

Asthma Symptom Utility Index: Reliability, validity, responsiveness, and the minimal important difference in adult asthmatic patients

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Background: The evaluation of asthma symptoms is a core outcome measure in asthma clinical research. The Asthma Symptom Utility Index (ASUI) was developed to assess the frequency and severity of asthma symptoms. The psychometric properties of the ASUI are not well characterized, and a minimal important difference (MID) is not established.

Objectives: We assessed the reliability, validity, and responsiveness to change of the ASUI in a population of adult asthmatic patients. We also sought to determine the MID for the ASUI.

Methods: Adult asthmatic patients (n = 1648) from 2 previously completed multicenter randomized trials were included.

Demographic information, spirometric results, ASUI scores, and other asthma questionnaire scores were obtained at baseline and during follow-up visits. Participants also kept a daily asthma diary.

Results: The internal consistency reliability of the ASUI was 0.74 (Cronbach α). Test-retest reliability was 0.76 (intraclass correlation). Construct validity was demonstrated by significant correlations between ASUI scores and Asthma Control Questionnaire scores (Spearman correlation $r = -0.79$; 95% CI, -0.85 to -0.75 ; $P < .001$) and Mini Asthma Quality of Life Questionnaire scores ($r = 0.59$; 95% CI, 0.51 - 0.61 ; $P < .001$). Responsiveness to change was demonstrated, with significant differences between mean changes in ASUI scores across groups of participants differing by 10% in percent predicted FEV₁ ($P < .001$) and by 0.5 points in Asthma Control Questionnaire scores ($P < .001$). Anchor-based and statistical methods support an MID for the ASUI of 0.09 points.

Conclusions: The ASUI is reliable, valid, and responsive to changes in asthma control over time. The MID of the ASUI (range of scores, 0-1) is 0.09. (J Allergy Clin Immunol 2012;■■■:■■■-■■■.)

Key words: Asthma Symptom Utility Index, reliability, validity, responsiveness, minimal important difference

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Asthma is a chronic disease associated with substantial morbidity.¹ Recent asthma guidelines highlight the need to achieve and maintain good disease control.^{1,2} Well-validated questionnaires, such as the Asthma Control Questionnaire (ACQ)³ and the Asthma Control Test,⁴ are often used to assess asthma control in research and clinical practice. Asthma-specific quality-of-life questionnaires, such as the mini Asthma Quality of Life Questionnaire (Mini AQLQ)⁵ and the Marks Asthma Quality of Life Questionnaire (AQLQ-Marks),⁶ gauge the effect of asthma on the patient's functioning and well-being. The evaluation of asthma symptoms is a recommended core outcome measure in asthma clinical research, yet there is currently no widely accepted instrument for the standardized measurement of asthma symptoms.⁷

A recent National Institutes of Health working group found the Asthma Symptom Utility Index (ASUI) to be promising but not adequately validated.⁷ The ASUI was developed in 1998 by Revicki et al⁸ to measure the degree of asthma symptoms and their effect on patients. Some items on the ASUI are similar to those on questionnaires that assess asthma control and asthma-related quality of life.^{3,5,9,10} However, composite scores obtained from these questionnaires allocate equal weight to each item, even though the effect of different symptoms on patients might vary. The ASUI is unique insofar as it is a weighted scale and thus particularly valuable in cost-utility analyses.⁸ It is increasingly being used in asthma clinical research.^{11,12} The initial study by Revicki et al⁸ showed that the ASUI had good reproducibility (intraclass correlation = 0.74), good construct validity (Pearson correlation coefficient with the AQLQ = 0.77), and good discriminant validity. Nonetheless, a comprehensive evaluation of the psychometric

Abbreviations used

ACQ: Asthma Control Questionnaire
 AQLQ: Asthma Quality of Life Questionnaire
 ASUI: Asthma Symptom Utility Index
 EPAC: Episodes of poor asthma control
 MID: Minimal important difference
 PEFr: Peak expiratory flow rate
 SARA: Study of Acid Reflux and Asthma
 SIIVA: Safety of Inactivated Influenza Vaccine in Asthma

properties of the ASUI is lacking. In addition, a minimal important difference (MID) for the ASUI has not been established. Our objectives were to assess the reliability, validity, and responsiveness to change of the ASUI in a population of adult asthmatic patients participating in 2 multicenter randomized trials. We also sought to determine the MID for the ASUI.

