Original research

For personal use only.

Not to be reproduced without the permission of the Primary Care Respiratory Journal

Factors affecting adherence to asthma treatment: patient and physician perspectives

Eric Van Ganse, Ann-Christin Mörk, Liesl M Osman, Paul Vermeire, Laurent Laforest, Alexia Marrel, Elisabeth Ståhl

Abstract

Aims: To identify important factors affecting treatment adherence of patients with asthma and to summarise this information as a guide for physicians.

Methods: Information from literature and interviews with 12 respiratory physicians (four each from France, Spain and UK) and 46 asthma patients was obtained. Factors affecting adherence to asthma treatment were identified, reviewed and a flow chart developed to indicate the relationship between key factors.

Results: Major factors influencing adherence included: the patient-physician relationship; the patient's understanding of the disease and its treatment; the patient's beliefs and perception of the disease and its treatment, and, importantly, the patient's willingness to take an active part in his/her asthma management.

Conclusion: Patient adherence to asthma can be improved, and the likelihood of treatment success increased, by paying attention to the factors that influence patients' willingness to participate in their treatment.

Key words: Asthma, adherence, patient beliefs, medication

Eric van Ganse CHU-Lyon

Ann-Christin Mörk AstraZeneca, Sweden

Liesl M OsmanUniversity of Aberdeen

Paul Vermeire University of Antwerp

Laurent Laforest CHLU-Lyon

Alexia Marrel Mapi Values, Lyon

Elisabeth Ståhl AstraZeneca, Sweden

Correspondence to:
Dr Eric van Ganse
Centre Hospitalier Lyon Sud
(CHLS)
Unité de
Pharmacoépidemiologie
Sainte Eugénie (bâtiment 5F)
69495 Pierre-Bénite
Cedex France

Tel +33 4 72 66 64 38 Fax +33 4 72 66 64 44

Email: eric.vanganse@chulyon.fr

Date submitted: 26/01/03 Date Accepted: 27/05/03

Prim Care Resp J 2003; **12(2)**:46-51

Introduction

Adherence† to treatment in asthma is mostly poor and may be a significant factor contributing to adverse outcomes, reduced health-related quality of life (HRQL) and high costs of the disease.¹ There are many reasons for poor adherence, including beliefs about medications, which may often be at variance with current scientific evidence.² It is important to understand the ways in which patients make their decisions to adhere to treatment, as this may be directly related to the benefits they obtain from treatment.³

In this article, information from a literature review and interviews from a small group of European respiratory physicians and asthma patients are used to identify patient and physician views on the important factors involved in treatment adherence. The aim was to process this information as a guide for physicians to assist them in improving the management of patients, more particularly by improving adherence.

Methods

Articles published from 1990 onwards with abstracts in French or English were identified from Medline or Excerpta Medica databases (keywords were asthma and patient compliance/adherence). These articles were screened for relevance based on the content of their abstracts. Individual factors affecting adherence were identified from individual studies measuring adherence and from previous review articles. An expert group, consisting of an epidemiologist and two respiratory physicians, reviewed and categorised the factors identified as influencing adherence and interrelated these in a flow chart.

Twelve respiratory physicians (four each from France, Spain and UK) with experience of treating asthma patients were selected from a database of physicians maintained by Mapi Values and interviewed by a

Clinical Research Associate (France, Spain) or a physician (UK). Interviews were carried out by phone in France and the UK and face-to-face in Spain. Physicians' views were obtained using a semi-structured interview guide; this was structured, to obtain information on: asthma, diagnosis, cause, treatment (medications and otherwise); patient-management practices; the impact of asthma on patients' lives; patient understanding of asthma and adherence; overall perspective. The physicians provided opinion on the preliminary flow chart and suggested changes either verbally or by annotation of the chart. The chart was faxed to physicians who were interviewed by phone, and annotated charts returned similarly.

