

## Validity and repeatability of the IUATLD (1984) Bronchial Symptoms Questionnaire: an international comparison

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*Validity and repeatability of the IUATLD (1984) Bronchial Symptoms Questionnaire: an international comparison. P.G.J. Burney, L.A. Laitinen, S. Perdrizet, H. Huckauf, A.E. Tattersfield, S. Chinn, N. Poisson, A. Heeren, J.R. Britton, T. Jones.*

**ABSTRACT:** The International Union against Tuberculosis and Lung Disease (IUATLD) Bronchial Symptoms Questionnaire (1984) was developed for use in studies of asthma and its reliability measured in an earlier survey in England. The association of the symptoms elicited by this questionnaire to bronchial response to histamine has also been described. This paper presents the results of studies of the questionnaire in four clinical centres in Europe. The reliability of the questionnaire and its ability to predict the bronchial response to histamine were compared for English, Finnish, French and German translations of the questionnaire in samples of diagnosed asthmatics and controls in Nottingham, Berlin, Helsinki and Paris. The answers to questions showed good repeatability, especially in Finland and Germany, particularly those questions on asthma and wheeze. The most sensitive symptom for predicting hyperresponsiveness was the question on wheeze, the most specific questions were those on waking at night with shortness of breath (Paris and Nottingham) and morning tightness (Helsinki and Berlin). This study shows that the IUATLD (1984) questionnaire may provide useful, valid and comparable data even in translation but these studies will need to be repeated in representative samples before such a possibility is accepted as fully demonstrated.  
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Asthma is an ill defined condition which, nevertheless, requires standardized methods of identification in epidemiological surveys [1]. Historically this has been done most often by asking questions about a diagnosis of asthma or by asking about a history of wheeze [2]. Answers to questions on asthma have been shown to be biased by access to and use of health care [3-5] and there is concern that wheeze may not be a symptom specific to asthma.

The search for an objective test for asthma has concentrated on tests of bronchial hyperreactivity [2]. These are not specific to asthma, at least as the term is generally understood in the United Kingdom [6], but nevertheless do provide an objective and reliable marker of one physiological characteristic strongly associated with asthma and with the need for treatment [7]. These tests have been simplified for use in epidemiological studies [8], but they remain expensive in the time that they require from skilled personnel. There remains a need for a simple questionnaire that could be used in surveys of large and widespread populations [9].

A number of authors have commented on the association between airway hyperreactivity and symptoms

[10-14]. Airway hyperresponsiveness has generally been associated with an increased prevalence of respiratory symptoms assessed using the British Medical Research Council (MRC) Respiratory Symptoms Questionnaire or a derivative. This has been the case particularly with wheeze and cough or cough and sputum production. MORTAGY *et al.* [11] developed their own questionnaire and noted associations with wheeze, shortness of breath at night and tightness in the chest in the early morning. A number of authors have, however, also remarked on the generally poor association between symptoms and hyperresponsiveness [10, 13], and a substantial number of subjects with rhinitis but without wheeze or chest tightness nonetheless have bronchial hyperreactivity as measured by several different methods [15, 16].

The International Union Against Tuberculosis and Lung Disease (IUATLD) has been developing a questionnaire for use in epidemiological studies of asthma. An early decision was taken to validate this against bronchial hyperreactivity as an available objective measure. The early development of the questionnaire in England has been described elsewhere [9, 17] and this paper describes a study designed to examine whether responses to the

questionnaire given in different languages in different countries relate in the same way to bronchial hyperresponsiveness as did the original questionnaire in a larger English sample [17].

### Methods

**Questionnaires.** The IUATLD (1984) questionnaire used in the initial English study was translated into French, German and Finnish and the translations checked by independent translation back into English.

**Samples.** In each centre approximately 20 subjects with diagnosed asthma and 20 without were selected. The base population from which they were selected and the methods of selection varied according to circumstances. In Finland subjects were military recruits, whereas in Paris (France), Berlin (Germany) and Nottingham (England) subjects were selected from new outpatients. In Paris and Nottingham all of the patients came from practices involved predominantly with respiratory disease, whereas those from Berlin who did not have a diagnosis of asthma came from a different medical clinic.

**Procedure.** After being selected and giving consent all subjects were asked to complete a questionnaire. If subjects were illiterate and the questionnaire was administered, interviewers were instructed to read the questions to the subjects without any more comment than appeared on the questionnaire. If the subject asked questions, the interviewer was asked to repeat the question and, if there was still no clear response, to mark the question as having been answered in the negative.

