

Compliance with inhaled asthma medication in preschool children

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Abstract

Background - Previous studies have shown poor compliance with regular drug therapy in children and adults with asthma. In preschool children the parents supervise and are responsible for drug administration, but little is known of compliance in this group. In addition, there are few data on the patterns of drug use of inhaled prophylactic asthma therapy or of the relation between compliance and symptom control. A study was undertaken to address these issues with the hypothesis that parental supervision would result in good compliance.

Methods - The subjects were 29 asthmatic children aged 15 months to five years already established on inhaled prophylactic medication delivered through a large volume spacer. The prescribed drug regimens varied between subjects. This was an observational study using an electronic inhaler timer device to record the date and time of each actuation of the aerosol canister. Diary cards were used for parallel recording of symptoms and parentally reported compliance with a drug regimen.

Results - Variable and generally poor compliance was demonstrated with a median of 50% of study days with full compliance (subject range 0-94%) and an overall median of 77% of prescribed doses of therapy taken during the study period. No relation was found between frequency of prescribed regimen and good compliance. Day care was associated with poorer compliance. No relation between good compliance and low symptom scores was found.

Conclusion - Compliance with inhaled prophylactic therapy is poor in preschool children with asthma whose medication is administered under parental supervision.

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Keywords: young children, asthma, drug compliance.

The prevalence of asthma is increasing worldwide, especially in young children. The general response to inhaled therapy in preschool children with asthma is variable. This may stem partly from the heterogeneity of the disease in young children, and partly from difficulties associated with inhaled drug delivery at this age.¹ Another potentially important factor affecting treatment success or failure which has not been addressed to date in this age group is the degree of compliance with inhaled drug therapy. We have previously shown that patient

compliance with inhaled prophylactic therapy in schoolchildren with asthma is poor, especially when the prescribed dose is more than twice a day.² However, we know of no studies of parental compliance and its effect on drug administration to their children.

Inhaled medication via a large volume spacer is increasingly being used in young children with asthma. In this study we have investigated the use of prophylactic medication in a group of preschool children using an electronic inhaler timer device. Such a group differs from older children in that their asthma therapy is administered either directly or under the close supervision of their parents. Supervision is a technique that has been used to improve compliance in other areas.³ In this study we hypothesised that parental involvement through supervision of drug administration would result in better compliance than that seen in other asthma patient groups.

Methods

SUBJECTS

A group of preschool children attending a specialised paediatric respiratory clinic were recruited. The entry criteria were that the child was receiving regular prophylactic asthma medication by metered dose inhaler through large volume spacer devices (chromoglycate, budesonide via Nebuhaler, or beclomethasone via Volumatic) and had been using such medication for at least a month before entry to the study. The study was observational in design and no changes were made in the children's treatment.

Parents were invited to participate and received written and verbal explanation of the study and its aims. The technique of administration by the tidal breathing method⁴ via the large volume spacer was checked and corrected if necessary. A study period of two months was planned. A troubleshooting telephone call was made after two weeks to check if there were any problems with the devices. All subjects were given an appointment at the end of the study period. There was open access by telephone for any problems encountered by the subjects.

ELECTRONIC TIMER DEVICE

To measure inhaler use we used the Nebulizer Chronolog NC300 (Forefront Technologies Inc, Lakewood, Colorado, USA) (fig 1). This is an electromechanical timer device which takes the place of the plastic holder of the metered dose inhaler. It incorporates a micro-

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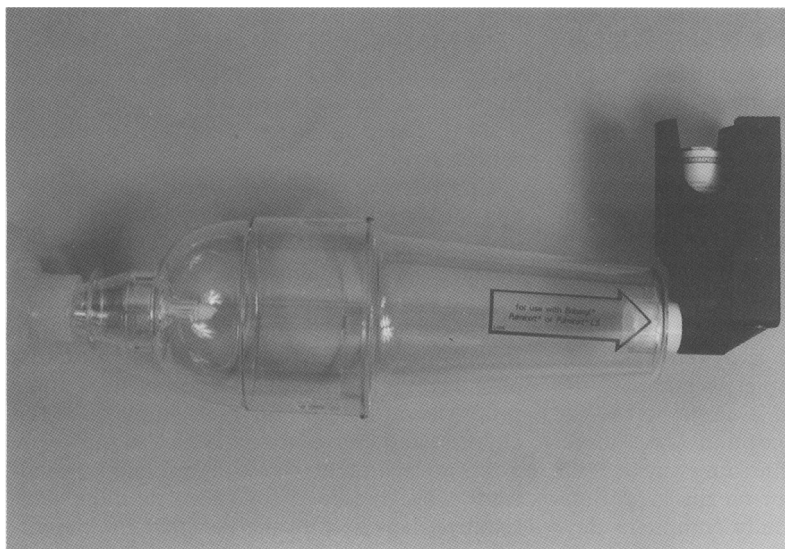