Face-to-face interviews were conducted with asthma patients referred by respiratory physicians (these included those interviewed) and general practitioners, who supplied details of their patient's treatments and disease status according to Global Initiative for Asthma (GINA) guidelines.⁴ Inclusion criteria were predefined. Patients were required to have asthma and have been treated with inhaled corticosteroids (ICS) with or without a long-acting \(\beta 2\)-agonist (LABA) as controller medication (≥2 years). It was intended that half of the patients would have had a recent asthma exacerbation (use of oral steroids within 6 months or a hospitalisation/emergency room visit within 2 years), a similar number would be male and female, and at least 18 patients (half male and female) would be aged between 20 and 35 years.

Their physician offered patients the opportunity to volunteer for the study. An explanation of the purpose of the study was given to the patients who volunteered by the interviewer, and verbal agreement was obtained before commencing the interview. Clinical Research Associates carried out interviews with the patients using a semi-structured interview guide, structured to obtain information and views on the following: socio-demographic characteristics;

Not to be reproduced without the permission of the Primary Care Respiratory Journal

patient knowledge of asthma; details of their current treatment; advantages and disadvantages of their treatment; purpose of treatments (e.g. differences between relievers and controllers); adherence to treatment (and reasons for non-adherence); their role in treatment; information provided on asthma and treatment; overall expectations and satisfaction with treatment and the management of their disease; information provided; impact of asthma on their lives; overall satisfaction with treatment. Patients were asked to rate the severity of their asthma as either mild, moderate, severe or very severe. The measure of agreement between patient ratings of asthma severity and the physician-assigned severity of asthma (GINA stage) was tested using a weighted kappa test.

Socio-demographic data from respiratory physicians and patients, and clinical data were analysed by descriptive statistics. Verbatim responses were tabulated from interviews and reviewed by the expert group, who subsequently revised the flow chart.

Results

Literature review

From 971 articles identified from the Medline and Excerpta Medica databases, 493 individual articles were identified with abstracts in English or French. Of these, 275 articles containing relevant information on factors affecting adherence were identified. The individual factors suggested or demonstrated to be associated with adherence in the articles reviewed, and any additions from subsequent expert review, are grouped in categories in Table 1.

Physician interviews

Physicians (11 male, one female) were aged between 33 and 55 years (mean 42 years). Types of practice were: hospital, five; private, two; both, five. On average each physician saw 24 patients per day (range 5-60), which included six (range 2-12) asthma patients.

Diagnosis and choice of treatment

All physicians based their diagnosis on medical history, symptoms and examination. Diagnosis was usually confirmed by tests (n=9), typically lungfunction measurements, and sometimes supported with other tests, e.g. allergy skin testing (n=2) and blood tests (n=2). Family history was the only factor commonly cited by physicians (n=8) as a determinant of asthma. The adverse effects of asthma on HRQL and relationship with severity of disease were generally recognised. The most frequently cited negative impacts of asthma were related to patients' work and scholastic activities (n=11); others included effects on sleep (n=3), restrictions on exercise, social and leisure activities (n=3), and partner/colleague relationships (n=1). As well as clinical status, the physician's choice of treatment took into account patient wishes (n=8), their intellectual ability (n=2), and ability to use an inhaler (n=6); the latter was considered a particular problem in the elderly (n=5).

Table 1. Factors that may affect patient adherence to asthma treatment.