After the questionnaire was completed all subjects underwent bronchial challenge with histamine using the method described by YAN *et al.* [8]. Doses of histamine ranged from 0.03–4.0  $\mu\text{mol}$ . The dose provoking a 20% fall in forced expiratory volume in one second ( $\text{FEV}_1$ ) ( $\text{PD}_{20}$ ) was estimated using the method of CHINN *et al.* [18].

At a minimum of two weeks later a second identical questionnaire was completed by each of the subjects in order to assess repeatability.

**Analysis.** Repeatability of the questions was assessed both in terms of absolute repeatability using  $\pi$  [19] and relative repeatability using  $\kappa$  [20]. The validity of the questions was measured as sensitivity, specificity and the index of YODEN [21], using the data from each country separately. In addition we tested for differences between the association of symptoms with reactivity ( $\text{PD}_{20}$ ) found in the original English survey [17] and the association found in the individual studies reported here. The comparisons were made with the first randomly selected half of the initial English subjects whose answers had been used to develop the method of scoring the questionnaires.

In addition to assessing individual questions a predictor of airway hyperresponsiveness developed in the initial survey, the discriminant function predictor (DFP),

was also evaluated. This predictor was positive if the subject had had wheeze, waking with shortness of breath, tightness in the chest or cough when entering a dusty room or contact with animals or feathers. It was also positive if the subject complained that they had either intermittent or continuous trouble with their breathing.

### Results

Table 1 shows the characteristics of the subjects. The populations studied were similar to each other with the exception of the Finns. Their method recruited a young male sample with relatively few exsmokers. The German subjects contained a high proportion of women (72%) and a relatively high proportion of subjects who were strongly reactive to histamine, 36% having a  $\text{PD}_{20} < 0.50$   $\mu\text{mol}$  and 64% responding to 8  $\mu\text{mol}$  or less.

Table 2 shows the repeatability of the questions. Absolute repeatability was good for all questions in all countries. Relative repeatability was also good for the most part. The answers in Finland and Germany seemed to be slightly more repeatable and answers to questions on wheeze and asthma also appeared particularly repeatable in all countries.

Table 3 shows the validity of the questions as predictors of bronchial hyperreactivity. Wheeze tended to be the most sensitive marker of bronchial response to histamine in the current study. It also had the highest Youden's Index in Helsinki and Berlin, although in Nottingham and Paris the symptom with the highest Youden's Index was waking at night with shortness of breath. Of the three symptoms the most specific were morning tightness in Helsinki and Berlin, and waking with shortness of breath in Paris and Nottingham.

Examining each question independently, using logistic regression, showed that the symptoms found to be predictive of reactivity in the first English survey were generally also associated with bronchial reactivity in this study. However, some questions had significantly weaker associations than were found in the English survey (table 4). Waking at night with shortness of breath was significantly less predictive in Berlin and in the three continental countries taken as a whole. Tightness in the chest in association with dust, animals or feathers was significantly less predictive in Nottingham, Paris and the three continental countries taken together. This remained true when multiple logistic regression was used to estimate the association between reactivity and symptoms after allowing for the information provided by other symptoms. In this case waking short of breath was significantly less closely associated with hyperresponsiveness in Germany and in the three continental countries taken together, and tightness in the chest or cough in the presence of animals, dust or feathers was significantly less closely related to reactivity in the three continental countries taken together.

Table 5 shows the association between the subjects' opinion of whether they have asthma and what the doctor thought. Doctors confirmed that 45/49 patients

Table 1. - Characteristics of selected populations

	Finland n=42	Germany n=42	France n=51	Nottingham n=40
Male %	100	28	58	62
Age range	17-24	16-60	20-66	21-64
Primary diagnosis of asthma %	52	42	41	51
Never smoked %	48	44	45	50
Exsmokers %	5	21	22	25
Current smokers %	48	35	29	25
Unknown smoking history %			4	
Number given at least 2 doses of histamine	42	42	50	40
PD <sub>20</sub>				
% > 0.12 < 0.50	5	19	4	3
% > 0.50 < 2.00	5	17	2	13
% > 2.00 < 8.00	12	14	12	23
% > 8.00	24	14	12	10
	55	36	68	53

PD<sub>20</sub>: provocative dose producing 20 % fall in forced expiratory volume in one second.

