



Validity and responsiveness of the Urticaria Activity and Impact Measure

A new patient-reported tool

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ABSTRACT

Background: Chronic spontaneous urticaria (CSU), also known as chronic idiopathic urticaria, may produce hives, itch, and angioedema. The Urticaria Activity and Impact Measure (U-AIM) is a newly developed 9-item patient-reported measure designed for use in routine clinical practice to assess CSU activity and impact during the previous 7 days.

Objective: To evaluate validity, responsiveness, and clinically meaningful change of the U-AIM.

Methods: Data from a 24-week, open-label, single-arm period of a randomized, placebo-controlled study of omalizumab were used to assess the psychometric properties of U-AIM items for itch, hives, and angioedema.

Results: A total of 206 patients (75% female; mean age, 44.6 years) were enrolled. At baseline, U-AIM results included prevalent severe itch (55%) and more than 12 hives (67%), angioedema (15%), and bother by itch (84%), hives (84%), and angioedema (49%). The Urticaria Patient Daily Diary (UPDD) mean weekly scores were 15.4 (itch severity), 16.8 (number of hives), and 32.2 (Urticaria Activity Score [UAS7]). At baseline, week 12, and week 24, U-AIM itch and hives items and UAS7 proxy scores (the sum of itch severity and number of hives during 7 days) demonstrated strong correlation coefficients with their corresponding measures from the UPDD (itch severity: 0.634–0.806; hives number: 0.735–0.843; UAS7 proxy: 0.724–0.852). Changes in U-AIM scores differentiated patients by their perspective of symptom improvement. Meaningful change thresholds were established for itch severity and number of hives scores (range, 0.8–1.0 for both) and the UAS7 proxy score (range, 10.5–12.5).

Conclusion: The U-AIM is valid and responsive to change and may help clinicians monitor CSU activity and track treatment effectiveness.

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Introduction

Chronic spontaneous urticaria (CSU), also known as chronic idiopathic urticaria (CIU), is characterized by the spontaneous occurrence of itchy hives and/or angioedema for more than 6 weeks without a specific trigger.^{1–3} Prevalence in the general population is approximately 1.0%.^{2,3} Approximately 20% of patients with CSU experience symptoms for more than 5 years.³ Individuals aged 20

to 40 years are most often affected, and women develop CSU twice as often as men.²

Many patients with CSU experience angioedema,^{4–7} either alone or together with hives and itch. The symptoms of CSU often have a significant negative effect on health-related quality of life, including sleep and emotional well-being,^{8–13} in part because of its unpredictable course and the potential for a lack of a clinical response to standard treatment.¹⁴

Antihistamines and omalizumab are the 2 licensed treatment options for CSU in the United States and Europe. Many patients can achieve symptomatic control with antihistamine therapy at approved or higher than approved doses. Omalizumab treatment is efficacious in most antihistamine-refractory patients.^{15,16} However, not all patients receive guideline-based care, and, even when they do, patients may exhibit various levels of symptom relief.

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The patient-reported Urticaria Activity Score (UAS) is the gold standard for measuring disease activity for CSU and is included within the Urticaria Patient Daily Diary (UPDD).¹³ The UAS7 measures intensity of pruritus and the number of hives or wheals.¹⁷ The UAS was developed specifically for use in patients with CSU and is the recommended method for assessing disease activity and response to treatment according to the European Academy of Allergy and Clinical Immunology/Global Allergy and Asthma European Network/European Dermatology Forum/World Allergy Organization guideline for urticaria.^{17,18} Currently, the most common versions of the UAS involve obtaining daily scores for 7 consecutive days (the UAS7 uses daily measurements and the UAS7TD uses the mean of twice-daily assessments^{19,20}), which may not always be practical and may require a high level of patient adherence. In addition, neither UAS7 version assesses angioedema.

The Urticaria Activity and Impact Measure (U-AIM) is a brief, newly developed, retrospective 9-item patient-reported outcome measure designed for use in clinical practice. A single administration, using a 7-day patient recall, assesses urticarial activity and impact during the previous 7 days. The current study sought to evaluate the psychometric properties of the U-AIM, including its validity and responsiveness, and to estimate what constitutes a clinically meaningful change in scale scores.

Methods

Data Sources and Study Population

Data from patients who were enrolled in a 24-week, open-label, single-arm period of a phase 4, multicenter, randomized, double-blind, placebo-controlled study (Xolair Treatment Efficacy of Longer Duration in Chronic Idiopathic Urticaria [XTEND-CIU]^{21,22}) to evaluate the efficacy and safety of omalizumab were included in the current study. Details of the XTEND-CIU inclusion and exclusion criteria have been previously published.²³ Briefly, patients aged 12 to 75 years with a diagnosis of CSU for at least 6 months refractory to histamine₁ (H₁)-antihistamines and use of a non-sedating H₁-antihistamines for CSU (also known as CIU) for at least 3 consecutive days before study screening were included.

