

Pediatric asthma assessment: Validation of 2 symptom diaries

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Accurate assessment of the value of asthma interventions in pediatric clinical trials is an essential step toward the improvement of the treatment of this disorder in children. Conventional pulmonary function measures can be infeasible and unreliable in younger children, particularly for use in multisite studies. As an alternative or supplemental approach, diary questionnaires completed by the patients or their caregivers may provide valuable data regarding the efficacy of asthma interventions in pediatric clinical trials. These questionnaires, however, have routinely not been validated for use in pediatric populations. Two pediatric diary questionnaires (the child-completed Pediatric Asthma Diary [PAD] and the parent/caregiver-completed Pediatric Asthma Caregiver Diary [PACD]) were designed to evaluate asthma symptoms in children aged 6 to 14 years and 2 to 5 years, respectively. The validity of these diary questionnaires was evaluated in 2 separate prospective studies that included children who were divided into 2 asthma groups: stable (requiring no additional asthma medication) and unstable (requiring either an increase in or the addition of asthma medication). Both scales displayed significant discriminant validity, construct validity, and responsiveness to change in asthma therapy. Only the PACD detected differences between groups in nighttime symptoms, such as awakenings caused by asthma. These validity studies suggest that diary questionnaires such as the PAD and PACD can be valuable as an alternative for the evaluation of interventions in pediatric asthma when pulmonary function testing is inappropriate or as an adjunct to such objective measures. (*J Allergy Clin Immunol* 2001;107:S465-72.)

Key words: *Pediatric clinical trials, questionnaires, diaries*

Because clinical trials designed to evaluate asthma interventions in children pose unique challenges, many asthma drugs have not been adequately tested in this population. As a consequence, product labeling typically is based on studies in adults, with dosing guidelines extrapolated to pediatric populations, a practice that can compromise efficacy and safety in children. A major challenge to designing adequate clinical trials in children with asthma is choosing meaningful measures to assess asthma symptoms and treatment outcomes.

When asthma measures are being selected for a study, there are a number of factors that should be considered. First, one needs to determine the purpose of the study. If

Abbreviations used

ICS: Inhaled corticosteroids
PACD: Pediatric Asthma Caregiver Diary
PAD: Pediatric Asthma Diary

the purpose is to determine the prevalence of asthma symptoms cross-sectionally at 1 point in time in a general pediatric population, the measure chosen should reliably and validly separate those patients with symptoms from those patients without symptoms. A different measure, again one that is reliable and valid, may be needed for a study designed to assess the severity or disability caused by symptoms in an asthmatic population. If the study is a clinical trial to examine the benefit of a therapeutic intervention, measures selected should be both reliable and valid but additionally must be sensitive to detect the expected changes. Other considerations on the selection of measures will include the age of the patient, who provides information (eg, patient-, parent/caregiver-, or physician-report), reliability and validity of the measure in the population being studied, and duration of the study (eg, assessment of health resource use may only be possible in longer studies).

In young children, developmental issues can prevent reliable perception and reporting of asthma symptoms. Other developmental issues can influence the accuracy of a young child's symptom reporting; young children do not possess a clear perception of time, and their ability to recall events may not be sufficiently reliable to permit accurate symptom reporting. Children are also often reluctant to acknowledge their asthma symptoms because, naturally enough, they want to be "normal" and not different from their peers. Parents/caregivers are often asked to provide an assessment of their child's asthma symptoms. Depending on the age of the child, the parent/caregiver has a different level of involvement in monitoring daily symptoms and in the administration of the child's asthma medication. Weak correlations have been reported between the symptom reports of children and those of the parent/caregiver.^{1,2} Additionally, the perception of airway obstruction remains poor for both the child with asthma and his or her parent/caregiver.³

Very young children also may not have adequate language skills that enable them to understand or follow complex instructions. Consequently, conventional methods of measuring airway obstruction in adults, such as the use of spirometry, which requires the patient to follow a multistep procedure, may be impractical and unreliable in children, especially those less than 8 years old.⁴

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Asthma symptoms and pulmonary function testing, when feasible in children, may in fact measure different aspects of the disease. Previous studies have shown that, in children and in adults, correlations between asthma symptoms and other measures of asthma (including standard pulmonary function assessments such as percent predicted FEV₁) are low.⁵⁻⁷

Asthma studies further indicate that children with chronic asthma who are undergoing controller therapy and their parent/caregiver generally report milder daily asthma symptoms than do adult asthma patients who are undergoing controller medication therapy.^{5,8,9} Symptoms in children are often, on average, characterized by either the parent/caregiver or the child as very mild or mild on a daily basis.^{10,11} In contrast despite similar pulmonary function criteria, average daily symptom scores in adult asthmatic patients who are undergoing chronic controller therapy tend to be reported by the patient as more moderate.^{5,8,9}

Generally, measures that assess asthma symptoms can be divided into 2 types: screening and evaluative questionnaires. The World Health Organization questionnaire¹² and the International Study of Asthma and Allergies in Children questionnaire are examples of established asthma screening tools.^{13,14} These measures are useful for establishing the prevalence of asthma in a general population but are often not useful as measures of response to therapy in an asthma population or may not have been designed and tested in this way.

