Monitoring childhood asthma: Web-based diaries and the asthma control test

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Background: Data from asthma diaries are frequently used as an end point in asthma studies; however, data on the validity of Web-based diaries are scarce.

Objectives: First, we examined the validity of a Web-based diary in assessing asthma control. Second, we determined the cutoff points for well-controlled asthma of the Childhood Asthma Control Test (C-ACT) and the Asthma Control Test (ACT), and calculated the minimal important difference for both tests.

Methods: Children with asthma, ages 4-18 years (n = 228) completed a 4-week Web-based diary, C-ACT, ACT, and an asthma-related quality-of-life questionnaire at baseline and after 1-year follow-up.

Results: The completion rate of the Web-based diaries was 89%. The diary scores correlated strongly with C-ACT and ACT scores ($r = -0.73$, $P < .01$; $r = -0.64$, $P < .01$, respectively) and the changes in diary scores correlated well with changes in C-ACT and ACT scores. The best cutoff points for well-controlled asthma were C-ACT ≥ 22 and ACT ≥ 23. The minimal important differences were 1.9 (95% CI, 1.3-2.5) for ACT and 1.6 (95% CI, 1.1-2.1) for C-ACT, and −0.7 points/d (95% CI, −1.1 to −0.4) for the Web-based diary.

Conclusions: Our Web-based diary was valid for recording asthma symptoms. Cutoff points of ≥22 (C-ACT) and ≥23 (ACT) define well-controlled asthma. We recommend a 2 C-ACT and ACT points difference as minimally important. (J Allergy Clin Immunol 2013;■■■:■■■-■■■.)

Key words: *Asthma, childhood asthma control test, asthma diaries, Internet diaries, asthma-related quality of life, GINA, minimal important difference, pediatrics, validity*

Asthma affects approximately 5% to 8% of all school-aged children in the Western world.[1] The ultimate goal of asthma treatment is to achieve and maintain clinical control and to reduce future risk; hence, measures of asthma control are important outcomes in clinical asthma trials.[2] Symptoms and symptom-free days as recorded in diaries are frequently used as end points that reflect control.[3,4] Symptom diaries are easy to use, cheap, and symptoms are important for the patients and parents. However, recall bias is a problem with paper-based diaries, especially if these are not filled in on a daily basis.[5] This problem might be minimized by Web-based diaries, which are easily accessible at any time. However, data on their feasibility and reliability are scarce. Other tools available for measuring asthma control are the Asthma Control Test (ACT) and Childhood Asthma Control Test (C-ACT). Both these questionnaires were developed and validated for detection of uncontrolled asthma and are available for children from the ages of 12 years (ACT) and 4 to 11 years (C-ACT).[6-8] They are frequently used by patients and physicians, and, although a cutoff of <20 has good sensitivity and enough specificity to detect uncontrolled asthma, only a few studies have proposed a cutoff point for well-controlled asthma.[9-11] Also, the minimal important difference (MID) in score for C-ACT and ACT, defined as the scores that reflect a clinically meaningful change for the patient, is currently lacking. We, therefore, studied the validity of a Web-based diary in assessing asthma control in children by using C-ACT and ACT as the criterion standards. Second, we determined C-ACT and ACT cutoff points for "well-controlled" asthma and calculated the MID in C-ACT, ACT, and the diary scores with the Pediatric Asthma Quality of Life score as the criterion standard.