Analyses to evaluate the psychometric properties of the U-AIM used interim data from the screening (week –2, week –1) and open-label treatment (week 0 through week 24) phases of the study. Data from the randomized double-blind (week 24 through week 48) or follow-up (week 48 through week 60) phases were not used to maintain separation from data to be used for the evaluation of treatment efficacy. The study sample included 206 patients (74.8% female), with a mean (SD) age of 44.6 (14.5) years and a mean (SD) time since CSU diagnosis of 5.9 (8.0) years. Most patients were white (81.6%) and employed (62.1%). Mean UAS7 score at baseline was 32.2 (Table 1), indicating fairly high levels of urticarial disease activity.

Study Instruments

Data from the U-AIM and additional PRO and clinician-reported collateral measures were used to examine the validity and responsiveness of the U-AIM and to explore clinically meaningful change in the U-AIM. The U-AIM includes 9 patient-reported items to assess urticarial activity and impact during the previous 7 days. Specifically, the U-AIM includes 3 items related to the severity of symptoms (itch severity, the number of hives, and the number of days with angioedema/swelling), 3 items of patient bother (itch, hives, and angioedema/swelling), 2 items that ask about the extent of interference urticaria has on daily activities and sleep, and a final item that asks about the current level of disease control. A composite score, referred to as the UAS7 proxy, was defined as the sum of itch severity and number of hives items, with that total multiplied by

Table 1
Baseline Characteristics

Characteristic	Finding (N = 206) ^a
Age, mean (SD), y	44.6 (14.5)
Female	154 (74.8)
Race/ethnicity	
White	168 (81.6)
Black/African American	23 (11.2)
Asian	5 (2.4)
American Indian/Alaskan Native	3 (1.5)
Multiple	3 (1.5)
Hispanic	44 (21.4)
Other	4 (1.9)
BMI, mean (SD) (n = 205)	84.7 (20.6)
Employment	
Working	128 (62.1)
Retired	19 (9.2)
Unemployed, unable to work	6 (2.9)
School, keeping house, on leave, other	13 (6.3)
Unknown	40 (19.4)
Time since CSU diagnosis, mean (SD), y	5.9 (8.0)
UPDD ^b at baseline, mean (SD) (n = 203)	
Weekly hives	16.8 (4.5)
Weekly itch	15.4 (3.6)
Weekly UAS, UAS7	32.2 (7.0)
DLQI ^c at baseline, mean (SD)	
Overall	14.8 (6.9)
Symptoms and feelings	4.5 (1.4)
Daily activities	3.5 (1.7)
Leisure	2.8 (2.0)
Work and school	1.4 (1.2)
Personal relationships	1.6 (1.8)
Treatment	1.1 (1.0)
UCT ^d at baseline (total score), mean (SD)	2.5 (2.5)
ISI ^e at baseline (total score), mean (SD)	15.9 (6.9)
WPAl ^f at baseline, mean (SD)	
Absenteeism (n = 162)	7.0 (15.6)
Presenteeism (n = 163)	43.1 (28.4)
Work productivity loss (n = 161)	44.7 (29.3)
Activity impairment (n = 203)	52.0 (26.9)
IC-UAS ² composite (n = 205), mean (SD)	4.9 (1.2)

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by the square of height in meters); CSU, chronic spontaneous urticaria; DLQI, Dermatology Life Quality Index; IC-UAS, In-clinic Urticaria Activity Score; ISI, Insomnia Severity Index; SD, standard deviation; UAS, Urticaria Activity Score; UCT, Urticaria Control Test; UPDD, Urticaria Patient Daily Diary; WPAl, Work Productivity and Activity Index.

^aData are presented as number (%) of patients unless otherwise indicated.

^bHigher scores represent worse functioning.

^cHigher scores represent greater impact.

^dHigher scores represent better functioning.

7. The collateral measures were also administered during the study and are described in detail in Table 2.

Descriptive Analysis

The mean and SD were calculated for age, time since CSU diagnosis, and UAS7 score 1 week before baseline (week –1). The count and percentage of patients were reported for sex, ethnicity, race, country, employment, marital status, and educational level. We provide descriptive information on all U-AIM items at baseline (week 0), week 12, and week 24. In addition to the mean and SD of individual items, ceiling and floor effects represent the percentage with the highest and lowest score, and skewness is described in terms of symmetry of the distribution of scores. Descriptive analyses on collateral measures characterized the study sample based on data obtained from the UPDD,¹³ the Dermatology and Life Quality Index (DLQI),²⁴ the Urticaria Control Test (UCT),^{25,26} the Insomnia Severity Index (ISI),²⁷ the Work Productivity and Activity Index (WPAl),²⁸ and the In-Clinic UAS (IC-UAS).