In contrast, measures that directly evaluate symptoms are used to assess the burden of asthma in children and may be useful in the assessment of changes in certain outcomes, and these measures may be suitable alternatives or adjuncts to standard pulmonary function assessments. Several types of scales have been either wholly or partially validated. These scales, developed for use in pediatric populations, may be completed either by the child or by the caregiver and include asthma-specific quality-of-life measures,^{15,16} asthma self-efficacy and self-management measures,¹⁷⁻¹⁹ and asthma symptom questionnaires.^{1,12,20,21} These questionnaires are used periodically and ask about symptoms in the past, and therefore depend on accurate recall of symptoms. As an example, a recent validated asthma scale from Lara et al²¹ asks the parent/caregiver to recall the frequency (responses range from "never" to "every day") and severity (responses range from "very mild" to "very severe") of asthma symptoms over the past 4 weeks for cough, wheeze, shortness of breath, chest pain, symptoms at night, and number of asthma attacks.

An alternative type of rating of symptoms and burden depends on physician assessment. Physician-rating scales are evaluative measures commonly used to rate the severity of asthma and response to treatment in children that are based on physical signs, but these scales are not useful measures of chronic asthma symptoms.²²

This article reviews validation studies for 2 pediatric asthma diary questionnaires and explores the potential benefits and limitations of these instruments for use in a clinical trial environment.

PEDIATRIC ASTHMA DIARY VALIDATION

Merck & Company, Inc, has developed 2 pediatric asthma diary questionnaires: the Pediatric Asthma Diary (PAD) and the Pediatric Asthma Caregiver Diary (PACD). These questionnaires have been designed to measure daily asthma symptoms in children who are participating in clinical trials. The PAD was designed for 6- to 14-year-old children and is completed by the child with or without assistance from the child's parent/caregiver.²³ The PACD was designed for 2- to 5-year-old children and is completed by the parent/caregiver.²³ Separate clinical studies evaluated the validity of these scales.

PAD questionnaire

The PAD is divided into 2 parts: daytime diary and nighttime diary. The daytime diary assesses the frequency and bother of daytime asthma symptoms and how they affect normal daily activities on a scale that ranges from 0 (no symptoms or activity limitation) to 5 (most symptoms or activity limitation). The nighttime diary examines the number of awakenings caused by asthma symptoms on a scale of 0 (no awakenings) to 3 (awake all night). A 3-week prospective clinical study evaluated the validity of the PAD symptom questionnaire in 106 children aged 6 to 14 years. Two groups of children were recruited into the study. One group, classified by physician investigators as being "stable," was required to be currently treated with anti-inflammatory controller medication (cromolyn or inhaled corticosteroids [ICS]) and required no change in their current asthma treatment. The other group was classified as "unstable." The asthma of these patients was either new in onset or worsening, requiring either an increase or an addition of an anti-inflammatory controller medication, either as cromolyn or ICS. Children completed the asthma symptom diary twice daily for the 3-week study period. For younger children who were unable to read the diary, the parent/caregiver was allowed to assist the child by reading the questions and responses to the child and soliciting the child's symptoms (Table I).

Significant differences were observed between the stable and unstable groups in percent predicted FEV₁ at baseline and daily β -agonist use over the first week (Table II). The symptom scores for both the stable and unstable groups were also significantly different, with the exception of the nighttime awakening scale for the first study week. The daytime questions were able to discriminate between the 2 groups at baseline, despite a fairly small (approximately 50 per group) sample size. The average scores were less than 1, which indicated very mild symptoms; the standard deviation reflected the consistency of scores between 0 and 1 (Table III).