METHODS

ASUI

The ASUI is a 10-item self-administered questionnaire with 4 questions on asthma symptoms (cough, wheeze, shortness of breath, and awakening at night) and 1 question about the side effects of asthma medications. For each symptom, there are 2 dimensions: frequency and severity. The questionnaire is based on a 2-week patient recall of symptoms and is scored by using a previously derived multiattribute utility function.⁸ The weighting scheme of the ASUI was developed by first constructing health states with single or multiple asthma symptoms at different frequencies and severities.⁸ Next, the participants were asked to attribute a relative value to various health states by using a visual analog scale and standard gamble methods.⁸ Finally, these data were used to derive a multiattribute utility function for scoring individual symptoms.⁸ The summary score is a continuous scale from 0 to 1, with lower scores indicating worse asthma symptoms.⁸ Details on the development of the ASUI have been previously published.⁸

Data collection

Patients. Data from 1648 adult asthmatic participants (≥ 18 years) enrolled in 2 completed clinical trials conducted by the American Lung Association Asthma Clinical Research Centers were included in this analysis.^{11,13} The Safety of Inactivated Influenza Vaccine in Asthma (SIIVA) trial was conducted between September 15 and November 30, 2000, and showed that the inactivated trivalent split-virus influenza vaccine was safe in adults and children with asthma.¹³ The Study of Acid Reflux and Asthma (SARA) trial was conducted between October 2004 and May 2008.¹¹ It showed that proton pump inhibitors did not improve asthma control in adults whose asthma was not well controlled on inhaled corticosteroids.¹¹

Procedures. The protocols for both studies were approved by institutional review boards in each of the participating centers, and informed consent was obtained from each participant. The SARA trial was registered at ClinicalTrials.gov (NCT00069823); the SIIVA trial was conducted before National Institutes of Health registration requirements were instituted. In the SIIVA trial baseline demographic data and ASUI scores were obtained for all participants ($n = 1236$). Baseline spirometric results were obtained in a subset of participants ($n = 704$). After administration of either vaccine or placebo, participants were followed for 14 days, during which they kept a daily asthma diary with information on asthma-related symptoms, peak expiratory flow rate (PEFR), health care use, and medication use. After crossover, there was another 14-day follow-up period.¹³ In the SARA trial ($n = 412$) baseline demographic data, spirometric results, ASUI scores, ACQ scores, and Mini AQLQ scores were obtained. Patients were then randomized to either 40 mg of esomeprazole twice daily or placebo in addition to their inhaled corticosteroid regimen for a total of 24 weeks. During follow-up

clinic visits that occurred every 4 weeks, ASUI, ACQ, and Mini AQLQ scores were obtained. Patients also kept an asthma diary that was returned during each clinic visit.¹¹

Assessments

Reliability. The Cronbach α coefficient was calculated by using baseline ASUI data from both the SIIVA and SARA trials to evaluate the internal consistency reliability. The Cronbach α coefficient measures the degree to which the items on the questionnaire measure the same unidirectional construct. Test-retest reliability was assessed by calculating the intraclass correlation coefficient between the baseline ASUI score and the ASUI score at the next follow-up visit (4 weeks apart) using data from participants in the SARA trial with stable asthma. Stable asthma was defined by the absence of an episode of poor asthma control (EPAC)¹¹ and no clinically significant change in the ACQ scores³ and Mini AQLQ scores⁵ (change < 0.5 points). An EPAC was defined by the occurrence of at least 1 of the following events: an increase in rescue medication use for asthma symptoms by 4 or more inhalations per day over baseline, the occurrence of an unscheduled contact with a health care provider for asthma, use of systemic corticosteroids for asthma, or a decrease of 30% or greater in morning PEFr on 2 consecutive days compared with the patient's best PEFr during the run-in period.¹¹

Construct validity. Construct validity of the ASUI was assessed with data from the SARA trial by computing Spearman correlations between baseline ASUI scores and (1) baseline ACQ³ scores and (2) baseline Mini AQLQ⁵ scores.