Figure 1 A Chronolog device loaded with an aerosol, attached to a Nebuhaler.

switch which is activated on each firing of the aerosol and allows the accurate recording of the date and time of each actuation of the metered dose inhaler. The Chronolog is initialised using dedicated computer software through a Medilog adapter attached to an IBM PC computer. It is then loaded with the metered dose inhaler canister and is ready for use with the large volume spacer. The battery life is over six months and the device can electronically store up to 4000 events. In a validation study we found it to be accurate to within 10 minutes over the course of one month of study (unpublished data). Hence, the device was capable of providing detailed information on the pattern of use of the metered dose inhaler over the course of the study.

A separate Chronolog was issued for each subject's inhaled "prophylactic" medication (inhaled steroids or cromoglycate) and for their bronchodilator (terbutaline or salbutamol). The result of study of the use of the bronchodilator medication is the subject of a separate paper³ and is not further discussed. The prescribed drug, its dose and frequency were detailed on a sticker attached to the back of each device (for example, cromoglycate two puffs four times a day).

When the device was returned at the end of the study period the Chronolog data were read by the program and a printout of all times and dates of use of the metered dose inhaler over the study period was prepared. The results were discussed with the parents and children. This allowed the opportunity to record comments and discuss any difficulties encountered.

INFORMATION GIVEN TO SUBJECTS

The prescribed medication regimen for each child was written on a standard asthma card (National Asthma Campaign, London, UK) which also gives advice on patient self-management. The regimen was also detailed on the symptom diary card, in addition to the label on the back of each Chronolog. Each subject also had written material that explained the

nature and accuracy of the timing device and the rationale of the study.

A symptom diary card was issued on which parents were asked to record daytime cough, night cough, and wheeze using a four point scale for each symptom, and also to record the use of the inhalers. Parents were asked to record on the symptom diary card any instances where they used asthma medication other than the study aerosol in the Chronolog and to note any firing of the aerosol when drug was not administered – for example, in play by the child. Subjects were not instructed to increase inhaled prophylactic therapy in the presence of increased symptoms.

ETHICS

The study was approved by the ethics committee of the Royal Hospital for Sick Children and informed written consent was obtained from all parents. As noted, it was made very clear in the written and verbal instructions that the device would record the date and time of each use of the metered dose inhaler.

MEASURES OF COMPLIANCE

In the initial instructions parents of subjects were asked to shake the canisters before use but not to "test fire" the metered dose inhaler. We therefore assumed that each recorded actuation represented administration of the medication. The data were assessed manually and each day scored for two measures of compliance. The first, "Daycomp", was the proportion of the total study days on which the prescribed number of puffs was recorded at the prescribed frequency. The spacing of actuations had to be consistent with the schedule of a preschool child – for example, two puffs at 08.00, 12.00, and 19.00 hours for a three times daily regimen. We accepted a gap of two hours between actuation times as the minimum acceptable spacing. Daycomp was therefore a measure of the number of days of strict adherence to the prescribed regimen. The second measure, "Dosecomp", was the proportion of actually administered to total prescribed doses over the entire study period. We ignored any "extra" puffs on the very rare study days on which more than the prescribed number of puffs was recorded. Dosecomp therefore gave an overall indication of use of the inhaled medication and provided a less demanding measure of compliance. A note was also taken of the number and pattern of days on which the Chronolog recorded no use of prophylactic medication.

A total symptom score for each day was calculated from the diary cards. The diaries were also used to score the parents' written record of compliance to the prescribed regimen, "Reported Compliance".

STATISTICAL ANALYSIS

As the number of fully compliant days is an integer and clearly dependent on the actual number of days studied separately for each

individual, cognisance of this must be employed in any analysis. This is achieved here by using a "logit" (or logistic) approach which models the ratio of the number of compliant to non-compliant days.