The ability of the diary questions to detect changes in asthma was evaluated by comparing week 3 symptom scores with week 1 scores (Table IV). There was a significant difference between the stable and unstable groups in changes of asthma bother score, the combined daytime scale score, and the percent of children experi-

TABLE I. PAD (completed by children 6 to 14 years old)

Table available in print only

encing a “day without asthma.” In this analysis, a day without asthma was defined as being a day with no β -agonist use, no daytime asthma symptoms, no nighttime awakenings, no unscheduled visits to a physician or emergency department, no admission to a hospital for asthma, and no use of oral steroids for asthma. Therefore, the diary was responsive to change in anti-inflammatory controller therapy; that is, it was able to detect changes in asthma between the stable and unstable groups over the 3 weeks. The study design does not allow for the determination of response to placebo; therefore, true responsiveness would need to be determined in a placebo-controlled trial environment.¹⁰

The assessment of the days without asthma for the 2 patient groups (Fig 1) shows that during the first, baseline week approximately 10% to 15% of the unstable group experienced days without asthma. The percent of unstable children having days without asthma progressively increased with treatment. On the contrary, the stable children experienced day-to-day variations, but the percent of children with days without asthma remained stable for the entire study period. As seen with the symptom scale, this combination endpoint appears to be responsive to treatment.

The longitudinal correlations between the change in symptoms reported and the change in other, more objective measures of asthma were generally low (Table V). For instance, the change from the study’s week 1 to week 3, individual and combined symptom scores correlated poorly with change in FEV₁ over the same period. The fact that childhood asthma symptoms vary daily and that the FEV₁ evaluations were completed weekly in the clinic may be, in part, responsible factors for these poor correlations. The low correlations are consistent with other research, however.^{5,7,11,24-26} Additionally, only low-to-moderate correlations were seen between diary symptom and overnight and daytime β -agonist puffs that were measured at the same time in the daily diary.

TABLE II. Baseline characteristics: 6- to 14-year-old children

Characteristic	Stable (n = 53)	Unstable (n = 53)
Age (y)*	9.2 $\pm$ 2.3	9.4 $\pm$ 2.4
Male (%)	66	70
FEV ₁ percent predicted (%)*	83.7 $\pm$ 10.9	77.8 $\pm$ 18.9 [†]
β -Agonist puff/day for week 1 (%)*	1.2 $\pm$ 1.7	3.1 $\pm$ 2.3 [‡]
Morning PEF (%)*	269.5 $\pm$ 80.7	258.8 $\pm$ 81.0

PEF, Peak expiratory flow.

*Value given as mean $\pm$ SD.

[†]P < .10.

[‡]P < .0001.

PACD questionnaire

A similarly designed study to evaluate the PACD included 125 children, 2 to 5 years old, with stable and unstable asthma and their parents/caregivers. For the patients whose asthma was stable and unstable, respectively, the mean ages were 4.3 and 4.0 years; there were 75% female and 68% male patients; cromolyn was used by 68% and 35%; ICS was used by 29% and 22%; and 35% of the unstable patients were using no controller asthma medication when they were entered into the study.

The parents/caregivers completed the PACD daily for 3 weeks. In this diary, the questions examined cough and wheeze severity, extent of breathing difficulty during the day, and limitations in the child’s normal daily activities because of asthma (Table VI). Based on an acceptable Cronbach α of 0.75, these 4 questions were combined to give an overall daytime symptom score. In addition, the daytime PACD explored other asthma-related factors that included resource use, school and daycare days lost, caregiver’s lost days from work, and β -agonist use during the day. The nighttime questions focused on the frequency of cough, caregiver disturbance because of the child’s

TABLE III. Discriminant validity (week 1 scores for children with asthma who were 6 to 14 years old)

Symptom	Stable (n = 53)	Unstable (n = 53)	P value
Trouble breathing	0.68 ± 0.78	0.93 ± 0.62	.008
Asthma bother	0.58 ± 0.61	0.95 ± 0.60	<.001
Activity limitation	0.41 ± 0.70	0.71 ± 0.64	.001
Combined daytime score	0.56 ± 0.67	0.86 ± 0.57	.001
Awakening score*	0.11 ± 0.20	0.17 ± 0.23	.103

Values are given as mean ± SD.

*Only 48 children (45%) experienced awakening with asthma in week 1.

TABLE IV. Responsiveness of diary questions (changes in scores from week 1 to week 3)

Question	Stable (n = 53)	Unstable (n = 53)	P value
Daytime diary			
Trouble breathing	-0.15 ± 0.64	-0.15 ± 0.85	.177
Asthma bother	-0.04 ± 0.56	-0.23 ± 0.80	.009
Activity limitation	-0.05 ± 0.77	-0.04 ± 0.85	.272
Combined daytime score	-0.25 ± 1.87	-0.42 ± 2.39	.037
Nighttime diary			
Awakening score*	0.02 ± 0.27	-0.02 ± 0.34	.198
Change in percent with day without asthma (%)	6.4 ± 26.9	24.5 ± 33.6	.004

Values given are mean ± SD.