METHODS

This study is part of the multicenter study BATMAN (Better Asthma Treatment: Monitoring with ACT and Nitric Oxide), a prospective, randomized controlled trial in the Netherlands on new monitoring strategies in children with asthma, with a follow-up of 1 year (trial no. NTR 1995). At baseline (t = 0), parents and children completed a C-ACT or an ACT (if ≥12 years), and fractional exhaled nitric oxide (FENO) was measured (Fig 1). Subsequently, the patients and/or their parents filled in a daily Web-based diary for 4 weeks (baseline diary). The participants who completed less than 50% of the diaries dropped out of the study because we thought that we did not have enough information on the primary end point (symptom-free

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Abbreviations used
ACT: Asthma Control Test
C-ACT: Childhood Asthma Control Test
FENO: Fraction of exhaled nitric oxide
GINA: Global Initiative for Asthma
IQR: Interquartile range
MID: Minimal important difference
PACQLQ: Pediatric Asthma Caregivers Quality of Life Questionnaire
PAQLQ: Pediatric Asthma Quality of Life Questionnaire
SFD: Symptom-free day

days). At visit 2 (t = 4 weeks), asthma control was assessed with the C-ACT or ACT; FENO and FEV_1 were measured and asthma-related quality of life was assessed with the Pediatric Asthma Caregivers Quality of Life Questionnaire (PACQLQ) or Pediatric Asthma Quality of Life Questionnaire (PAQLQ if ≥12 years).[12,13] After 1 year follow-up, all the children filled in a second daily Web-based diary for 4 weeks (follow-up diary), and C-ACT and ACT, PACQLQ and PAQLQ, FEV_1, and FENO were repeated at the end of this 4-week period (t = 13 months).

Study population

Children 4 to 18 years of age, with a physician's diagnosis of atopic asthma based on clinical symptoms, and FEV_1 bronchodilator response of >9% of predicted and/or airway hyperresponsiveness and/or FENO > 25 ppb, were recruited from 3 tertiary referral centers and 4 general hospitals. The patients had been using inhaled corticosteroids for at least 3 months before inclusion and had Internet access at home. Exclusion criteria were active smoking, pulmonary diseases other than asthma, recent (<1 year) admission to an intensive care unit for asthma, an inability to perform FENO measurements, and the use of omalizumab. The medical ethics committee of the Erasmus University Medical Center, Rotterdam, approved the study. All the patients (if 12 years or older) and their parents gave written informed consent before entering the study.

Web-based diaries

The Web-based diary recorded daytime and nighttime symptoms (coughing, wheezing, shortness of breath), limitation in activity, and use of reliever medication (see Tables E1 and E2 in this article's Online Repository at www.jacionline.org). The diary score for nighttime as well as daytime symptoms ranged from 0 (no symptoms) to 21 (severe symptoms) plus the number of occasions when reliever medication was used. Diaries were sent out twice daily (5:00 am and 3:30 pm), were automatically date and time stamped, and the participants received an e-mail reminder once daily. Data entry was possible at the latest 5 days later. The Web-based diary is a Web version of an existing paper diary based on the Global Initiative for Asthma (GINA) criteria.[4] To correct for different completion rates, the diary scores were divided by the number of completed days ("corrected diary score"). For assessing the validity of the Web-based diaries and determination of the GINA levels that were used for the calculation of cutoff values, only patients who completed at least 75% of the diaries were selected.

Childhood asthma control

The ACT was used to assess asthma control in children from the age of 12 years old.[8] This patient-completed questionnaire consists of 5 questions on shortness of breath, awakenings at night, limitation of activity, rescue use of inhaled bronchodilators, and patient rating of asthma control over the past 4 weeks. Total score ranges between 5 and 25, with a score of less than 20 corresponding to uncontrolled asthma.[8,14,15] In this study, we used the Dutch validated version of the ACT. The translated C-ACT was used in children 4 to 11 years old.[7] The C-ACT is a 7-item questionnaire that also addresses the previous 4 weeks and is divided into 2 parts. The first part is filled in by the child with the aid of a visual scale and consists of 4 questions on perception of asthma control, limitations of activities, coughing, and nocturnal awakenings. The second part is filled in by a parent or caregiver and consists of 3 questions on daytime complaints, daytime wheezing, and awakenings at night. The C-ACT score may range from 0 (poorest asthma control) to 27 (optimal asthma control). A score of ≤19 indicates uncontrolled asthma.[7]

Lung function and FENO

FENO was measured online (NIOX NO-analyzer or NIOX MINO; Aerocrine, Stockholm, Sweden) with an expiratory flow of 50 mL/s.[16] Spirometry was performed by using a MasterScreen electronic spirometer (Jaeger/Carefusion, Würzburg, Germany). FEV_1 was recorded and expressed as percentage predicted.

