 (0.90,0.99)	0.89 (0.68,0.98)	0.94 (0.86,0.98)	0.76 (0.54,0.90)
BHR vs. diagnosis	0.39 (0.21,0.61)	0.90 (0.80,0.96)	0.55 (0.31,0.79)	0.82 (0.71,0.90)	0.29 (0.09,0.51)
questionnaire + BHR vs. diagnosis	0.37 (0.20,0.59)	0.99 (0.95,1.00)	0.94 (0.65,1.00)	0.83 (0.73,0.91)	0.36 (0.18,0.58)
Children:					
questionnaire vs. diagnosis	0.85 (0.73,0.93)	0.81 (0.76,0.86)	0.61 (0.50,0.71)	0.94 (0.88,0.98)	0.66 (0.53,0.76)
BHR vs. diagnosis	0.54 (0.40,0.67)	0.89 (0.83,0.94)	0.64 (0.49,0.77)	0.85 (0.79,0.90)	0.43 (0.29,0.57)
questionnaire + BHR vs. diagnosis	0.47 (0.35,0.60)	0.94 (0.90,0.97)	0.74 (0.58,0.86)	0.84 (0.78,0.89)	0.41 (0.28,0.55)

^a Values tabulated for point estimates are the medians of posterior distributions based on non-informative prior distributions for the underlying multinomial parameters.²³ These are very close to the values that result from substitution of simple proportions from the data into the appropriate weighted formulae such as that outlined in the Methods section. Ninety-five per cent confidence intervals are the lower and upper 2.5% points of the same posterior distributions.

are generally valid measures of asthma as they are in close agreement with asthma diagnosis by a respiratory physician. For adults and children the responses to questionnaires were both sensitive and specific for physician diagnosed asthma. For adults and children, at least 80% of current asthmatics were identified by the questionnaire and only 3% of adults without current asthma were incorrectly labelled asthmatic by the questionnaire. Reported asthma symptoms by questionnaire were estimated to identify correctly asthma (positive predictive value) in adults 89% of the time, and negative reports of symptoms were estimated to identify correctly non-asthmatic adults and children (negative predictive value) 94% of the time. The questionnaire was more accurate at identifying asthmatic adults than asthmatic children where the positive predictive value was 61%. This indicated that interpreting all symptoms of reported recent wheeze as being asthma, may result in over-estimating the prevalence of childhood asthma. Those subjects who are not familiar with wheezing may use the term for a variety of respiratory noises and sensations. This may be the reason why more children than adults, who were diagnosed as non-asthmatic by a respiratory physician, reported that they had wheezed in the past 12 months. Despite a lower positive predictive value, sensitivity was reasonably high (85%) reflecting that the great majority of the childhood asthmatics were detected by the questionnaire.

The estimates of Youden's index (0.76 for adults, 0.66 for children) indicate that comparisons of questionnaire-based prevalence estimates between populations will underestimate differences in the true prevalence by between 30% and 50% (see Methods; $1/0.76 = 1.3$, $1/0.66 = 1.5$).

In contrast, around one in three children and approximately half of all adults with BHR to hypertonic saline were not asthmatic, and only about half of all childhood asthma and 39% of adult asthma was detected with BHR. While the majority of asthmatics did have BHR and the majority of those without BHR did not have asthma, this instrument's usefulness in detecting asthma was unsatisfactory.

Although challenge tests give objective measurements, which are readily reproducible and can be used across different population groups, no challenge test has been shown to be sufficiently sensitive or specific, in population studies, to be used in isolation to make a diagnosis of asthma. The specificity of our study is consistent with other community based studies in children, using a variety of different challenges (Table 4). Other published studies have reported a higher sensitivity for HS, but these have been hospital based studies, where asthmatic subjects tended

TABLE 4 *Validity of self-report asthma using bronchial hyperresponsiveness to various agents in several community based studies of children*

Challenge test	Age range (years)	Sensitivity (%)	Sepecificity (%)
Hypertonic saline ¹⁷	13-15	47	92
Exercise ¹⁷	13-15	46	88
Distilled water ³⁰	7-10	36	92
Cold air ³¹	9-11	31	88
Histamine ¹⁰	8-11	53	87

to have more severe asthma, with more chronic symptoms, rather than infrequent episodic asthma, with no intercurrent symptoms, which was the pattern of asthma experienced by most of our subjects. Some of our subjects were taking regular asthma medication. Inhaled steroids were not withheld prior to the study, although subjects were requested to withhold other medication, as described in the methods. Inhaled steroids could have modified the degree of BR to HS, but exclusion of those subjects taking inhaled steroids would not have significantly improved the sensitivity.

The sensitivity and specificity of challenge tests is dependent upon the change in lung function chosen as the cutoff limit which represents BHR. A fall in FEV1 of 15% was chosen in this study, as this level was optimal, in terms of sensitivity and specificity, in 13-15 year olds.¹⁷ In our study a smaller proportion of adults than children with current asthma was responsive to HS. This raises the issue of comparing BHR across different age groups. For example, is a 15% fall in FEV1 in adults a comparable measure of airways reactivity to a 15% fall in FEV1 in 13-14 year olds?²⁵

It has been suggested that BHR plus a positive response to symptom-based questionnaire should be used to define asthma.¹¹ However we found that although such a definition was highly specific for asthma in adults (99%) and children (94%), the sensitivity was low (37% for adults and 47% for children). This definition would therefore not be appropriate for population-based epidemiological studies as it would underestimate the true prevalence of asthma. The majority of asthmatics would be missed because of the low sensitivity of such a combined definition.

Three methods of validation have been employed in reported studies:²⁶ comparing questionnaire response to a clinical physiological investigation, such as a bronchial challenge test;¹³ comparing questionnaire response with a previous doctor diagnosis,²⁷ and comparing

questionnaire response with responses from another questionnaire.^{28,29} These studies reflect the lack of a true gold standard for diagnosing asthma, but since asthma is a clinical diagnosis, our approach of using a respiratory physician diagnosis of asthma, as a gold standard, appears reasonable.¹⁵

Questionnaires by themselves have some limitations. They cannot necessarily be used for international studies, as direct translation of some terms into another language is not always possible. For example, some languages do not have a single word which means wheeze. The ISAAC questionnaire used in this study has been translated from English to several languages including French, German and Finnish. It is important to validate questionnaires in the country, language and the situation for which they have been designed. This may be difficult, as the gold standard, physician diagnosis of asthma, may also differ from country to country. Not only are there potential problems in validating questionnaires in different countries, but any problems are compounded because the concept of what actually constitutes asthma has been changing over a period of time. In our study, all subjects were fluent in English, and given the same questionnaire.

Despite the limitations of using tests of bronchial responsiveness in the diagnosis of asthma, such objective measures may be useful for comparisons between countries where questionnaire results cannot be directly compared. Further they provide objective measures which do not change over time, as the physician diagnosis of asthma may do. However, our estimates of Youden's index indicate that comparison between the prevalence of BHR in different countries may give considerable underestimates of differences in the prevalence of asthma; for example given $Y = 0.29$ (adults) the difference in asthma prevalence is approximately $1/0.29 = 3.5$ times the difference in BHR prevalence (see Methods).

In conclusion, in this study in which we compare self-reported asthma with the diagnosis of a respiratory physician, we have shown that asthma questionnaire items determining wheeze are valid instruments for measuring current asthma in children and adults in epidemiological surveys.

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