*Categories of factors considered of greatest importance

Patient characteristics: Age; gender; educational level; socio-economic level; ethnic origin; physical ability; comorbid diseases

Environment and support: Attitudes and involvement/support of family/friends; social relationships; lifestyle

Patient knowledge and understanding of asthma:* Asthma, symptom recognition, understanding severity and variability of symptoms; how to manage symptoms; triggers; medications

Psychological state: Anxiety; depression; stress; forgetfulness

Beliefs/attitudes and perception of disease/treatment:* Factors that control health; locus of control - internal (patient controls their own destiny), self-efficacy (ability to manage the disease themselves) and external (something or someone else has control); fate (chance); helplessness - neither he nor she or the physician can do anything to help. Cultural beliefs. Perceptions of control - feeling the disease is well controlled; severity of the disease; necessity for and success/benefit of medication; perceived success of treatment; the burden of treatment (cost, complexity, social embarrassment); the medication (side-effects, dependence, fear of steroids, general beliefs)

Patient's willingness:* Desire to take active part in the management of disease; denial and rejection of diagnosis; laziness; disturbance/limitation of normal daily and social/recreational activities

Medication: Frequency of dosing; integration with other medications; simplicity of directions and use; taste; degree and nature of side effects; convenience and embarrassment in using; cost

Patient-physician relationship:* Communication; patient satisfaction with relationship with physician; confidence in physician skills; therapeutic alliance (patient takes active part in treatment decision); patient expectations; patient information (on the disease, on the treatment, on the device); continuity of care; failure to analyse medication behaviours; physician training in communication skills; inappropriate medication or dose prescribed.

Specialist-general practitioner relationship: Consistency of advice and treatment; trust and mutual respect

Access to medical care and advice: Location of amenities; financial situation (cost of medication and transport); availability of medication; availability of educational literature

Severity and duration of the disease: Ability to cope with symptoms; motivation to take medication; length of therapy; experiences of previous medications

Adherence and efficacy of treatment

Estimates of adherence to treatment of their asthma patients varied widely between physicians; ratings for the percentage of patients who were non-adherent were highest in the UK (France, 10-50%; Spain, 15-50%; UK, 30-70%). Physicians expressed a wide range of opinions towards adherence and efficacy of treatments, which are summarised in Table 2. All but one physician felt that the fear of side effects or addiction outweighed efficacy benefits as influencing factors for stopping treatment. All physicians considered patient beliefs and perceptions of disease were important issues in adherence.

Review of the flow chart

The physicians all agreed with the flow chart presented; however, six physicians suggested the following additional items: general practitioner-specialist relationship (n=2), nurse-patient relationship; family attitude; use of explanatory leaflets; severity of asthma (n=2); health system (availability, access, cost) (n=2); concomitant disease; use of peak flow meters.

†Adherence

Adherence was defined as the extent to which patient's behaviour with respect to their treatment for asthma coincides with the clinical treatment intended by the physician. The term "adherence" is used throughout in this article to imply a voluntary choice of the patient in deciding whether or not to follow a treatment plan offered to them by the physician. The term "compliance", though frequently used interchangeably with "adherence", is less preferred as it implies a passive submission to the prescriber's instruction."

Original research

For personal use only.

Not to be reproduced without the permission of the Primary Care Respiratory Journal