Known-groups validity. Known-groups validity was assessed by using data from the SIIVA trial, comparing the mean baseline ASUI score across 3 categories of baseline percent predicted prebronchodilator FEV₁: (1) less than 60%, (2) 60% to 79%, or (3) 80% or greater. The mean baseline ASUI score was also compared across a 4-point scale of ascending asthma severity among SIIVA participants based on asthma medication use at baseline (1, intermittent; 2, mild; 3, moderate; and 4, severe).¹⁴ Asthma severity was assessed according to an approximate Global Initiative for Asthma medication classification.¹⁴ Data on other methodologies for assessing asthma severity, such as the National Asthma Education and Prevention Program and Global Initiative for Asthma classifications, were not available for this *post hoc* analysis. Previous studies have shown that current asthma medication use complements other classifications of asthma severity.^{15,16} One-way ANOVA was then used to test the significance of differences in mean ASUI scores across groups of patients who differed by percent predicted FEV₁ and asthma severity categories.

Predictive validity. By using data from the SIIVA trial, predictive validity was assessed by comparing the frequency of EPACs and asthma exacerbations over the next 2 weeks by quartiles of baseline ASUI scores. An asthma exacerbation was defined by new use of systemic corticosteroids or an unscheduled contact with a health care provider. The ASUI was classified by quartiles because on exploratory data analysis, baseline ASUI scores had a skewed distribution, such that a majority of patients had very high scores and fewer patients had low scores. By using the highest ASUI quartile as the reference, the relative risk for each quartile of baseline ASUI scores was then calculated.

Responsiveness. Data from the SARA trial were used to determine the responsiveness to change in ASUI score. For each participant, there were 7 clinic visits, each separated by 4-week intervals from randomization to the end of the study. During each clinic visit, ASUI, ACQ,³ and Mini AQLQ⁵ scores were obtained. All participants were instructed to keep a daily asthma diary that was returned to the clinic during subsequent visits. Linear regression with robust variance estimates and an exchangeable correlation structure was used to compare mean changes in ASUI scores across groups of participants who differed by more than 10% in percent predicted FEV₁ and by greater than 0.5 points in ACQ scores while adjusting for visit period.¹⁷ The participant groups for each measure were derived as follows:

1. *Percent predicted FEV₁*: Previous studies have used 10% as the cutoff for significant change in percent predicted FEV₁.^{9,10,18} In the

population with chronic obstructive pulmonary disease, the MID of percent predicted FEV₁ is approximately 10%.¹⁹ The change in percent predicted FEV₁ was derived by subtracting baseline percent predicted FEV₁ from follow-up percent predicted FEV₁ and dividing by the baseline percent predicted value. Participants were categorized as better if the increase in percent predicted FEV₁ was greater than or equal to 10%. They were categorized as worse if percent predicted FEV₁ decreased by greater than or equal to 10%. If the change was less than 10% in either direction, they were categorized as unchanged. The mean changes in ASUI scores were then compared among the 3 groups.

2. **ACQ scores:** The MID for the ACQ score is 0.5 points.³ Participants were categorized as better if the decrease in ACQ score was greater than or equal to 0.5. They were categorized as worse if the increase in ACQ score was greater than or equal to 0.5, and they were categorized as the same or unchanged if the change was between −0.5 and +0.5 points. The mean changes in ASUI scores were then compared among the 3 groups: better, same, or worse.

MID. The MID is the smallest difference in score of an instrument that represents a clinically noticeable change.²⁰ In this study anchor- and distribution-based methods were used to determine the MID of the ASUI score.^{5,18,20}

Anchor-based analysis. Two groups of change in percent predicted FEV₁ (<10% vs ≥10% improvement from baseline) and 7 groups of changes in ACQ scores from baseline ($\Delta\text{ACQ} \geq -1.5$, $-1.0 \leq \Delta\text{ACQ} < -1.5$, $-0.5 \leq \Delta\text{ACQ} < -1.0$, $+0.5 > \Delta\text{ACQ} < -0.5$ [no change], $+1.0 > \Delta\text{ACQ} \geq +0.5$, $+1.5 > \Delta\text{ACQ} \geq +1.0$, $\Delta\text{ACQ} \geq +1.5$) were used as “anchors” to evaluate meaningful differences in ASUI scores. One-way ANOVA was used to compare mean changes in ASUI scores across the groups in each case. The occurrence of an EPAC, as well as individual EPAC components, also served as anchors. The mean difference in ASUI scores between visits with an EPAC in the prior period and those without an EPAC were calculated by using repeated-measures ANOVA.