*Only 48 (45%) of 106 patients had awakenings because of asthma in week 1.

TABLE V. Correlation coefficients for change in symptoms versus change in other measures from week 1 to week 3 in children 6 to 14 years old

Symptoms	Percent predicted FEV ₁	Morning PEF	Evening PEF	Overnight puffs	Daytime puffs
Trouble breathing	-0.08	-0.38*	-0.43*	0.31*	0.36*
Asthma bother	-0.11	-0.41*	-0.48*	0.30*	0.43*
Activity limitation	-0.12	-0.29*	-0.30*	0.26*	0.41*
Awakening	-0.03	-0.19*	-0.19*	0.37*	0.10
Combined daytime scale score	-0.11	-0.40*	-0.44*	0.31*	0.41*

PEF, Peak expiratory flow.

*Significant at $P < .05$. As the diary symptom score improved (decreased), significant improvements were seen in PEF (increases) and in β -agonist use (decreases).**TABLE VI.** PACD (completed by children 2 to 5 years old)

Overnight					
How much did your child cough last night after being put to bed for the night until awaking this morning? (<i>Check 1 response.</i>)					
0	Did not cough at all	2	Coughed several times	4	Coughed almost all night
1	Coughed very little	3	Coughed frequently	5	I do not know
Daytime symptoms					
How severe was your child's cough today? (<i>Check 1 response.</i>)					
0	No cough	2	Mild cough	4	Severe cough
1	Very mild cough	3	Moderate cough	5	Very severe cough
How severe was your child's wheezing today? (<i>Check 1 response.</i>)					
0	No wheezing	2	Mild wheezing	4	Severe wheezing
1	Very mild wheezing	3	Moderate wheezing	5	Very severe wheezing
How severe was your child's trouble breathing today? (<i>Check 1 response.</i>)					
0	No trouble breathing	2	Mild trouble breathing	4	Severe trouble breathing
1	Very mild trouble breathing	3	Moderate trouble breathing	5	Very severe trouble breathing
How much did your child's asthma symptoms interfere with your child's activities today? (Your child's activities could include any sort of physical activity such as running, playing, jumping, sports, bike-riding, climbing, or school activities.) (<i>Check 1 response.</i>)					
0	Did not interfere	2	Mildly interfered	4	Severely interfered
1	Very mildly interfered	3	Moderately interfered	5	Very severely interfered

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FIG 1. Percentage of children, aged 6 to 14 years, with days without asthma over the 3-week study. *Blue line/circles* represent children with stable asthma; *orange line/triangles* represent children with unstable asthma. A day without asthma equals all of the following: no daytime and nighttime symptoms and no β -agonist, oral steroid, and urgent care use. (From Santanello NC, Davies G, Galant SP, Pedinoff A, Sveum R, Seltzer J, et al. Validation of an asthma symptom diary for interventional studies. *Arch Dis Child* 1999;80:414-20. With permission from the BMJ Publishing Group.)

TABLE VII. Discriminant validity: week 1 scores on parent/caregiver-completed symptom questions for children with asthma who were 2 to 5 years old

Symptom measure	Stable mean	Unstable mean	P value
Daytime cough	0.67 $\pm$ 0.09	1.37 $\pm$ 0.10	.0001
Daytime wheeze*	0.25 $\pm$ 0.08	0.84 $\pm$ 0.09	.0001
Trouble breathing*	0.29 $\pm$ 0.08	0.83 $\pm$ 0.09	.0001
Activities limited*	0.29 $\pm$ 0.09	0.89 $\pm$ 0.10	.0001
Combined daytime symptom score	0.37 $\pm$ 0.04	0.98 $\pm$ 0.09	.0001
Nighttime cough†	0.46 $\pm$ 0.07	0.93 $\pm$ 0.08	.0001

Values given are mean $\pm$ SE.

*Daytime symptoms measured by severity on a scale of 0 to 5.

†Nighttime symptoms based on awakenings (0 = none to 3 = up all night).

asthma, and β -agonist use at night. The baseline scores on the variables collected for these young children are displayed in Table VII.

As was seen with the PAD in older children, the symptom scores were on average low, which indicates that the parent/caregiver reported very mild symptoms in this population. The PACD, however, was able to distinguish between children with stable and unstable asthma at baseline, despite low symptom scores between 0 and 1 and a small sample size. Significant ($P < .01$) differences were also detected in the nighttime symptoms (Table VIII). Of note, the percentage of young children with reported nighttime symptoms, up to 93%, was much higher than that seen in the study of older children (45%). Although the precise reason for this difference is unclear, one explanation may be that nighttime asthma symptoms may be more disturbing to the parent/caregiver than to the child, which would increase the frequency of reports on the parent/caregiver-completed PACD. There also may be differences in the types of asthma symptoms in younger versus older children.