Table 2. Opinions of physicians regarding adher of treatment.	ence and entracy	Table 3. Patient cha
	Number of	Socio-demographic
	physicians (of 12)*	Nationality
	(01 12)	Age (y)
Reasons why patients stop treatment:		Gender (male/female)
side-effects	3	()
feeling better	3	
forgetfulness	3	Occupational status
reatment inappropriate or of no benefit	3	
general dislike of medication	2	
fear of addiction	1	
embarrassment	1	Educational level
osychiatric illness	1	
Factors motivating patients to adhere to medicat		
perceived efficacy	4	
understanding the reasons for adherence	3	Family status
ease of use medication	2	Tuning States
naving severe asthma	1	Smokers
ow cost	1	Living with someone
adverse experience of other asthma sufferers	1	with asthma
a good physician-patient relationship	1	***************************************
Main reasons for inefficacy of inhaled treatment		Clinical characterist
failure to master the use of the inhaler	8	
poor adherence	4	Duration of asthma (y
nappropriate treatment for severity	2	Duration of treatment
neffective medication	1	Use of oral steroids w
insufficient dose	1	Hospitalisation within
wrong diagnosis	1	Emergency department
Methods used to improve efficacy:	•	24 months (yes/no)
change the type of device	3	Other disease (yes/no
check how the patient uses treatment and consider a		Current asthma contro
check for adherence	1	ICS (budesonide/ bec
(re-)educate the patient	1	fluticasone/ undefined
ncrease dosage	1	ICS plus LABA (sepa
re-evaluate the patient	1	Current asthma reliev
Actions taken if non-adherence is suspected:	1	Short-acting \(\beta 2\)-agon
provide information, advice and stress importance of	of adherence 6	Ipratropium/salbutam
with maintenance medication	n adherence o	ipianopium/saioutam
prescribe combination inhalers	2	ICS = inhaled corticoste
encourage the patient	1	a. Use of oral steroids
nake sure the patients know how to take their medi		room visit within 2 y
provide written advice	1	b. One patient was incl
suggest that, if the patient was not happy with his/h		he/she had experience
reatment, he/she should go and see another doctor		c. Duration of ICS trea
reatment, ne/sne should go and see another doctor		hence values of 0 we d. Data not provided fo
		a linto not provided to

Table 3. Patient characteristics	able 3. Patie	haracteristic
----------------------------------	---------------	---------------

characteristics

Nationality	Number (French/Spanish/British)	46 (16/15/15
Age (y)	Mean (range)	34 (18-53)
Gender (male/female)	Total	20/26
	Between ages 20 and 35	10/15
	With recent asthma exacerbation ^a	10/17
Occupational status	Working	28
	Student	4
	Retired due to asthma	6
	Other or missing data	8
Educational level	Elementary	6
	Secondary	21
	College	14
	Postgraduate or other	5
Family status	Living with partner/family	43
	Living alone	3
Smokers	Present/past/never smoked	13/12/21
Living with someone with asthma	Yes/No	14/32

stics (according to physicians)

Duration of asthma (y); mean (range)	15 (1-45) ^b
Duration of treatment with ICS (y); mean (range)	10 (0-28) ^c
Use of oral steroids within last 6 months (yes/no)	22/23 ^d
Hospitalisation within last 24 months (yes/no)	9/35 ^d
Emergency department treatment within the last	11/34 ^d
24 months (yes/no)	
Other disease (yes/no)	15/27 ^d
Current asthma controller medication:	
ICS (budesonide/ beclomethasone/	40(16/14/6/4)
fluticasone/ undefined)	
ICS plus LABA (separate and combination)	6
Current asthma reliever medication:	
Short-acting ß2-agonist (salbutamol/terbutaline)	45(34/11)
Ipratropium/salbutamol combination	1

eroid; LABA = long-acting \(\beta \)-agonist

- within 6 months or a hospitalisation/emergency
- luded with a duration of asthma of 1 year, because ced emergency room treatment
- atment was unknown in several Spanish patients, ere assigned
- or all patients

Patient interviews

Information on socio-demographics and clinical characteristics of patients (supplied by physicians) are summarised in Table 3. Although there was a statistically significant agreement between patient perceptions of their asthma severity (mild-very severe) and severity of asthma (GINA stages) assigned by the physician (weighted kappa 0.53, p<0.001), there were several instances of disagreement for individual patients (Table 4). Most patients defined asthma in terms of the symptoms and how they felt, although 14 patients attempted to explain their asthma in terms of lung function, as explained by their physicians. Only four patients mentioned inflammation. Most of them appreciated the widespread occurrence and increasing prevalence of asthma. Allergy (n=20) and heredity

(n=17) were the two most frequently mentioned causes of asthma. Most frequent triggers stated (often multiple) included dust and feathers (n=24); smoking (n=17); stress (n=17); air quality (n=16), weather (n=16); animal fur (n=16); pollen (n=15); and a respiratory infection (cold/bronchitis) (n=7).