Distribution-based analysis. The SDs of the baseline ASUI scores for each study sample were calculated, and ½ SD was used as an estimate of the MID.²⁰ The SEM of the baseline ASUI scores for each sample was also computed as follows: $SEM = SD_{ASUI} \times \sqrt{(1 - reliability_{ASUI})}$.^{18,20}

For the SIIVA sample, the Cronbach α coefficient was used to estimate the reliability coefficient of the ASUI, and for the SARA sample, the test-retest reliability coefficient was used. By convention, 1 SEM of baseline ASUI score is a good estimate of the MID.^{18,20}

RESULTS

Study population

Data from 1236 study participants aged 18 years and older from the SIIVA trial were included. The mean age of these asthmatic patients was 42 years (SD, 12 years). A majority of them were female (75%) and white (67%). Data from 412 participants in the SARA trial were also included. The mean age of asthmatic patients in the SARA trial was 41 years (SD, 13 years). The majority were female (68%), 50% were white, and 38% were black. A summary of the baseline characteristics of the study participants from the SIIVA and SARA trials is presented in Table I.²¹

Reliability

The internal consistency reliability (Cronbach α) was 0.74 ($n = 1223$) in the SIIVA sample and 0.71 ($n = 412$) in the SARA sample. Test-retest reliability (intraclass correlation coefficient) among the 55 participants in the SARA trial with stable asthma over a 4-week period was 0.76.

TABLE I. Patients' characteristics at baseline

Characteristic	SIIVA trial (n = 1236)	SARA trial (n = 412)
Age, y (SD)	42 (12)	41 (13)
Female sex (%)	923 (75)	279 (68)
Race or ethnic group, no. (%)		
White	828 (67)	205 (50)
Black	281 (23)	157 (38)
Hispanic	79 (6)	41 (10)
Other	44 (4)	9 (2)
Asthma questionnaire scores, mean (SD)		
ASUI↑ (0-1)	0.82 (0.18)	0.76 (0.16)
ACQ↓ (0-7)	NA	1.7 (0.9)
Mini AQLQ↑ (1-7)	NA	4.7 (1.2)
Pulmonary function, mean (SD)*	SIIVA (n = 704)	SARA (n = 412)
Prebronchodilator FEV ₁ (L)	2.6 (0.9)	2.4 (0.7)
Prebronchodilator FEV ₁ (% predicted)	83.4 (21)	76.7 (15)

ASUI scores range from 0 to 1, with higher scores indicating less severe asthma symptoms. ACQ scores range from 0 to 7, with lower scores indicating better asthma control and 0.5 being the minimal clinically important difference. Mini AQLQ scores range from 1 to 7, with higher scores indicating better quality of life and 0.5 as the minimal clinically important difference. FEV₁ and the predicted values are from Hankinson et al.²¹

*Pulmonary function results were available for 704 (57%) SIIVA participants.

TABLE II. Known-groups validity tests on mean ASUI scores at baseline (SIIVA trial)

	No. of participants	Mean (SD) ASUI score	F statistic/P value
Percent predicted FEV ₁			
<60%	97	0.76 (0.18)	
60% to 79%	188	0.81 (0.17)	
≥80%	405	0.85 (0.15)	12.5/<.0001
Asthma severity based on baseline medication use			
Intermittent	332	0.85 (0.14)	
Mild	453	0.83 (0.16)	
Moderate	298	0.80 (0.19)	
Severe	137	0.71 (0.20)	25.4/<.0001

FEV₁ and predicted values are from Hankinson et al.²¹

Construct validity

Statistically significant Spearman correlations were observed between baseline ASUI scores and baseline ACQ ($r = -0.79$; 95% CI, -0.85 to -0.75 ; $P < .001$) and baseline Mini AQLQ ($r = 0.59$; 95% CI, 0.51 - 0.61 ; $P < .001$) scores.

Known-groups validity

The difference in mean ASUI scores between patients with poor baseline lung function (percent predicted FEV₁ <60%) and those with good baseline lung function (percent predicted FEV₁ ≥80%) was statistically significant (0.76 vs 0.85, $P < .0001$, Table II). There was a positive linear relationship between the mean ASUI score and category of percent predicted FEV₁ (Fig 1). The difference in mean ASUI scores between patients with severe asthma and those with intermittent asthma was statistically significant (0.71 vs 0.85, $P < .0001$, Table II). There was a negative linear relationship between mean ASUI scores and asthma severity based on asthma medication use at baseline (Fig 2).