Pediatric asthma quality of life

In children 12 years and older, asthma-related quality of life was measured with the 23-item self-reported Dutch validated version of the PAQLQ for children.[13,17] This questionnaire consists of domains related to emotions, activity, and symptoms, which are all equally weighted. Results were expressed as overall asthma-related quality of life. In children younger than 12 years old, asthma-related quality of life was measured by using the PACQLQ, which measures how caregivers are limited in their own quality of life by their child's asthma.[12,17] In both tests, the maximal score is 7, which indicates optimal quality of life.

Defining asthma control

Based on the diary data, the patients were categorized as having either well-controlled, partly controlled, or uncontrolled asthma according to GINA guidelines, including FEV_1.[1] In this survey, the definition of partly controlled was adapted from "any measure present in any week" to "any measure present per week" in the previous 4 weeks. The features "daytime symptoms" and "need for rescue treatment" were scored as present if patients recorded these for more than 2 days a week.[11] After 4 weeks, an overall GINA asthma control level was determined, which was the mean score of control status of all weeks. Three completed weeks were considered the minimum in the final assessment of GINA asthma control level (75% of the diaries).

Statistical analysis

To validate the Web-based diary, symptom scores from diaries were correlated with C-ACT or ACT scores. Both cross-sectional and longitudinal construct validity were evaluated by comparing associations (Pearson correlation coefficient) between C-ACT or ACT and the Web-based diary data. Responsiveness (sensitivity of change) of the Web-based diary was evaluated by comparing changes in the score between baseline and after 1-year follow-up with changes in the C-ACT and ACT score over the same period. Sensitivity, specificity, and positive and negative predictive values for well-controlled asthma as defined by GINA criteria were calculated for different cutoff points of C-ACT and ACT. The highest Youden index (sensitivity – [1 – specificity]) was considered the optimal cutoff.[18] The MID for the C-ACT, ACT, and symptom scores from the diary were calculated by using the PAQCLQ or PAQLQ score. In a linear regression model, we calculated the change in C-ACT, ACT, and symptom scores that corresponded to a change in PACQLQ or PAQLQ score of 0.5, which has been considered as a clinically significant and relevant change.[19,20] Data were analyzed by using SPSS version 20.0 (SPSS Inc, Chicago, Ill). All statistical tests used were 2-tailed. The level of significance was set at 5%.

RESULTS

Two hundred twenty-eight patients (67% boys) participated; their mean (SD) age was 10.5 ± 3.0 years. Baseline characteristics are shown in Table I. Seven patients dropped out because

FIG 1. Study design.

TABLE I. Baseline characteristics of the patients

	Age group 4-11 y old (n = 151)	Age group 12-18 y old (n = 77)
Age (y), mean (SD)	8.7 ± 1.8	13.8 ± 1.6
Boys, absolute no. (%)	106 (70)	43 (56)
Duration of asthma (y), mean (SD)	4.5 ± 2.8	8.3 ± 3.9
Daily dose of inhaled corticosteroids, absolute no. (%)		
≤400 μg budesonide or equivalent	116 (77)	42 (55)
>400 μg budesonide or equivalent	35 (23)	34 (45)
Use of long-acting β_2-agonists, absolute no. (%)	57 (38)	54 (70)
Use of leukotriene receptor antagonist, absolute no. (%)	12 (8)	15 (20)
Self-reported medication adherence, median (IQR)*	7.0 (6.0-7.0)	7.0 (6.0-7.0)
C-ACT or ACT score, median (IQR)	22.0 (19.0-24.0)	22.0 (20.0-23.0)
FENO (ppb), geometric mean (SD)	15.9 ± 2.2	19.9 ± 2.2
FEV_1 (% predicted), mean (SD)†	97 ± 14	96 ± 15

*Range, 1-7 d/wk.
†Measured after the baseline diary.

they did not complete 50% of all diaries or they did not show up at their second visit.