In these young children, the FEV₁ could not be reliably measured at multiple clinical sites; consequently, changes in parent/caregiver symptom reports were correlated with other more subjective measures, including change in caregiver quality of life as measured by the Pediatric Asthma Caregiver Quality of Life Asthma Questionnaire,¹⁶ physician and caregiver global change in asthma assessment at the end of the 3-week study, and change in β -agonist use (Table IX). For these young children, changes in symptoms reported by the caregiver were most highly correlated with changes in β -agonist use, a correlation higher than that detected in the 6- to 14-year-old group or in adults.^{5,23} The high correlation between symptoms and β -agonist use in younger children may suggest an interaction between these 2 measures. The locus of control in younger children for the administration of asthma therapy generally lies with the parent/caregiver. Therefore, the child may have been perceived to be more symptomatic by the caregiver because more β -agonist treatments were perceived to be necessary.

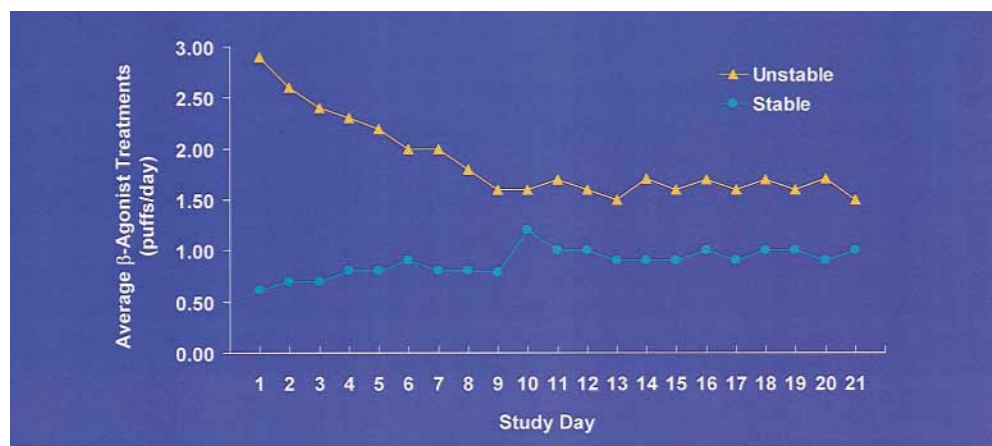


FIG 2. Average daily use of β -agonist (puffs/d) over the 3-week study in children aged 2 to 5 years. Blue line/circles represent children with stable asthma; orange line/triangles represent children with unstable asthma.

TABLE VIII. Discriminant validity of nighttime symptom questions

Question	Stable (n = 65)		Unstable (n = 65)	
	n	%	n	%
Parent/caregiver awakened	35	53.9	47*	78.3
Child coughed	48	73.9	56*	93.3
β -Agonist used	10	15.4	28*	46.7
Any 1 of 3	48	73.9	56*	93.3

* $P < .01$ for differences between groups at baseline.

In the PACD, all questions demonstrated significant ($P < .05$) discriminant validity in distinguishing between the stable and unstable groups on all questions, except for time lost from work by the caregiver, perhaps because most of the mothers in this study population did not work outside the home. In terms of responsiveness, all questions differed significantly between groups, except for lost time from school or daycare (a low percentage were in school or daycare). Unlike the PAD in older children, nighttime symptoms discriminated between stable and unstable asthma; these symptoms were shown to be responsive over time to therapy.

Fig 2 shows the clear discriminant validity of the PACD's measure of β -agonist use during the 3 weeks of the study. The stable group shows a more consistent use of less than 1 treatment per day; the unstable group's use starts high, at nearly 3 treatments per day, and is reduced with treatment. Similarly, the percent of patients having days without asthma symptoms differentiates the 2 groups (Fig 3).²⁴ In the unstable group, the percent of children who experience a day without asthma symptoms is rare initially, but with therapy, the incidence increases. In the stable group, the percent of patients remains between 30% and 40% throughout.

Overall, these studies suggest the PAD and PACD are valid and reliable and may be responsive instruments for the evaluation of asthma interventions in clinical trials with children as young as 2 to 5 years of age.

DISCUSSION

The results of studies in pediatric populations support the validity of the PAD and PACD questionnaires in the assessment of the severity of children's asthma symptoms and suggest that they can be valuable tools for evaluating asthma treatments in the clinical trial setting, as an alternative or adjunct to pulmonary function testing.