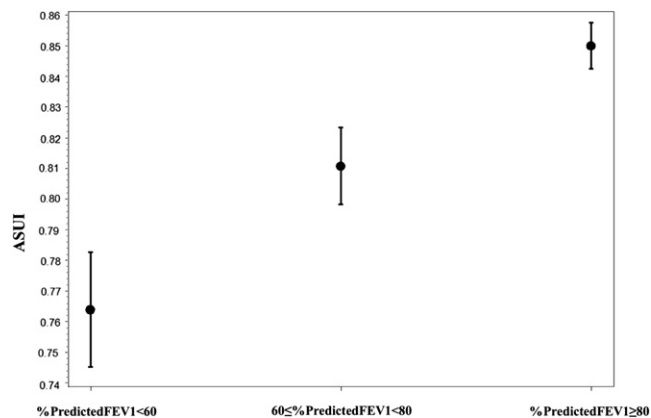


FIG 1. Mean ASUI scores with SEs by category of percent predicted FEV₁.

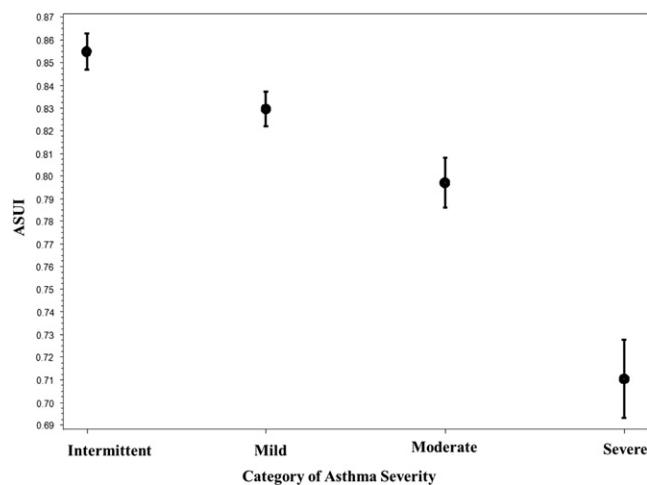


FIG 2. Mean ASUI scores with SEs by category of asthma severity.

Predictive validity

The frequency of EPACs ranged from 13% in the highest quartile of ASUI scores to 39% in the lowest quartile. Compared with patients in the highest quartile of baseline ASUI scores (score >0.95), SIIVA participants with a baseline ASUI score of 0.73 or less (lowest quartile) were 40% more likely to experience an EPAC over the next 2 weeks. There was a dose-response relationship with increasing likelihood of an EPAC by decreasing quartile of baseline ASUI scores (Table III). The overall frequency of asthma exacerbations, as defined by new or increased oral corticosteroid use or an unscheduled health care contact for asthma, was low (4% to 11%) across all 4 groups. Participants in the lowest quartile were 8% more likely to experience an exacerbation compared with those in the highest quartile (Table III).

Responsiveness

The ASUI demonstrated good responsiveness to change. As hypothesized, ASUI scores improved significantly among participants whose percent predicted FEV₁ improved by greater than or equal to 10% compared with those with no change in percent predicted FEV₁ (Table IV). Likewise, there was a significant change in ASUI scores (in the hypothesized direction) when ACQ scores

changed by more than the MID of 0.5 points compared with when the ACQ scores were unchanged (Table IV). After adjusting for visit period, there was a statistically significant difference in mean change in ASUI scores between visits with an EPAC in the prior period and those without an EPAC ($P < .0001$, Table V). Similar significant differences were seen for all 4 EPAC components (Table V).

MID

Anchor-based results. The absolute mean change in ASUI score corresponding to a small change in ACQ score ($-0.5 \leq \Delta\text{ACQ} < -1.0$ or $+1.0 < \Delta\text{ACQ} \leq +0.5$) was 0.09 (Table IV). The mean difference in ASUI scores between visits with an EPAC in the prior period and visits without an EPAC was also 0.09 (Table V). For the EPAC components, the mean difference ranged from 0.08 to 0.16 (Table V). The mean differences in ASUI scores for the less serious EPACs of peak flow decrease and increased use of rescue inhalers were 0.08 and 0.10, respectively. For the more serious EPAC components of oral steroid use and unscheduled urgent care contact, the mean differences in ASUI scores were 0.16 and 0.15, respectively. These results support an MID of approximately 0.09.