Validation of Web diaries

Patients reported more symptoms in the baseline diary than in the follow-up diary 1 year later; median corrected diary scores were 1.1 (IQR, 0.3-3.1) (<12 years old; n = 127) and 1.4 (IQR, 0.5-2.7) (≥12 years old; n = 67) versus 1.0 (0.3-3.0) (<12 years old; n = 93) and 0.8 (IQR, 0.3-3.3) (≥12 years old; n = 53) in the follow-up period. The median C-ACT and ACT scores at the end of the baseline period were 22 (IQR, 19-25) (n = 146) and 22 (IQR, 19-23) (n = 75), respectively. After completion of the follow-up diary, the median C-ACT score was 23 (IQR, 20-25) (n = 114) and the median ACT score was 23 (IQR, 20-24) (n = 66). There was a strong correlation between ACT or C-ACT scores and the diary scores of both baseline diary and follow-up diary (Table II). A total of 134 children completed both ACTs and at least 21 diary days in both periods. There was a good correlation between the change in diary score and the change in C-ACT ($r = -0.48$; $P < .01$) and ACT score ($r = -0.69$; $P < .01$) (Table II).

C-ACT and ACT cutoff points for well-controlled asthma

According to the GINA criteria, after the baseline period, 20% of patients (n = 39) were classified as well controlled, 40% (n = 78) as partly controlled, and 40% (n = 77) as uncontrolled.[1] Children with well-controlled asthma had a median C-ACT of 25.0 (IQR, 23.0-26.0) and a median ACT score of 24.0 (IQR, 23.0-25.0) (Table III). GINA levels of control were used to determine a cutoff point for well-controlled asthma. The best C-ACT cutoff score for well-controlled asthma was ≥22 (area under the curve, 0.81). When using the ACT, the best cutoff score for well-controlled asthma was ≥23 (area under the curve, 0.91). Receiver operating characteristic curves are shown in Fig 2, *A* and *B*.

FENO and lung function

At baseline, geometric mean FENO was 18.0 ppb in children with controlled asthma, 19.7 ppb in children with partly controlled asthma, and 17.8 ppb in children with uncontrolled asthma ($P = .61$). There was no significant correlation between FENO and C-ACT ($P = .78$) or ACT ($P = .37$). FEV_1 values per GINA level were 97% for controlled asthma, 96% for partly controlled asthma, and 98% for uncontrolled asthma ($P = .71$). Again, there was no significant correlation with C-ACT ($P = .72$) or ACT ($P = .43$) and FEV_1.

After a 1-year follow-up, the geometric mean for FENO was significantly higher for all GINA levels (all $P < .02$), 27.3 ppb for controlled asthma, 26.9 ppb for partly controlled asthma, and 23.0 ppb for uncontrolled asthma. There was no significant difference between the GINA levels ($P = .42$). FEV_1 values at follow-up were 99% for controlled asthma, 97% for partly controlled asthma, and 95% for uncontrolled asthma ($P = .40$). We also assessed the predictive value of FENO to predict well-controlled asthma, which was poor (area under the curve, 0.55) (data not shown).

Asthma control and quality of life

At baseline, children younger than 12 years old had a median asthma-related caregiver quality of life score (PACQLQ-score) of 6.5 (IQR, 5.9-6.9) (n = 138). Adolescents with asthma reported lower asthma-related quality of life (PAQLQ), with median PAQLQ scores of 6.2 (IQR, 5.9-6.6) (n = 78). Children with well-controlled asthma had PACQLQ and PAQLQ scores that were significantly higher than those with children with partly controlled or uncontrolled asthma (both $P < .001$) (Table III). Quality of life scores and C-ACT or ACT were strongly correlated for children ≥12 years old ($r = 0.81$; $P < .001$), whereas the correlation was moderate in children <12 years old ($r = 0.48$; $P < .001$). Also the changes in ACT or C-ACT scores correlated strongly with the change in PAQLQ score ($r = 0.64$; $P < .001$) and PACQLQ score ($r = 0.52$; $P < .001$).