Most patients recognised the different roles and benefits of the reliever and controller in treatment. Of 44 respondents, given a choice of medication, 32 chose the reliever and 10 the controller; and 2 insisted that both were needed. Almost half of the patients reported at times both forgetting and stopping controller treatment for a variety of reasons (Table 5).

Most patients (n=28) thought their first treatment would be temporary, and of these 23 considered that

Not to be reproduced without the permission of the Primary Care Respiratory Journal

medication would cure them. Only six patients reported that their physician kept them well informed. Most had received instruction on the use of the inhalers (by physician 26; pharmacist, 3; nurse 10; a friend, 1) and three reported not having received any instructions. An equal number of patients (n=10) mentioned that they had or had not discussed pros and cons of treatment with their physician. Nevertheless, most patients expressed confidence in their physicians, and only three patients were dissatisfied with the medical help they received. Most patients (n=36) considered they were capable of managing their asthma themselves. Seven patients deplored the lack of psychological support, whereas 38 patients felt that they had sufficient support from their families and friends, although four patients did not discuss their asthma with them.

Derivation of the final flow chart

Additional categories of factors (medication; specialist-general practitioner relationship; disease severity) were added to finalise the flow chart after consideration of the views of physicians and patients (Figure 1).

Discussion

Information from an extensive literature review and interviews with 12 respiratory physicians and 46 patients with asthma confirmed a high frequency of inadequate controller use and identified many individual patient- and medication-related factors that influenced adherence. The inter-relationship between potentially influencing factors is complex, and, we did not attempt to rank individual factors with regard to their relative importance in positively or negatively influencing adherence to treatment. Nevertheless, we identified four categories of factors as being of the most importance in influencing adherence to treatment: (1) the patient-physician relationship, (2) patient understanding of the disease and its treatment, (3) patient's beliefs/attitudes and perception of disease/treatment and (4) patient willingness (to take an active part in asthma management).

Overall, patients interviewed had good knowledge of their asthma, trigger factors and treatment and felt there were advantages for the use of controller medications; nevertheless, in many cases patients decided to stop treatment because of inconvenience and lack of perceived benefit. Results of this study confirm the necessity for patients to appreciate the benefits of regular controller treatment and to make the medications simple and convenient to use.

Although side effects were a common cause of concern, they were not a commonly expressed reason for stopping treatment. Interestingly, some patients cited the lack of an immediate bronchodilating effect as a reason for their perception of inefficacy of controller medication. In this respect, it is possible that a single inhaler containing a combination of a rapid- and long-acting ß2-agonist and an ICS may help to encourage regular therapy. Unfortunately,

Table 4. Classification of patients according to physician assessments of the GINA stage of asthma severity⁴ and severity as perceived by patients^a

	GINA stage				
Patients' rating ^b	No. of	1	2	3	4
	patients				
Mild	12	6	4	1	1
Moderate	16	1	12	2	1
Severe	9	0	2	2	5
Very severe	3	0	0	0	3
a. Complete informat	ion was not obta	ained for all	patients		
b. There was a signifi	cant agreement	between pat	tients' rating a	nd GINA stag	ge (weighted
1	1)				

kappa = 0.53, p < 0.001)