Table 2. - Repeatability of selected questions

	Absolute repeatability (average "correct" classification rate)				Repeatability relative to prevalence of response ( $\kappa$ )			
	Finland	Germany	France	Nottingham	Finland	Germany	France	Nottingham
1 Wheeze	0.96	0.99	0.96	0.93	0.85	0.95	0.83	0.73
2 Morning tightness	0.91	0.94	0.88	0.84	0.67	0.66	0.60	0.46
3 Attacks of shortness of breath	0.85	0.90	0.85	0.83	0.46	0.40	0.56	0.46
4 Waking with shortness of breath	0.91	0.96	0.93	0.92	0.63	0.85	0.77	0.71
5 Phlegm	0.87	0.95	0.85	0.88	0.52	0.74	0.51	0.55
6 Breathing problems continuous, intermittent rare	0.94	0.95	0.80	0.88	0.78	0.77	0.51	0.66
12 Asthma ever	0.92	1.00	0.93	0.83	0.71	1.00	0.74	0.70
12.4 Asthma last 12 months	0.92	0.99	0.88	0.92	0.73	0.94	0.59	0.85
Discriminant function predictor	0.99	0.99	0.82	0.86	0.95	0.96	0.54	0.53

Table 3. - Ability of selected questions to predict a PD<sub>20</sub> less than or equal to 8  $\mu$ mol of histamine

	Finland			Germany			France			Nottingham		
	Sens	Spec	Youden	Sens	Spec	Youden	Sens	Spec	Youden	Sens	Spec	Youden
1 Wheeze	0.95	0.74	0.69	0.59	0.80	0.39	0.73	0.65	0.38	0.89	0.62	0.51
2 Morning tightness	0.74	0.87	0.61	0.33	0.93	0.26	0.53	0.72	0.25	0.79	0.57	0.36
3 Attacks of shortness of breath	0.58	0.78	0.36	0.11	0.80	-0.09	0.73	0.68	0.41	0.74	0.67	0.41
4 Waking with shortness of breath	0.47	0.83	0.31	0.37	0.80	0.17	0.69	0.77	0.46	0.74	0.97	0.71
5 Phlegm	0.63	0.74	0.37	0.26	0.87	0.13	0.50	0.62	0.12	0.74	0.79	0.23
6 Breathing problems i continuous or intermittent vs rare ii continuous vs intermittent or rare	0.89	0.83	0.72	0.30	0.80	0.10	0.80	0.57	0.37	0.78	0.65	0.43
12 Asthma ever	0.74	0.91	0.65	0.33	0.93	0.26	0.80	0.74	0.54	0.53	1.00	0.53
12.4 Asthma last 12 months	0.68	0.91	0.59	0.26	0.93	0.19	0.50	0.76	0.26	0.47	1.00	0.47
Discriminant function predictor	1.00	0.57	0.57	0.67	0.67	0.29	0.83	0.41	0.24	0.89	0.47	0.36

PD<sub>20</sub>: provocative dose producing a 20 % fall in forced expiratory volume in one second; Sens: sensitivity; Spec: specificity; Youden index [21].

Table 4. – Odds ratio between bronchial response to histamine (PD<sub>20</sub> <8 μmol) and selected symptoms, calculated from logistic regression

		Current study					
		English Standard <sup>#</sup>	Continental Europe <sup>##</sup>	Finland	Germany	France	Nottingham
<b>Simple regression</b>							
1	Wheeze	15.38	7.29	51.01	6.40	5.04	13.82
4	Waking with breathlessness	16.53	3.54**	4.28	2.35*	7.50	50.40
6	Continuous problems with breathing	8.81	2.13*	+	+	4.93	8.77
9.3	Tightness or cough with animals, dust or feathers	24.02	4.18**	35.56	3.18	3.43*	0.50***
<b>Multiple regression</b>							
1	Wheeze	6.13	5.83	57.63	9.23	1.53	\$
4	Waking with breathlessness	5.84	0.93*	0.59	0.39*	2.25	\$
6	Continuous problems with breathing	3.00	1.11	+	+	3.01	\$
9.3	Tightness or cough with animals, dust or feathers	12.23	2.52*	36.34	1.63	1.76	\$

<sup>#</sup>: initial analysis of English community survey; <sup>##</sup>:Finnish, German and French studies combined. Significance of difference of odds ratios from those in the English standard +: specificity = 100 %; \*: p<0.05; \*\*: p<0.01; \*\*\*: p<0.001; \$: insufficient data; PD<sub>20</sub>: provocative dose producing a 20 % fall in forced expiratory volume in one second.