MIDs

The MID that corresponded to a clinically relevant change of 0.5 in PAQLQ or PACQLQ score[19,20] was 1.9 (95% CI, 1.3-2.5) for the ACT and 1.6 (95% CI, 1.1-2.1) for the C-ACT. The MID

TABLE II. Diary scores, C-ACT and ACT-scores, and correlations

	Diary score, <12 y old, median, (IQR)	C-ACT, median (IQR)	Correlation diary-C-ACT, *r**	*P* value	Diary score, ≥12 y old, median (IQR)	ACT, median (IQR)	Correlation diary-ACT, *r**	*P* value
Cross-sectional								
Baseline	1.1 (0.3-3.1)	22 (19-25)	−0.64†	<.001	1.4 (0.5-2.7)	22 (19-23)	−0.72‡	<.001
Follow-up	1.0 (0.3-3.0)	23 (20-25)	−0.70§	<.001	0.8 (0.3-3.3)	23 (20-24)	−0.58‖	<.001
Longitudinal (baseline follow-up)								
Change, mean (SD)	−0.2 (2.2)	0.5 (4.0)	−0.48¶	<.001	−0.3 (2.0)	0.6 (3.8)	−0.69#	<.001

*Pearson correlation coefficient.
†No. = 131.
‡No. = 67.
§No. = 124.
‖No. = 68.
¶No. = 117.
#No. = 60.

TABLE III. ACT, C-ACT, PACQLQ, and PAQLQ scores in children with well-controlled, partly controlled, and uncontrolled asthma according to GINA criteria, based on the baseline diary data

	Well-controlled, n = 40 (20%)*	Partly controlled, n = 81 (41%)†	Uncontrolled, n = 76 (39%)‡	*P* value§
C-ACT, median (IQR)	25.0 (23.0-26.0)	24.0 (20.0-25.0)	19.0 (17.0-21.0)	<.001
ACT, median (IQR)	24.0 (23.0-25.0)	22.0 (21.0-23.0)	19.0 (16.5-21.5)	<.001
FENO, geometric mean (SD)	18.0 (2.0)	19.7 (2.4)	17.8 (1.9)	.61
FEV_1 % predictive, mean (SD)	97 (10)	96 (14)	98 (17)	.71
% SFD, mean (SD)	92 (9)	69 (23)	23 (19)	<.001
Symptom score, mean (SD)	0.12 (0.15)	0.60 (0.57)	2.39 (1.14)	<.001
PACQLQ, median (IQR)	6.8 (6.5-7.0)	6.7 (6.1-7.0)	6.0 (5.6-6.5)	<.001
PAQLQ, median (IQR)	6.8 (6.6-7.0)	6.5 (6.0-6.7)	5.9 (5.4-6.1)	<.001

SFD, Symptom-free days.
*Age < 12 y, n = 31; age ≥ 12 y, n = 9.
†Age < 12 y, n = 52; age ≥ 12 y, n = 29.
‡Age < 12 y, n = 47; age ≥ 12 y, n = 29.
§Kruskal-Wallis test.

for the Web-based diary, also corresponding to a change of 0.5 PAQLQ or PACQLQ points, was −0.7 points (95% CI, −1.1 to −0.4).

Adherence to Web-based diary

Of the baseline diary, 89.2% of the morning entries were completed after a median of 16 hours (IQR, 11-39 hours). Similarly, the evening entries were filled in after a median of 18 hours (IQR, 4-40 hours), with a completion rate of 88.5%. During the 4-week baseline diary period, adherence to filling in diary cards remained stable (88.4% in week 1 and 89.6% after 4 weeks). Fifty-four percent (n = 124) of the children filled in all diaries twice daily, and 85% (n = 194) at least 21 days. A total of 199 patients (87%) filled in the follow-up diary after 1 year. In this 4-week diary period, 88.3% of the morning entries were completed after a median of 28 hours (IQR, 12-53 hours) and 87.3% of the evening entries after a median of 24 hours (IQR, 5-49 hours). Here, 160 children (80%) completed at least 21 diary days.