Distribution-based results. The SD of baseline ASUI scores was 0.18 for the SIIVA trial and 0.16 for the SARA trial. On the basis of the $\frac{1}{2}$ SD criteria as an estimate of MID, the MID of the ASUI is 0.09 and 0.08, respectively. The 1 SEM criteria produced MID estimates of 0.07 for the SARA sample and 0.09 for the SIIVA sample. Overall, from our study samples, we estimate the MID of the ASUI to be approximately 0.09.

DISCUSSION

The results of this study demonstrate that the ASUI, an asthma-specific utility index designed to summarize the frequency and severity of selected asthma-related symptoms,⁸ has good psychometric properties in 2 groups of asthmatic patients. We confirmed the findings of Revicki et al⁸ that ASUI scores have good construct validity, test-retest reliability, and discriminant validity. We also showed that baseline ASUI scores predict the occurrence of EPACs or asthma exacerbations in the subsequent 2 weeks. Patients with the lowest baseline ASUI scores were 40% more likely to have an EPAC and 8% more likely to have an asthma exacerbation over the next 2 weeks compared with those with the highest baseline ASUI scores. The ability to predict EPACs and asthma exacerbations suggests that the ASUI could be useful in guiding asthma therapy in clinical practice. In addition, we have shown that the ASUI is responsive to changes in asthma control. Using well-established anchor-based and statistical methods,^{5,9,18,20} we estimated the MID of the ASUI to be approximately 0.09 points.

Some items on the ASUI are similar to those on other questionnaires that assess asthma control and asthma-related quality of life.^{3,5,9,10} Asthma control as measured by the ACQ is a normative construct developed by physicians and validated against the physician's assessment of asthma.³ Asthma-related quality-of-life instruments measure the extent to which asthma symptoms interfere with physical functioning in daily life.⁵ The ASUI is complementary to these other tools by focusing on the frequency and severity of asthma symptoms. It is a patient preference-weighted scale and thus suitable for economic analyses that incorporate disability-adjusted life years.⁸

TABLE III. Predictive validity of the ASUI: relationship to the frequency of EPACs and exacerbations

Quartiles of ASUI	EPACs*		Exacerbations†	
	Frequency (%)	Relative risk (RR) (95% CI)	Frequency (%)	Relative risk (RR) (95% CI)
>0.95 (n = 321)	13	Reference = 1.00	4	Reference = 1.00
0.87-0.95 (n = 263)	24	1.13 (1.05-1.23)	4	1.00 (0.96-1.03)
0.74-0.86 (n = 290)	30	1.24 (1.13-1.35)	7	1.03 (0.99-1.07)
≤0.73 (n = 304)	40	1.44 (1.30-1.60)	11	1.08 (1.03-1.13)

RR, Relative risk.

*Any one of the following: (1) peak flow decrease of 30% or greater from personal best, (2) increased rescue medication use of greater than the average reported during the 2 weeks before randomization, (3) new or increased oral corticosteroids for asthma, and (4) an unscheduled use of health care for the treatment of asthma.

†Any one of the following: (1) new or increased oral corticosteroids for asthma and (2) an unscheduled health care encounter for treatment of asthma.

TABLE IV. Mean changes in ASUI scores as a function of changes in percent predicted FEV₁ and ACQ scores

	No. (patients)*	Mean change in ASUI score (95% CI)	P value
Changes in percent predicted FEV ₁			
Better ($\Delta\text{FEV}_1 \geq 10\%$)	213 (163)	0.05 (0.03 to 0.07)	
Same ($-10\% \leq \Delta\text{FEV}_1 < 10\%$)	1657 (384)	0.01 (0.00 to 0.01)	
Worse ($\Delta\text{FEV}_1 \leq -10\%$)	222 (170)	-0.03 (-0.05 to -0.02)	<.0001
Changes in ACQ† (ΔACQ)			
Better			
$\Delta\text{ACQ} \geq -1.5$	76 (68)	0.32 (0.28 to 0.35)	
$-1.0 \leq \Delta\text{ACQ} < -1.5$	111 (100)	0.15 (0.13 to 0.18)	
$-0.5 \leq \Delta\text{ACQ} < -1.0$	255 (198)	0.09 (0.08 to 0.10)	
Same			
$+0.5 > \Delta\text{ACQ} < -0.5$	1254 (369)	0.00 (-0.00 to 0.01)	
Worse			
$+1.0 > \Delta\text{ACQ} \geq +0.5$	233 (175)	-0.09 (-0.10 to -0.07)	
$+1.5 > \Delta\text{ACQ} \geq +1.0$	78 (69)	-0.17 (-0.20 to -0.14)	
$\Delta\text{ACQ} \geq +1.5$	61 (53)	-0.32 (-0.36 to -0.28)	<.0001

Note: The MID for the ACQ is 0.5 points.