Table 5. – Comparison of doctors' and subjects' opinion of whether the subject had asthma

Subjects' opinion			Doctors' opinion of whether the subject had asthma									
			Finland		Germany		France		All continental Europeans <sup>#</sup>		Nottingham	
			yes	no	yes	no	yes	no	yes	no	yes	no
12	Asthma ever	yes	15	1	10	0	15	7	40	8	10	0
		no	7	19	8	25	5	23	20	67	11	18
12.4	Asthma last 12/12	yes	14	1	8	0	14	3	36	4	9	0
		no	8	19	10	25	6	27	24	71	12	18
Total			22	20	18	25	20	30	60	75	21	18

<sup>#</sup>: Finnish, German and French studies combined.

Table 6. – Doctors' diagnoses according to the patients' opinion of whether they had had asthma in the previous twelve months and results of histamine challenge

Subjects with asthma in previous 12 months		Subjects without asthma in the previous 12 months	
Reactive 34 asthmatics	Unreactive 9 asthmatics	Reactive 21 asthmatics	Unreactive 14 asthmatics
1 Acute bronchitis	1 Pulmonary tuberculosis	1 Goitre	61 Various
1 Abnormal X-ray		1 Hyperparathyroid	
1 Allergic Rhinitis		1 Vitamin B Co deficiency	
		3 Hypertension	
		2 Arrhythmias	
		2 Allergic rhinitis	
		2 Chronic obstructive bronchitis	
		2 COPD	
		1 Polymyositis	
		1 Cough	
		1 Pneumonia	
		1 Post viral hyperreactivity	
		1 Bronchial neoplasm	
	1 Not known	3 Not known	7 Not known

who said they had had asthma in the last 12 months, had asthma, but 31/81 (38%) of those whom their doctors thought had asthma claimed never to have had the condition.

Table 6 shows the doctors' diagnoses according to whether the subjects thought that they had had asthma in the previous 12 months and the results of the histamine challenge. Of eleven unreactive subjects ( $PD_{20} > 8 \mu\text{mol}$  histamine) who claimed to have had asthma in the previous 12 months, nine were also thought by their doctors to be asthmatic. Of 44 reactive subjects who claimed not to have had asthma in the last 12 months, 21 were believed by their doctors to be asthmatic but 20 were given other diagnoses. No diagnosis was given for three subjects.

### Discussion

This study represents an attempt to standardize a questionnaire for the prediction of bronchial reactivity across different languages. The study was restricted in terms of manpower and other resources and only provides a provisional result. However, the findings of the study do give some grounds for believing that approximately equivalent information may be collected by using questionnaires in different languages and populations. This study was not large enough to give more precise information on the extent of any biases.

We have provided estimates of repeatability in both absolute and relative terms. Because  $\kappa$  is dependent on prevalence this will be affected by the choice of sample. As the prevalence falls from that in this sample the value of  $\kappa$  would also fall.

The questionnaire did best at predicting reactivity in the Finnish sample in which smoking is likely to have had the least confounding effect because of the young age of the subjects. There is also a notable consistency between the countries considering the differences in samples and languages. Of the individual symptoms the question on wheeze is consistently the most sensitive. This is surprising as the German translation was a paraphrase that did not bear an immediate resemblance to the original question (Haben Sie eine ziehende Atmung oder Pfeifen zu irgendeiner Zeit in den Letzten 12 Monaten gehabt?), there being no suitable colloquial term for wheeze in German. The symptoms of waking with shortness of breath at night, or of waking with tightness in the chest in the early morning were the most specific symptoms in each country. There was little to choose between the two except in the Nottingham sample where waking with tightness in the chest in the morning seemed to have poor specificity. Finally the question with the highest Youden's index was consistently the question on wheeze.

Choosing an ideal question for predicting bronchial reactivity under all circumstances is not possible. The question that gives the least biased estimate of the difference between two prevalences is that with the highest Youden's index [17]. That which gives the least misclassification where the prevalence is less than 50% as in the

case with bronchial hyperreactivity, is the question with the greatest specificity. Under some circumstances the best screening test for selecting a population prior to using a further confirmatory test may be the test with the greatest sensitivity.