The effects of possible factors influencing compliance, such as frequency of prescription, daycare, etc were analysed by means of generalised linear models taking the logarithm of the odds ratio of the compliance measure as a response variable. Individuals were modelled by means of random effects with estimated variances determined by the above "logit" transformation. For example, to compare the daily compliance rates on average across the three frequencies of prescription (two, three, or four times daily) a weighted one way analysis of variance was carried out on the logarithms of the number of actual fully compliant days divided by the number of days on which the subject did not comply.

Results

Over a 13 month period the parents of 36 children were approached to seek participation. In seven children the parents declined to participate, most frequently after expressing concern at the commitment of time necessary for proper conduct of the study. Twenty nine children aged 15 months to five years were therefore recruited. Details of the children are included in the table. Most found the timer device to be acceptable, but some difficulties were experienced. One subject did not return the Chronolog devices or diary cards. Two subjects were withdrawn from the study after difficulties with the fit of the cromoglycate aerosol into the Chronolog which resulted in the electronic switch "sticking" with the documentation of large numbers of actuations and difficulty in using the metered dose inhaler. One further subject had poor symptom control and was changed from cromoglycate to inhaled steroids 18 days into the study. The data for

that subject were only analysed for the first 18 day period. Satisfactory Chronolog data were therefore available for 26 subjects. The median number of days studied was 58 days (range 15-94). Three subjects did not keep or did not return diary cards.

Compliance with inhaled prophylactic therapy was variable and often very poor as shown in the values for Daycomp and Dosecomp in the table. We were interested to note that there was no relation between either good Daycomp or good Dosecomp and low symptom scores. Inspection of the data printouts showed that only 11 of the 26 subjects took at least some prophylactic therapy on each study day. Ten children had consecutive days when they were given no treatment; five children had no medication use recorded for seven or more consecutive days despite the fact that the parents reported their child to have symptoms on a mean of 63% of study days. Many parents continued to record symptoms during periods when they were not apparently administering the prophylactic treatment. The symptom diary card data also showed that most parents reported compliance to be better than that actually measured (table).

Undercompliance, when it occurred, usually consisted of missing a time of administration rather than omitting doses at actuation times. From examination of the printouts it was clear that in those with a three or four times/day regimen it was generally the doses in the middle of the day that were omitted. Examples of the patterns of compliance to the prescribed regimens are shown in fig 2. It can be seen that most show variation in compliance, but this variation did not correlate with fluctuations in symptoms. When the first 20 days of the study were compared with the next 20 days there was a significant drop of 7% in both Daycomp ($p < 0.05$) and Dosecomp ($p < 0.05$). This suggests that there may have been a study effect resulting in improved compliance at the beginning of the study.

Characteristics of children included in the study

Patient no.	Age (years)	Day care	Drug	Frequency (per day)	Study days with symptoms (%)	Reported compliance (%)	Daycomp (%)	Dosecomp (%)
1	4.8	N	Cromoglycate	4	58	98	91	99
2	3.6	Y	Cromoglycate	4	95	89	87	97
3	2.8	N	Cromoglycate	4	73	77	61	88
4	2.9	N	Cromoglycate	4	4	92	36	77
5	4.7	Y	Cromoglycate	4	100	11	0	39
6	1.3	N	Cromoglycate	4	74	13	40	77
7	2.0	Y	Cromoglycate	4	100	18	3	17
8	2.1	N	Cromoglycate	4	100	50	48	59
9	4.1	Y	Budesonide	3	65	40	45	55
10	5.0	N	Cromoglycate	3	39	73	41	75
11	3.0	Y	Budesonide	3	38	92	65	90
12	2.2	Y	Cromoglycate	3	29	25	26	68
13	3.7	Y	Budesonide	3	100	99	67	89
14	3.8	Y	Cromoglycate	3	No data	No data	50	71
15	4.8	N	Budesonide	2	58	100	51	73
16	3.4	N	Budesonide	2	85	90	82	91
17	4.6	Y	Budesonide	2	41	85	82	90
18	4.8	Y	Budesonide	2	100	81	23	48
19	3.8	Y	Budesonide	2	100	95	4	15
20	4.8	N	Budesonide	2	45	88	84	89
21	4.9	N	Beclomethasone dipropionate	2	27	No data	94	97
22	3.3	Y	Beclomethasone dipropionate	2	45	100	12	22
23	3.8	Y	Budesonide	2	No data	No data	82	91
24	3.2	Y	Budesonide	2	94	67	33	54
25	2.3	N	Budesonide	2	100	100	82	94
26	1.5	N	Budesonide	2	No data	No data	88	93