*No. denotes frequency of events, and *patients* indicates the number of patients.†Better, Decrease by 0.5 points or more; *same*, change by less than 0.5 points; *worse*, increase by 0.5 points or more.**TABLE V.** Mean difference in ASUI scores by EPAC status for all visits

	No. of EPACs (% visits)	ASUI		
		Mean difference*	95% CI	P value*
Any EPACs	750 (35)	0.09	0.01-0.10	<.0001
EPAC components				
Peak flow decrease	426 (20)	0.08	0.06-0.10	<.0001
Rescue inhalers	414 (19)	0.10	0.01-0.12	<.0001
Oral steroid use	168 (8)	0.16	0.12-0.20	<.0001
Urgent care contact	103 (6)	0.15	0.11-0.20	<.0001

Two thousand one hundred fifty-five follow-up visit periods were evaluated among 390 participants.

*Mean difference in scores between visits with an EPAC in the prior period and those without an EPAC adjusted for visit period (repeated measures with independent correlation).

A key strength of this analysis is that data from 2 separate trials conducted at different time periods with different entry criteria and different interventions were used. However, because of the differing study designs, we were not able to perform the same validation analyses in both trials. It was necessary to use data from both studies to fully characterize the psychometric properties of the ASUI and to determine the MID. The SIIVA study included asthmatic patients with a wide range of clinical disease severity, but the ASUI was only administered at baseline,¹³ and therefore test-retest reliability and longitudinal validity could not be

assessed in this study population. Also, patients in the SIIVA trial had only 28 days of follow-up data, which might have limited the number of events, especially exacerbations. Nonetheless, because of the large population, we were able to demonstrate predictive validity based on the frequency of EPACs. In addition, ACQ and Mini AQLQ scores were not available for the SIIVA trial participants, and therefore construct validity could not be determined. The SARA trial, which included multiple ASUI measurements, as well as ACQ and Mini AQLQ scores, provided a good opportunity to determine responsiveness and construct validity.¹¹ Even though only patients with poorly controlled asthma were enrolled in the SARA trial, exploratory data analysis showed a skewed distribution of baseline ASUI scores, such that a majority of patients had very high scores and only a few patients had low scores.

A limitation of this study is the use of percent predicted FEV₁, ACQ scores, and EPACs as anchors for determining the MID. Data on other anchors, such as physician's global rating of asthma severity or control, were not available in this *post hoc* analysis.^{9,10,18} Studies evaluating the psychometric properties of other asthma questionnaires have used changes in percent predicted FEV₁ and changes in ACQ scores as anchors to determine the MID.^{9,10,18}

Generalizability to other patient populations is an important aspect of health utility tools.²⁰ The initial development and validation of the ASUI included asthmatic patients who were relatively well educated and mostly white.⁸ The current scoring of

the ASUI in the United States is based on the multiattribute utility function that was originally derived by Revicki et al.⁸ The preference weights, utility functions, and mean ASUI scores derived in the United States differ significantly from those obtained in other countries in Europe (Italy, France, and the United Kingdom).²² However, the relative rank ordering of the mean ASUI scores by asthma severity is maintained.²² In the current analysis we included participants with a good representation of women and racial minorities.^{11,13} Data on education level or socioeconomic status were not available. However, many of the study sites were located in large urban centers in the United States that generally serve patients of low socioeconomic status. This study therefore expands the generalizability of the ASUI to a more diverse population of asthmatic patients. The ASUI score can be complex to calculate for an individual patient in the clinical setting compared with the Asthma Control Test,⁴ and this could limit its routine use in clinical practice. However, computers can address this problem.

In summary, we demonstrated that the ASUI has good psychometric properties among adult asthmatic patients when used in the context of clinical trials in the United States. The MID of the ASUI in our population has been determined to be about 0.09 points. Further studies are needed to determine the psychometric properties of the ASUI in children and other demographic groups of the asthmatic population.

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Clinical implications: The established MID of 0.09 points for the ASUI will aid clinicians in interpreting the results of clinical research and improve monitoring of asthma symptoms in clinical practice.

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