Table 5. Patient interview respon	nses r		
Reliever	n	Controller	n
Use of reliever		Use of controller	
when having an attack	29	three times daily	3
before exercise	5	twice daily	29
before going to bed	5	daily	2
preventing an attack	2	infreqently	1
after too much exercise	2		
after smoking a lot	1		
Advantages/Disadvantages		Advantages/Disadvantages	
Benefit outweighs disadvantages	38	Benefit outweighs disadvantages	38
Benefits did not outweigh	2	Benefits did not outweigh	4
disadvantages		disadvantages	
Advantages		Advantages	
helps breathing and prevents need	29	easy to use	15
for emergency treatment		relieves symptoms	8
provides immediate benefit	23	helps control asthma	8
user-friendly	19	none	7
easy to carry	5		
opens the airways	3		
straightforward treatment	2		
Disadvantages		Disadvantages	
none	13	side effects	19
side effects	13	no immediate benefit	8
dependence	6	contains cortisone/steroids	4
difficult to use	4	need to take every day	4
embarrassment	3	too many medications	4
inefficient	2	none	3
		embarrassment	2
		dependence	1
Concerns about side effects		Concerns about side effects	
none	21	none	24
cough/dry mouth/after taste	11	horse voice/sore throat/dry mouth	
shaking	7	mouth ulcers	3
tachycardia	4	can weaken bones	3 2 2
weight gain	1	weight gain	2
mouth ulcers	1	shivering	
		itch	1

Reasons for non-adherence with controller treatment Forgetting (n=25) Deciding to stop treatment (n=19)

		(,
work (time/stress)	7	Didn't need it/felt fine	7
when feel good or symptoms	6	fear of side effects	3
not bad		physician request	3
no particular reason	5	too complicated	3
weekends	3	to see how I coped	1
away from home	3	too many treatments	1
see no benefit in taking it	2	asthma not serious	1
		travelling	1
		no money	1

n =the number of patients who expressed the opinion. As not all patients provided an answer to every question, the sum of the answers is not always 46 for each question. Furthermore, multiple answers (occasionally given) were given equal weight

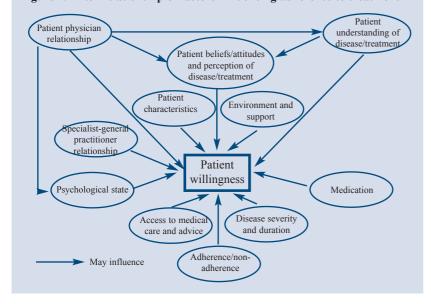
Not to be reproduced without the permission of the Primary Care Respiratory Journal

previous attempts to improve compliance by combining short-acting B2-agonists and ICS have been unsuccessful in improving compliance.^{5,6} In contrast, however, improved compliance with regular ICS use has been demonstrated when a long-acting B2-agonist was added to ICS maintenance therapy.⁷

Patients will inevitably balance potential risks against the benefits to be obtained from medications when deciding whether or not to take their medications as prescribed; non-adherence may be a logical attempt to moderate the perceived risks by taking less. The physician has a key role in making sure that the patient's informed choice is not made on mistaken beliefs, either about the disease or the medication. Patients may have very different viewpoints on what the objective of asthma therapy is and their level of asthma control; this is illustrated by the discrepancy between patient perceptions of severity and physician-assessed severity reported in a large European survey.

There were also several instances in the present study of differences between patients' assessment of their own asthma severity (mild-very severe) and physicians' assessment of asthma severity (GINA stage). If patients underestimate their disease severity, it is likely that they will also underestimate the need for treatment. Educating patients about their disease and role of medication is important for improving adherence; however, good knowledge alone is no guarantee of good adherence. 10 Communication skills of the physician are clearly important, and there is evidence that training physicians can improve patient self-management. 11 To achieve patient willingness to actively participate in the effective treatment of the disease the physicians' approach should be adapted depending on the individual circumstances, beliefs and attitudes of the patient. Furthermore, in aiming to achieve willingness, the physician should not lose sight of clinical outcome. As Chapman et al (2000)12 state "it is better to achieve complete asthma control with an effective medication taken less than that prescribed than it is to achieve perfect compliance

Figure 1. Inter-relationship of factors influencing adherence to treatment



with an ineffective medication that fails to control the disease". Thus adherence and effectiveness of medications are both important.