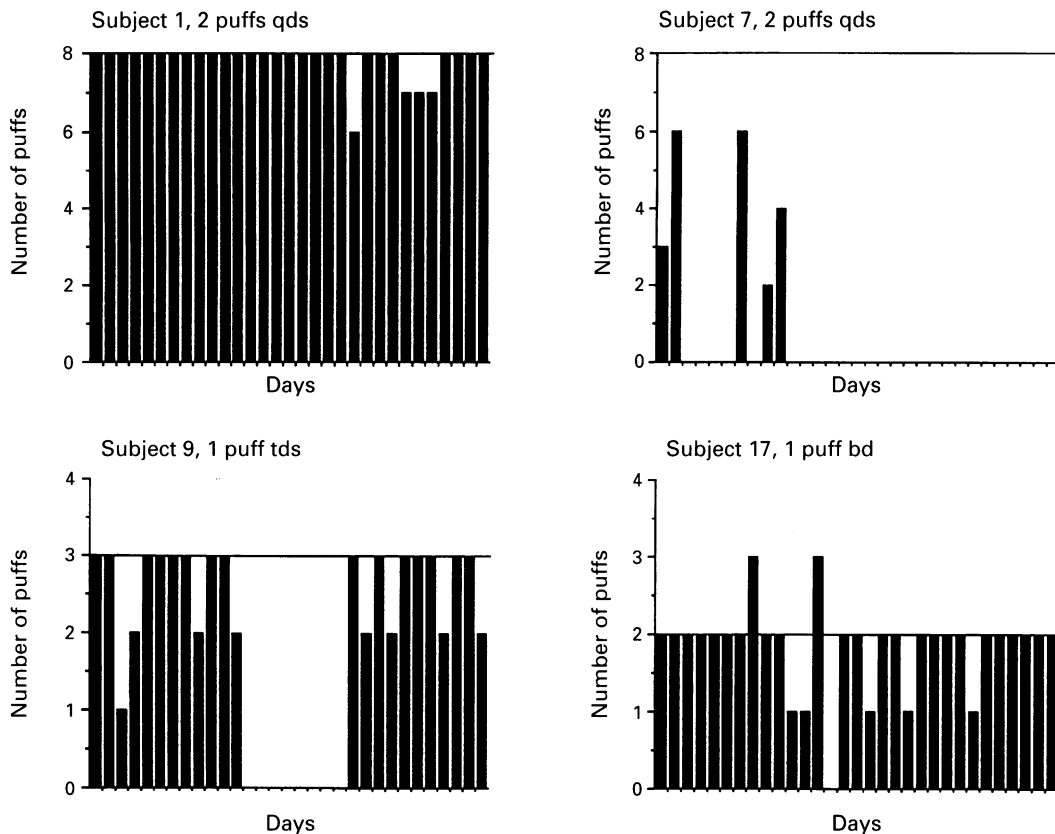


Figure 2 Each graph represents the pattern of use of inhaled prophylactic medication over the first 31 days of the study in a single subject. The vertical axis is the number of puffs taken on a particular day. Each study day is represented as a bar. The horizontal line represents the number of puffs that denotes full compliance with the prescribed regimen.

Day care was used for 17 of the children but was full time in only two, both of whom had poor Daycomp (23% on a twice daily regimen and 26% on a three times daily regimen). There was a significant adverse effect on Dosecomp of those in day care ($p < 0.05$) but not for Daycomp. This finding was interesting as enquiry at study entry had revealed that no child was normally given their prophylactic drug at day care. The poorer compliance in children in day care is not therefore due to the omission of doses by carers in day care, but rather to poorer overall parental compliance in children who attended day care.

In this group of children we found no significant difference in compliance between regimens of two, three, or four times daily, with each group showing marked variation in Daycomp and Dosecomp as demonstrated in fig 3.

When the discrepancy between reported compliance and recorded compliance was revealed at the end of the study parents were often keen to offer explanations of happenings within the family that had had an adverse effect on compliance. They were often at pains to explain these as unusual – for example, deaths of elderly relatives, hospitalisation of relatives, holidays.