Despite generally low symptom scores, the PAD and PACD displayed significant discriminant validity and responsiveness to treatment interventions. Average symptom scores reported were low, which indicated that daily asthma symptoms were generally infrequent or very mild in the children who were studied. The diary responses in the PAD and PACD apparently support the assertion that the nature of asthma in children, episodic with fewer symptoms overall, is different from the more persistent, more symptomatic asthma often seen in adults. These results, however, should be interpreted with caution because of the previously mentioned reluctance of children to acknowledge their disability.² This tendency can reduce the child's and the parent's/caregiver's perceptions of the severity and frequency of airway obstruction, which could result in an underreporting of the actual severity or symptom frequency.^{5,8,9}

Steps can be taken to encourage increased perception of asthma symptoms among children and their caregivers. The mere use of a spirometer or peak flow meter where feasible, for example, may enhance symptom awareness, increasing the frequency and possibly the accuracy of the questionnaire's symptom reports. Indeed, with adequate training of caregiver and child, spirometry and peak flow rates have been shown to be feasible in children as young as 4 years of age. Nevertheless, because spirometry training can be time-consuming, the usefulness of this method in younger children is questionable in certain settings, especially large, multicenter clinical trials where the need for training would be extensive and costly. Also, the collection of daily symptoms will more accurately reflect the day-to-day variation in

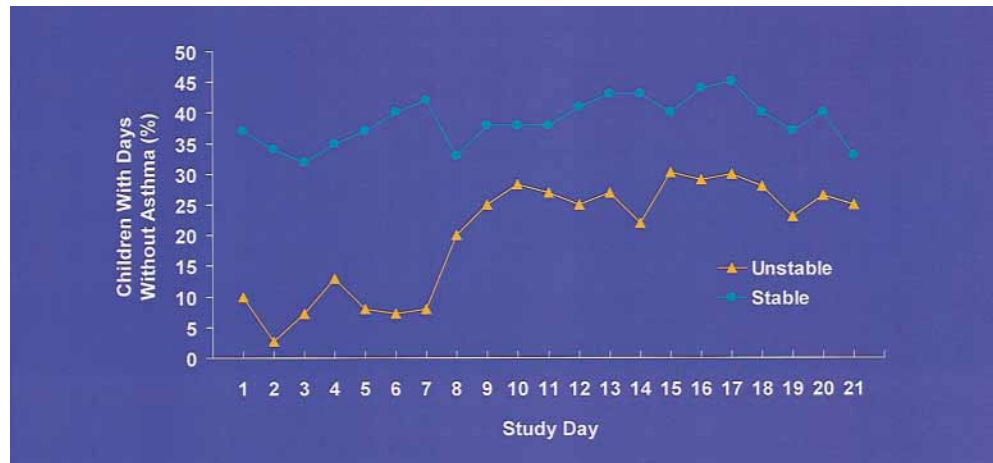


FIG 3. Percentage of children, aged 2 to 5 years, who experienced each day without asthma symptoms during the 3-week study. Blue line/circles represent children with stable asthma; orange line/triangles represent children with unstable asthma. (From Santanello NC, DeMuro-Mercon C, Davies G, Ostrom N, Noonan M, Rooklin A, et al. Validation of a pediatric caregiver diary. *J Allergy Clin Immunol* 2000;106:861-6. With permission.)

TABLE IX. Correlation coefficients for change in symptoms versus change in other measures from week 1 to week 3 in children 2 to 5 years old

Symptom	Change in QOL domain scores*		Global change in assessments		
	Activity	Emotion	Physician	Caregiver	Change in β -agonist treatments per day
Daytime cough	-0.23 [†]	-0.29 [†]	0.36 [†]	0.40 [†]	0.61 [†]
Daytime wheeze	-0.19	-0.25 [†]	0.30 [†]	0.39 [†]	0.67 [†]
Trouble breathing	-0.18	-0.25 [†]	0.28 [†]	0.36 [†]	0.58 [†]
Activity limitations	-0.28 [†]	-0.37 [†]	0.39 [†]	0.51 [†]	0.65 [†]
Combined daytime symptom scores	-0.27 [†]	-0.34 [†]	0.39 [†]	0.47 [†]	0.65 [†]
Nighttime cough	-0.27 [†]	-0.31 [†]	0.42 [†]	0.47 [†]	0.46 [†]

QOL, Pediatric Asthma Caregiver Quality of Life Questionnaire.

*Reported by pediatric caregiver.