Two important potential sources of bias have been introduced by the design of the study. Firstly, and less seriously, we were not able to test the comparability of the histamine challenge tests in the different centres. It was not practicable to assemble all testers to train together and to be tested for comparability using the same subjects. We were, however, able to standardize the method. If the tests of reactivity were biased in one country this would alter the estimates of sensitivity and specificity in different directions, whereas the tendency was for sensitivity and specificity to be correlated between countries. The possible exception is Germany, where sensitivity was generally lower and specificity higher than in other countries (table 3). This difference could equally be explained by the German population being less likely to report symptoms or by the provocation used in Germany being weaker.

The more serious problem arises from the method of sampling. Studies of this nature are best carried out on representative samples of the general population. This was not feasible in this instance. The condition for the accurate estimation of sensitivity and specificity from these samples is that the subjects should be selected by reactivity and not by symptoms. In asking for asthmatics and non asthmatics this condition is unlikely to be fulfilled although it might be hoped that no one symptom has influenced the choice of subjects more than another.

Where a symptom has influenced the choice of subjects this will tend to increase the estimated sensitivity and reduce the estimated specificity of this symptom as a predictor of reactivity as measured in the study.

We assessed the association between symptoms and reactivity in terms of the odds ratio. This will be an unbiased estimate of how much more common increased bronchial reactivity is in those with symptoms compared with those without symptoms only if reactivity is rare and if the sample has been selected in such a way that selection factors associated with symptoms are independent of those associated with reactivity. In an already preselected population it is not possible to assess the extent to which this latter condition has been met. Reactivity as measured in this study affects approximately 14% of the English population surveyed earlier [17]. This will have had the effect of exaggerating the odds ratios quoted in table 4 in all but the "standard" English population.

This study has shown that the characteristics of questions as predictors of bronchial hyperreactivity appear to be qualitatively similar between selected countries and languages. This conclusion will, however, require confirmation in larger studies on representative samples of subjects which should also give a better estimate of any bias in the questionnaire between countries. On the strength of these findings we have edited the original IUATLD (1984) questionnaire into a shorter version, the IUATLD (1986) Bronchial Symptoms Questionnaire. This

is available from the IUATLD in several languages including Chinese, Japanese and Spanish. Further studies of its characteristics are in progress.

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*Validité et reproductibilité du questionnaire de l'Union Internationale contre la Tuberculose et les Maladies Respiratoires (1984) sur les symptômes bronchiques: une comparaison internationale.* P.G.J. Burney, L.A. Laitinen, S. Perdrizet, H. Huckauf, A.E. Tattersfield, S. Chinn, N. Poisson, A. Heeren, J.R. Britton, T. Jones.

RESUMÉ: L'Union Internationale contre la Tuberculose et les Maladies Respiratoires a développé en 1984 un "questionnaire des symptômes bronchiques" en vue de son utilisation dans les études de l'asthme; sa valeur a été mesurée dans une enquête antérieure en Grande-Bretagne. L'on a également décrit l'association des symptômes mis en évidence par ce questionnaire à la réponse bronchique à l'histamine. Ce travail expose les résultats d'étude du questionnaire dans quatre centres cliniques en Europe. La validité du questionnaire et sa potentialité de prédiction pour la réponse bronchique à l'histamine ont été comparées pour les traductions anglaise, finnoise, française et allemande du questionnaire, dans des échantillons d'asthmatiques et de contrôles diagnostiqués à Nottingham, Berlin, Helsinki et Paris. Les réponses aux questions ont montré une bonne reproductibilité spécialement en Finlande et en Allemagne, et particulièrement sur les questions concernant l'asthme et les sifflements. Le symptôme le plus sensible pour la prédiction de l'hyperréactivité était celui se rapportant aux sifflements. Les questions les plus spécifiques furent celles se rapportant à l'éveil nocturne avec oppression (Paris et Nottingham) et l'oppression matinale (Helsinki et Berlin). Cette étude montre que le questionnaire de l'Union Internationale (1984) peut fournir des données utiles, valables et comparables, même après traduction. Ces études doivent toutefois être répertoriées dans des échantillons représentatifs avant que l'on considère que cette possibilité est démontrée de façon formelle. *Eur Respir J.*, 1989, 2, 940-945