Discussion

In this study we found clear evidence of variable and often poor compliance with inhaled prophylactic medication in preschool children with

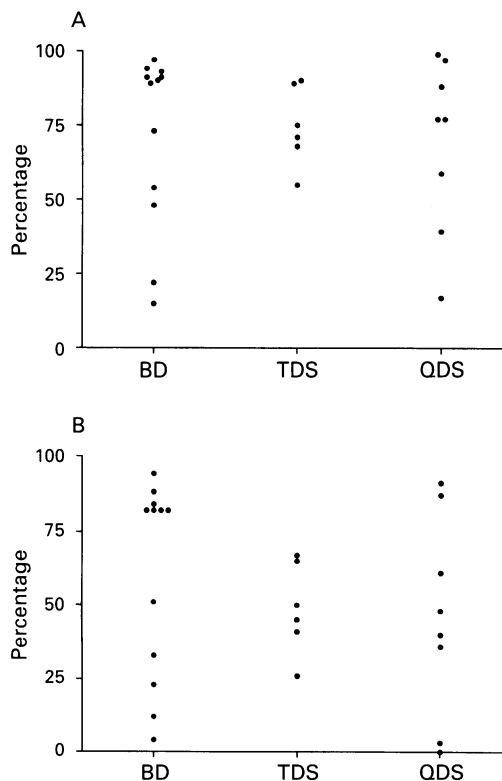


Figure 3 Scatter of values for (A) Dosecomp and (B) Daycomp. Each subject is plotted once on each graph. BD=twice daily; TDS=three times daily; QDS=four times daily.

asthma. This occurred despite the fact that the subjects of the study were having medication administration supervised by their parents. The measured compliance was little better than in a previous study in school age children² or in adult studies of aerosol use.^{6,7}

It has been reported that participation in a trial or study⁸ may lead to improved compliance with treatment. This was particularly likely in this study as the Chronolog's ability to time and date each actuation was carefully explained to the parents at enrolment to the study. Indeed, our data provide some evidence for an effect of study participation on compliance as we have shown a significant deterioration in compliance with the prescribed regimen over time. This suggests that our results may, in fact, be an overestimation of true medication compliance in the preschool asthmatic population. However, Rand and colleagues⁷ showed that the use of a Chronolog *per se* did not appear substantially to improve compliance during a long term study, but that if feedback was given the compliance improved.⁹ We did not restudy these subjects after the feedback was given at the end of the study.

One potential confounding factor could be the actuation of the inhaler without the dose being inhaled such as in "test firing". This was actively discouraged at enrolment to the study. In any event, test firing, if it occurred, would lead to apparently better compliance. In this respect we noted that most undercompliance was due to omission of times of administration and that taking too many puffs per administration was not a phenomenon observed in this study population. Another finding noted in children² and well demonstrated in adults⁷ is that of "canister dumping" – that is, large numbers of actuations occurring in a very short time period thought to be due to repetitive actuations without inhalation. This unexpected behaviour has been thought to be due to a patient attempting to get up to the "correct" number of actuations during the study period by "catching up" for previously omitted doses. As noted, we took care to make our subjects aware of the abilities of the Chronolog and we did not see this phenomenon with prophylactic therapy in the present study. We did see some subjects for whom doses of prophylactic medication were noted very late in the evening or in the early hours of the morning, well after a preschool child's likely bedtime. These were generally explained by the parents as administration to a sleeping child.

A trend towards better compliance with less frequent administration times was noted in a previous study in older children² and has been seen in other conditions in different age groups.^{10,11} In a study of school aged asthmatic children Williams *et al*¹² attributed the better compliance with a twice daily regimen to the availability of parental supervision of inhaler use in the morning and evening. Our data suggest that in preschool children the involvement of parents does not significantly alter inhaled medication use. Furthermore, from our data there was no clear trend towards better compliance when fewer daily administration

times were prescribed. The striking finding is that, within each group of two, three, or four times a day administration there is a wide variation in the use of inhaled prophylactic medication.