The patients interviewed in the study were not selected at random, and it is possible that physicians chose patients with whom they were most familiar and had a good patient-physician relationship; a factor that would be expected to improve adherence. It is possible, therefore, that the population sampled may not have been fully representative of the general asthma patient population, i.e. more adherent. However, as many patients interviewed reported poor adherence, the numbers were considered sufficient to provide a general overview on factors affecting adherence from the patient perspective, and this was not considered a major limitation of the study.

The small numbers of patients and physicians interviewed precluded quantitative ratings of the importance of individual factors to be assigned and did not allow inter-country differences in practices and opinions to be evaluated; more controlled studies involving larger numbers are needed for this.

Although the respiratory specialists provided their opinions from a broad perspective, the inclusion of general practitioners and respiratory nurses in future surveys would increase the credibility of these findings for primary care. Furthermore, as we only interviewed adults with asthma, specific factors influencing adherence in childhood asthma may not have been identified. For younger children the parents have a key-influencing role in adherence, and obtaining their willingness to actively participate in the treatment of their children is as important as it is for older patients who take full responsibility for administering their medications.

The present review identified multiple factors that should be considered for obtaining patient commitment to follow the intended treatment regimen. Other reviews^{7,11} have highlighted the complex interrelationship between factors that affect patient ability and motivation to adhere to treatment, and generally support the central position of patient willingness in our model. Our flow chart offers a reminder to physicians of the major factors involved in improving adherence. In particular, the chart highlights the importance of fostering a good patient-physician relationship, understanding patient beliefs, attitudes and perceptions of disease and treatment, and to provide the necessary education to improve patient understanding of their condition and the value of prescribed treatment. As well as prescribing safe and effective medications, obtaining the willingness of patients to participate in the management of their asthma is important for increasing adherence and improving the chance of successful therapy.

Conclusion

Patient adherence to asthma can be improved, and the likelihood of treatment success increased, by paying attention to the factors that influence patients' willingness to participate in their treatment.

Not to be reproduced without the permission of the Primary Care Respiratory Journal

References

- 1. Schmier JK, Leidy NK. The complexity of treatment adherence in adults with asthma: challenge and opportunities. *J Asthma* 1998; **35**: 455-72.
- Royal Pharmaceutical Society of Great Britain.
 From compliance to concordance. Achieving shared goals in medicine taking. London: Royal Pharmaceutical Society of Great Britain, London, 1997.
- 3. Jones PW. Health status, quality of life and compliance. *Eur Respir Rev* 1998; **8**: 243-6.
- 4. National Institutes for Health, National Heart, Lung and Blood Institute. Global Initiative for Asthma. Publication Number 96-3659B, 1998.
- 5. Bosley CM, Parry DT, Cochrane GM. Patient compliance with inhaled medication: Does combining β2-agonists with corticosteroids improve compliance? *Eur Respir J* 1994; 7: 504-9.
- 6. Braunstein GL, Trinquet G, Harper AE. Compliance with nedocromil sodium and a nedocromil sodium/salbutamol combination. *Eur Respir J* 1996; **9**: 893-8.

- 7. van der Woude HJ, Aalbers R. Compliance with inhaled glucocorticoids and concomitant use of longacting β2-agonists. *Respir Med* 2001; **95**: 404-7. 8. Clark N, Jones P, Keller S, Vermeire P. Patient factors and compliance with asthma therapy. *Respir Med* 1999;**93**:856-62.
- 9. Vermeire PA, Rabe KF, Soriano JB, Maier WC. Asthma control and differences in management practices across seven European countries. *Respir Med* 2002;**96**:142-9.
- 10. Tettersell MJ. Asthma patients' knowledge in relation to compliance with drug therapy. *J Adv Nurs* 1993;**18**:103-13.
- 11. Clark NM, Gong M, Schork MA, Evans D *et al.* Impact of education for physicians on patient outcomes. *Pediatrics* 1998; **101**: 831-6.
- 12. Chapman KR, Walker L, Cluley S, Fabbri L. Improving patient compliance with asthma therapy. *Respir Med* 2000;**94**:2-9.