DISCUSSION

In this study, we established the feasibility and validity of a Web-based asthma diary to monitor asthma control in children. The correlation between diary scores and C-ACT and ACT was high, and the Web-based diaries were able to detect changes in asthma control. We determined the optimal cutoff for defining well-controlled asthma and the clinically relevant changes in C-ACT score, ACT score, and diary score. Evaluation of symptoms should be a core asthma outcome measure in clinical research, as was stated by the National Institutes of Health. In this report, the importance of validation studies and comparison of diaries versus retrospective questionnaires was recommended.[21] Indeed, in this study, we showed that a Web-based diary was valid to assess symptoms and asthma control over a wide pediatric age range and correlated well with the C-ACT or the ACT, which are retrospective questionnaires, and determined the MID. The Web-based diary was highly feasible in assessing asthma control in children 4-18 years old. The completion rate was high and did not decrease over 4 weeks. The high completion rates were in line with earlier studies that used Web-based diaries. Moloney et al[22] used Internet-based diaries to register headache symptoms in adults, and they showed that, in their population, 75% of diaries were completed within 2 days. Also, 87% of the patients would have been willing to continue the diary for another 2 months. Sorbi et al[23] registered migraine symptoms by using a Web-based diary. They reported a completion rate of 87%. One earlier study used a Web-based diary to record asthma symptoms in children, and a completion rate of 80% was found, which is in line with our data.[11]

Paper-based diaries carry the risk of recall bias, errors, falsification, and omissions.[5,24] These risks may be reduced if electronic diaries are used.[24-26] Recently, Ireland et al[27] showed