One feature of concern was the number of days that patients received no prophylactic therapy at all, on occasion for several days at a time (fig 2). While it is possible that another metered dose inhaler was used during these periods, parents were asked to record and report such occurrence. We also noted that in general there was no clear relation between high scores for compliance and low scores for symptoms. This may be an important factor in explaining the poor compliance as perceived effectiveness is said to be a promoter of drug compliance.¹³ In these preschool asthmatic patients positive feedback from good symptom control was not present to reinforce good compliance with the prophylactic drug regimen. Adult data have also shown a similar lack of correlation between symptoms and compliance to a regimen of four times a day inhaled steroid.¹⁴

Why do parents adhere poorly to prescribed treatment regimens for their preschool asthmatic children? An important feature may well be that those responsible for drug administration are not those who experience the symptoms first hand. Nevertheless, it was the parents who both scored their child's symptoms and gave the treatment. We took great care to emphasise by written and verbal instructions the prescribed medication and its mechanism of action. Despite this, misunderstanding of the rationale of regular prophylactic therapy still persists. It is also likely that some parents remain unconvinced of the benefits or are fearful of the side effects of regular medication.¹⁵ The home of an average toddler is a busy environment and a degree of disorganisation may be implicit and contribute to the poor observed compliance. However, against this it has to be noted that the number of siblings was not significantly associated with either Dose-comp or Daycomp.

These findings potentially have an important bearing on the planning of therapy in preschool asthmatic children. For example, once daily anti-inflammatory medication in these children would probably not have been appropriate as 58% of subjects had days on which no treatment was taken at all. Interestingly, adult data^{10,11} suggest that compliance with a once daily medication is little better than with twice daily, and the pharmacotherapeutic importance of a missed day of once daily medication may be greater. Hopefully, measurement of actual inhaler use may lead to the prescription of more empirically based medication to young children in the future.

We conclude that compliance with inhaled prophylactic therapy in preschool asthmatic children is poor. We speculate that poor compliance is likely to be an important factor in the difficulty experienced in achieving control of symptoms in such children. In future we think it will be important to address specifically the issue of drug compliance and factors which

affect it in studies of prophylactic inhaled medication in young children.

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- 1 British Thoracic Society. Guidelines on the management of asthma. *Thorax* 1993;**48**:S1-24.
- 2 Coutts JAP, Gibson NA, Paton JY. Measuring compliance in asthma. *Arch Dis Child* 1992;**76**:332-4.
- 3 Sumartojo E. When tuberculosis treatment fails. *Am Rev Respir Dis* 1993;**147**:1311-20.
- 4 Gleeson JGA, Price JF. Nebuhaler technique. *Br J Dis Chest* 1988;**82**:172-4.
- 5 Ferguson AE, Gibson NA, Aitchison TC, Paton JY. Measured bronchodilator use in pre-school children with asthma. *BMJ* 1995;**310**:1161-4.
- 6 Spector SL, Kinsman R, Mawhinney H, Siegel SC, Rachelefsky GS, Katz RM, et al. Compliance of patients with asthma with an experimental aerosolized medication: implications for controlled clinical trials. *J Allergy Clin Immunol* 1986;**77**:65-70.
- 7 Rand CS, Wise RA, Nides M, Simmons MS, Bleecker ER, Kusek JW, et al. Metered-dose inhaler adherence in a clinical trial. *Am Rev Respir Dis* 1992;**146**:1559-64.
- 8 Reiser J, Warner JO. Value of participating in an asthma trial. *Lancet* 1985;i:206-7.
- 9 Nides MA, Tashkin DP, Simmons MS, Wise RA, Li VC, Rand CS. Improving inhaler adherence in a clinical trial through the use of the Nebulizer Chronolog. *Chest* 1993;**104**:501-7.
- 10 Greenberg RN. Overview of patient compliance with medication dosing: a literature review. *Clin Therap* 1984;**6**:592-9.
- 11 Cramer JA, Mattson RH, Prevey ML, Scheyer RD, Ouellette VL. How often is medication taken as prescribed? A novel assessment technique. *JAMA* 1989;**261**:3273-7.
- 12 Williams H, Verrier Jones ER, Sibert JR. Twice daily versus four times daily treatment with beclomethasone dipropionate in the control of mild childhood asthma. *Thorax* 1986;**41**:602-5.
- 13 Eraker SA, Kirscht JP, Becker MH. Understanding and improving patient compliance. *Ann Intern Med* 1984;**100**:258-68.
- 14 Mann MC, Eliasson O, Patel K, ZuWallack RL. An evaluation of severity-modulated compliance with q.i.d. dosing of inhaled beclomethasone. *Chest* 1992;**102**:1342-6.
- 15 Radius SM, Becker MH, Rosenstock IM, Drachman RH, Schuberth KC, Teets KC. Factors influencing mother's compliance with a medication regimen for asthmatic children. *J Asthma Res* 1978;**15**:133-49.