[†]Significant at $P < .05$.

asthma, whereas spirometry is measured periodically. This is consistent with the slightly better correlations (although still low) observed between daily symptoms and peak flow meters.

In the PAD evaluation, correlations between objective measures of pulmonary function, such as FEV₁, correlated poorly with actual symptom reports over the study period. These findings are consistent with what has been reported in the literature for adults.^{5,11,25-27} Symptoms and objective assessments of pulmonary function may measure different aspects of the disease, underscoring the need to measure both parameters when possible. Underestimation or under recognition of symptoms by children and parent/caregiver may explain, at least partially, the typically poor correlation observed between these parameters.^{6,7} Daily symptom reports may more accurately reflect the day-to-day variation in asthma, whereas spirometry is generally measured episodically and hence will not provide an assessment of asthma variability. This is consistent with the slightly better correlations observed between change in daily symptom mea-

asures and change in daily peak flow measures, although these are still quite low.

Importantly, guidelines for the treatment of asthma in both adults and children are based on disease severity response by symptom control, activity level, β -agonist use, and response to treatment and are not determined solely by pulmonary function assessments.^{14,28,29} A question arises as to whether assessments of pulmonary function are appropriate in young children, a group in which standard pulmonary function testing is often unreliable. Clinical trials in young children may require symptom outcome measures to properly evaluate the effects of treatment and to establish proper dosing when measurement of pulmonary function is not possible.

Despite generally excellent validity for most measures, the older child-completed PAD did not distinguish differences in nighttime symptoms between children with stable and children with unstable asthma. In contrast, the caregiver-completed PACD, which evaluated young children 2 to 5 years of age, detected significant differences between these groups on all nighttime symptoms. The

reason for this difference in sensitivity between the PAD and PACD questionnaires may be attributed to the much greater percentage of younger children who experienced nighttime asthma symptoms, according to reports by their caregivers. It was not clear, however, whether the caregiver was more sensitive to a child's nighttime asthma symptoms, increasing the frequency of reports, or whether the younger children actually experienced a greater incidence of nighttime asthma symptoms.

Symptom reports and β -agonist use were the most highly correlated in young children, although this relatively high correlation may reflect the possibility that caregivers may expect and thus report more symptoms if they are providing more β -agonist medication. Moreover, the percentage of days without asthma, a combination measure that primarily represents symptom- and medication-free days, displayed excellent discriminant validity and clearly distinguished between stable and unstable asthma on both the PAD and PACD.

CONCLUSIONS

Validated diary questionnaires, such as the PAD and PACD, can provide one alternative for the evaluation of the effectiveness of asthma interventions in pediatric clinical trials, especially in young children in whom pulmonary function testing is often inappropriate or exceptionally challenging. Because they may measure different aspects of the disease state, symptom and pulmonary function assessments should be used together when feasible to provide the most complete assessment of asthma severity and the value of treatment. When that is not possible, reliable, valid, and responsive measures of symptoms should be used to provide quality data and useful information.