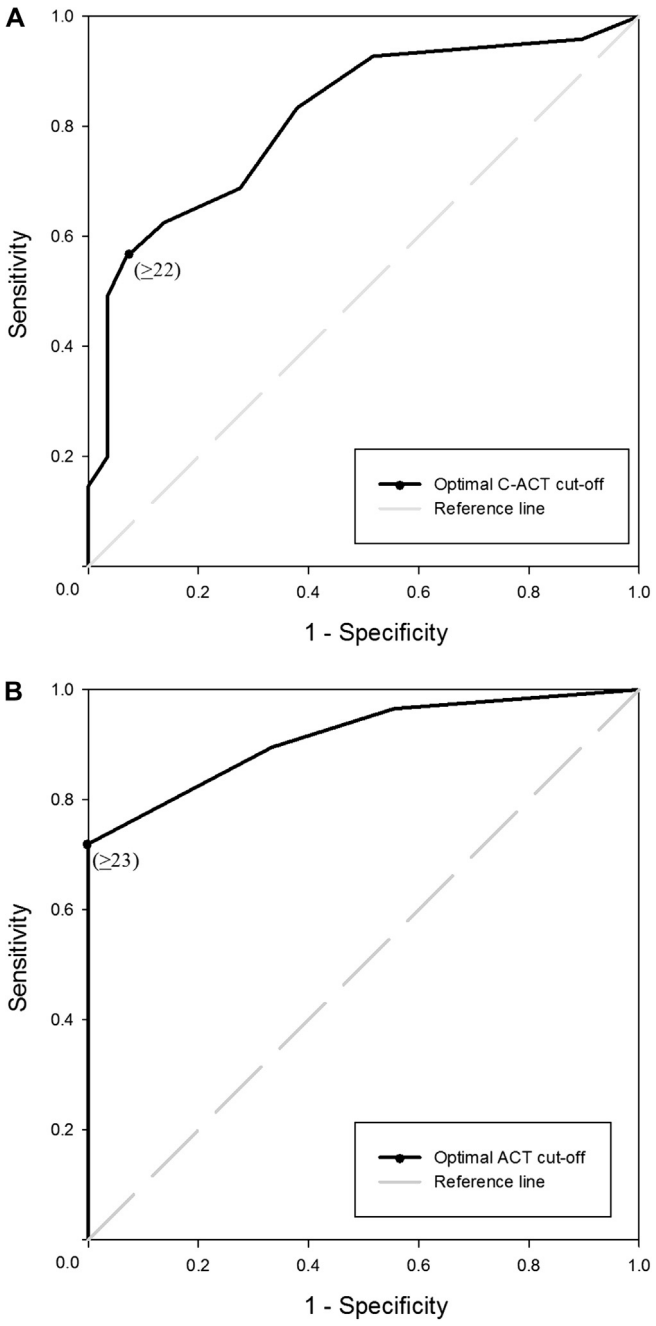

FIG 2. Receiver operating characteristic curves for C- ACT **(A)** and ACT **(B)**. Area under the receiver operating characteristic curve 0.81 (C-ACT) and 0.91 (ACT). The best C-ACT cutoff score for well-controlled asthma was ≥22 (sensitivity, 93.1%; specificity, 56.3%). The best ACT cutoff score for well-controlled asthma was ≥23 (sensitivity, 100%; specificity, 71.9%).

that an electronic diary is more reliable than a paper diary. Although we did not compare Web-based diaries with paper-based diaries, we confirmed the high accuracy of Web-based diaries in daily symptom recording. Also we found a good correlation among the diary data, C-ACT and ACT scores, and PAQLQ scores. This is in line with earlier studies by Juniper et al,[19,28] who showed strong correlations among diary data, the Asthma Control Questionnaire, and PAQLQ scores.

Why did we use a 4-week diary to assess asthma control? In asthma studies symptom scores and symptom-free days or asthma days are frequently used as a primary end point.[29] Therefore, we wanted to assess the validity of diaries as we used in this study in comparison with other measures of asthma control, which are frequently used in daily practice, such as the C-ACT and ACT. We found that asthma diaries are valid for use in studies, although we realize that, in daily practice, simple questionnaires or GINA criteria are much more feasible and easier to use. In the same way, Okupa et al[30] recently concluded that daily diaries might be more sensitive than the ACT for assessing differential treatment responses with respect to asthma control.

For analyzing the diary data, we only used data from patients who completed at least 21 diary days of the 28 days. It could be argued that the correlation between C-ACT or ACT and symptom scores might have been even better in children who filled in their diaries every day because these may have been better aware of their symptoms. However, this might introduce a bias toward children with good symptom perception. Still, there was no difference in corrected symptom scores, C-ACT and ACT scores, and PAQLQ scores between the children who did fill in at least 21 of 28 days and the children who filled in fewer days. Hence, there does not seem to be an important bias as a result of including those with only 21 days recording.

We determined C-ACT and ACT cutoff points for well-controlled asthma and the MID of both tests based on the quality-of-life information of these children. The C-ACT and ACT were initially developed to detect uncontrolled asthma, and earlier studies showed that the cutoff points for uncontrolled asthma for both C-ACT and ACT were ≤19, with 68% to 71% sensitivity and 71% to 76% specificity.[7,8] However, a C-ACT or ACT score of ≥20 does not necessarily indicate well-controlled asthma.[31] The primary goal of clinical asthma management is to achieve control, but, until now, little attention has been paid to cutoff points for well-controlled asthma. Ito et al[10] recommended a higher C-ACT cutoff score of 23 for well-controlled asthma when taking lung function into account. We found an optimal ACT cutoff point of ≥23 and a C-ACT cutoff point of ≥22 for well-controlled asthma. We propose to use these higher cutoff scores to accurately assess if a patient has well-controlled asthma.

For the Asthma Control Questionnaire, Juniper et al[19] calculated a MID based on minimal important changes in asthma-related quality of life. We followed a similar approach for ACT and C-ACT and the Web-based diary score. To our knowledge, we are the first who determined MIDs in children. Schatz et al[32] recommend a MID of 3 points in ACT score in adults, which is based on distribution- and anchor-based analyses instead of changes in quality of life. These different analyses may be an explanation for the difference between the MID of 2 in our study and 3 in the study by Schatz et al.[32] Second, we included adolescents rather than adults, and MID might differ for these 2 age groups.

A limitation of this study is the lack of a criterion standard for asthma control. We used the C-ACT and ACT scores as reference tests to assess validity of the Web-based diaries. The C-ACT and ACT are well-validated questionnaires to assess asthma control over a wide age range,[7,8,14] and we and others found that they correlated well with GINA criteria of asthma control.[11,31] In our opinion, the C-ACT and ACT were the best available standards of asthma control for our purpose. The same is true for establishing MIDs. In the absence of a criterion standard for MIDs, we decided to use quality-of-life scores to define

MIDs. Quality of life is an important and clinically relevant patient-centered outcome. We did not choose to determine MID on objective parameters as FEV_1 or FENO. First, in the majority of children with asthma, FEV_1 is normal, and clinically important differences of C-ACT or ACT based on changes in FEV_1 may not be easy to establish. Second, FENO was not considered an appropriate measure for determining MID, despite the large amount of literature on FENO because the role of FENO in monitoring asthma control is not evident. Similar to earlier studies, we found no correlation between asthma control scores and FEV_1 or FENO.[33-35] Also, in our study, FENO could not predict well-controlled asthma, and changes in FENO were not correlated with the level of asthma control. Symptoms, lung function, and airway inflammation represent different domains of the asthma phenotype and show limited agreement. Presently, the role of FENO in monitoring of children with asthma seems limited.[29,36]

We believe that the widespread use of user-friendly electronic devices such as tablets and smartphones will increasingly facilitate the use of Web-based diaries in asthma research and clinical practice. Children and adolescents in particular are an attractive population for Web-based studies because they are very active on the Internet, with 75% of all European children of 6-17 years using the Internet and even 86% of the 15-17-year-olds; whereas, in some countries, for example, the Netherlands, even 100% of all children of 15-17 years use the Internet.[37] Indeed, randomized controlled pediatric trials on Internet-based asthma monitoring have already been published, with mostly promising results.[38,39] However, potential difficulties with Web-based monitoring in less literate or technologically sophisticated populations warrant further research in these populations.

We conclude that our Web-based diary was feasible and valid in recording symptoms in children with asthma; hence, we recommend its use in clinical intervention studies. We established the C-ACT and ACT cutoffs for well-controlled asthma in children and found a MID to be 2 C-ACT or ACT points.

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Clinical implications: This study shows that Web-based diaries are valid for assessing asthma control in studies; however, the ACT (and C-ACT) is a good alternative. The minimal important difference of ACT (and C-ACT) is 2 points.

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TABLE E1. Web-based diaries: morning diary to register nighttime symptoms

Coughing	None (0)	One episode (1)	Two or more episodes (2)	Coughing during the whole night (3)
Wheezing	None (0)	One episode (1)	Two or more wheezing episodes (2)	Wheezing during the whole night (3)
Shortness of breath	None (0)	One episode (1)	Two or more episodes (2)	Shortness of breath during the whole night (3)
Use of reliever medication _____ times				

TABLE E2. Web-based diary: evening diaries to register daytime symptoms

Coughing	None (0)	One episode (1)	Two or more episodes (2)	Coughing during the whole day (3)
Wheezing	None (0)	One episode (1)	Two or more wheezing episodes (2)	Wheezing during the whole day (3)
Shortness of breath	None (0)	One episode (1)	Two or more episodes (2)	Shortness of breath during the whole day (3)
Limitation of activity	No limitation (0)	Little complains, no limitation of activities (1)	Some limitation of activities (2)	Much limitation of activities (3)
Use of reliever medication _____ times				