REFERENCES

- Fritz GK, Overholser JC. Patterns of response to childhood asthma. *Psychosom Med* 1989;51:347-55.
- Townsend M, Feeny DH, Guyatt GH, Furlong WI, Seip AE, Dolovich J. Evaluation of the burden of illness for pediatric asthmatic patients and their parents. *Ann Allergy* 1991;67:403-8.
- Sly PD, Landau LI, Weymouth R. Home recording of peak expiratory flow rates and perception of asthma. *Am J Dis Child* 1985;139:479-82.
- Henry R, Sly P, Godfrey S, Van Asperen P, Staugas R, Le Souef P, et al. Assessment and treatment of childhood asthma. *J Paediatr Child Health* 1991;27:218-20.
- Santanello NC, Barber BL, Reiss TF, Friedman BS, Juniper EF, Zhang J, et al. Measurement characteristics of two asthma symptom diary scales for use in clinical trials. *Eur Respir J* 1997;10:646-51.
- Sly PD. Relationship between change in PEF and symptoms: questions to ask in paediatric clinics. *Eur Respir J Suppl* 1997;24:80S-3S.
- Shingo S, Zhang J, Reiss TF. Correlation of airway obstruction and patient-reported endpoints in clinical studies. *Eur Respir J* 2001;17:1-5.
- Condemni JJ, Chervinsky P, Goldstein MF, Ford LB, Berger WE, Ayars GH, et al. Fluticasone propionate powder administered through Diskhaler versus triamcinolone acetonide aerosol administered through metered-dose inhaler in patients with persistent asthma. *J Allergy Clin Immunol* 1997;100:467-74.
- Reiss TF, Chervinsky P, Dockhorn RJ, Shingo S, Seidenberg B, Edwards TB. Montelukast, a once-daily leukotriene receptor antagonist, in the treatment of chronic asthma: a multicenter, randomized, double-blind trial: Montelukast Clinical Research Study Group. *Arch Intern Med* 1998;158:1213-20.
- Knorr B, Matz J, Bernstein JA, Nguyen H, Seidenberg BC, Reiss TF, et al. Montelukast for chronic asthma in 6- to 14-year-old children: a randomized, double-blind trial: Pediatric Montelukast Study Group. *JAMA* 1998;279:1181-6.
- Santanello NC, DeMuro-Mercon C, Davies G, Ostrom N, Noonan M, Rooklin A, et al. Validation of a pediatric caregiver diary. *J Allergy Clin Immunol* 2000;106:861-6.
- Brunekreef B, Groot B, Rijcken B, Hoek G, Steenbekkers A, de Boer A. Reproducibility of childhood respiratory symptom questions. *Eur Respir J* 1992;5:930-5.
- The International Study of Asthma and Allergies in Childhood (ISAAC) Steering Committee. Worldwide variation in prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema. *Lancet* 1998;351:1225-32.
- Florey CV, Leeder SR. Methods for cohort studies of chronic airflow limitation: World Health Organization Regional Office for Europe. Copenhagen, Denmark: WHO Regional Publications European Series, No. 2; 1982.
- Christie MJ, French D, Sowden A, West A. Development of child-centered disease-specific questionnaires for living with asthma. *Psychosom Med* 1993;55:541-8.
- Juniper EF, Guyatt GH, Feeny DH, Ferrie PJ, Griffith LE, Townsend M. Measuring quality of life in children with asthma. *Qual Life Res* 1996;5:35-46.
- Taylor GH, Rea HH, McNaughton S, Smith L, Mulder J, Asher MI, et al. A tool for measuring the asthma self-management competency of families. *J Psychosom Res* 1991;35:483-91.
- Schlösser M, Havermans G. A self-efficacy scale for children and adolescents with asthma: construction and validation. *J Asthma* 1992;29:99-108.
- Wu AW, Algatt-Bergstrom P, Diette GB, Skinner EA, Fitterman L, Clark R, et al. Development of the pediatric asthma control score [abstract]. *Am J Respir Crit Care Med* 1999;159:A911.
- Usherwood TP, Scrimgeour A, Barber JH. Questionnaire to measure perceived symptoms and disability in asthma. *Arch Dis Child* 1990;65:779-81.
- Lara M, Sherbourne C, Duan N, Morales L, Gergen P, Brook RH. An English and Spanish pediatric asthma symptom scale. *Med Care* 2000;38:342-50.
- Parkin PC, MacArthur C, Saunders NR, Diamond SA, Windees PM. Development of a clinical asthma score for use in hospitalized children between 1 and 5 years of age. *J Clin Epidemiol* 1996;49:821-5.
- Santanello NC, Davies G, Galant SP, Pedinoff A, Sveum R, Seltzer J, et al. Validation of an asthma symptom diary for interventional studies. *Arch Dis Child* 1999;80:414-20.
- Malo JL, L'Archeveque J, Trudeau C, d'Aquino C, Cartier A. Should we monitor peak expiratory flow rates or record symptoms with a simple diary in the management of asthma? *J Allergy Clin Immunol* 1993;91:702-9.
- Malo JL, Cartier A, Merland N, Ghezzi H, Burek A, Morris J, et al. Four-times-a-day dosing frequency is better than a twice-a-day regimen in subjects requiring a high-dose inhaled steroid budesonide, to control moderate to severe asthma. *Am Rev Respir Dis* 1989;140:624-8.
- Van Essen-Zandvliet EE, Hughes MD, Waalkens HJ, Duiverman EJ. Effects of 22 months of treatment with inhaled corticosteroids and/or beta-2-agonists on lung function, airway, responsiveness, and symptoms in children with asthma. The Dutch Chronic Non-specific Lung Disease Study Group. *Am Rev Respir Dis* 1992;146:547-54.
- McFadden ER. Clinical physiologic correlates in asthma. *J Allergy Clin Immunol* 1986;77:1-5.
- Pediatric Asthma: Promoting Best Practice. Guide for Managing Asthma in Children. American Academy of Allergy, Asthma & Immunology; 1999.
- Global Initiatives for Asthma (GINA). Pocket guide for asthma management and prevention (revised 1998). Bethesda (MD): US Department of Health and Human Services, Public Health Service, National Institutes of Health, National Heart, Lung, and Blood Institute; November 1998. NIH Publication No. 96-3659B.