Table 2
Overview of Collateral Patient- and Clinician-Reported Measures

Measure	Overview
Patient reported	
Dermatology and Life Quality Index (DLQI) ²⁴	10 items, patient reported, assesses symptoms, feelings, activities, leisure, work/school, personal relationships, and treatment over the past week, higher scores indicate more impact
Urticaria Control Test (UCT) ^{25,26}	4 items, patient reported, assesses control and used to screen patients with poorly controlled urticaria, uses a 4-week recall, lower scores indicate more poorly controlled diseases
Insomnia Severity Index (ISI) ²⁷	7 items, patient reported, assesses self-perceptions of insomnia symptoms and effect on health and daily life, higher scores indicate greater insomnia severity
Work Productivity and Activity Index (WPAI) ²⁸	6 items, patient reported, assess reduced productivity through 4 aspects: absenteeism, presenteeism, work productivity loss, and activity impairment, uses 7-day recall, higher scores indicate more productivity problems associated with the health state
Patient Global Impression of Change (P-GIC)	1 item, asks patients to rate change in their CSU since the beginning of the study on a 7-point scale (1, very much improved; 7, very much worse)
Urticaria Patient Daily Diary (UPDD) ¹³	Daily (morning and evening) diary asking patients about urticaria during the last 12 or 24 hours, assesses itch severity, number and size of hives, sleep interference, daily activity interference, diphenhydramine use, and occurrence of angioedema
Urticaria Activity Score (UAS)	Developed as part of the UPDD, based on the number of wheals and intensity of itch; the UAS7 represents the sum of UAS during 7 consecutive days, higher scores indicate more wheals and intensive itching
Clinician reported	
In-Clinic Urticaria Activity Score (IC-UAS)	A clinician's rating (through an interview with the patient) of the patients itch and number of hives during the 12 hours before the visit, the composite score is calculated as a sum of the number of hives (0, none; 3, >12) and severity of pruritus (0, none; 3, severe and difficult to tolerate), higher scores indicate more severe activity
Clinician Global Impression of Change (C-GIC)	1 item, asks clinicians to rate the change in patients CSU since the beginning of the study on a 7-point scale (1, very much improved; 7, very much worse)

Abbreviation: CSU, chronic spontaneous urticaria.

Evaluation of Psychometric Properties

Response characteristics of items and 3 scales (itch severity, the number of hives, and the UAS7 proxy) were examined, and the following were assessed: construct validity (known-groups validity and convergent validity), responsiveness, and clinically meaningful change. To assess convergent validity, correlation coefficients were calculated between U-AIM scale scores and collateral measures (ie, UPDD, DLQI, UCT, ISI, WPAI, IC-UAS) at weeks 0, 12, and 24. The choice of Spearman vs Pearson correlations was based on the Kolmogorov-Smirnov test for distributional normality. For scales that measure similar constructs (as determined after the U-AIM scale structure had been finalized), correlations greater than 0.30, a medium effect as defined by Cohen standards,²⁹ were used to establish convergent validity.

Known-groups validity was assessed by categorizing patients into groups on the basis of IC-UAS itch and hives scores separately at baseline (week 0) and week 24 and comparing patients on U-AIM scale scores using nonparametric tests for omnibus comparisons. Where omnibus tests were significant, pairwise post hoc comparisons between groups were performed using the Tukey honest significant difference post hoc tests.³⁰ Calculated partial η^2 values represent the proportion of the variance of U-AIM scores accounted for by group differences. Cohen²⁹ characterizes an η^2 value of approximately 0.14 as a large effect. To assess longitudinal known-groups validity, patients were divided into groups based on the Patient Global Impression of Change (P-GIC) and the Clinician Global Impression of Change (C-GIC) ratings separately at week 24. These groups were then compared on changes in U-AIM scores from baseline to week 24 using analysis of variance. The Tukey honest significant difference post hoc tests³⁰ were used to determine differences between individual groups; nonparametric tests were used if distributional assumptions were not met.

Correlation coefficients were calculated between changes in U-AIM scale scores and changes in collateral measures (UPDD, DLQI, UCT, ISI, WPAI, and IC-UAS) to examine longitudinal construct validity. Analyses were performed separately for changes from baseline to week 12 and changes from baseline to week 24. The type of correlation (ie, Pearson or Spearman) was based on the Kolmogorov-Smirnov test for distributional normality. Correlations greater than

0.30, a medium effect as defined Cohen,²⁹ were used to establish longitudinal convergent validity.

The responsiveness of a measure reflects its ability to detect clinically important changes, even if the changes are small.³¹ Three measures of responsiveness were calculated using the difference in means between baseline and week 12 and between baseline and week 24. The first measure, the standardized effect size (SES),²⁹ was calculated as that difference divided by the SD at baseline. The standardized response mean (SRM)³² divided that difference by the SD of the change score, and the responsiveness statistic³¹ divided that difference by the SD of the change score for stable patients. We defined stable patients as those rating themselves as unchanged on the P-GIC at week 24. We calculated coefficients of responsiveness separately by week 24 P-GIC and C-GIC ratings, as well as combined across the entire sample.

Clinically Meaningful Change

To determine clinically meaningful change estimates, both distribution- and anchor-based methods were used. Distribution-based measures included the SEM, Cohen *d* or SES,²⁹ and Guyatt's responsiveness statistic.³¹ The SES and Guyatt's statistic used thresholds for the magnitude of the effect of 0.20 (small), 0.50 (medium), and 0.80 (large).³³ Several anchor-based approaches were used, including correlations between changes in U-AIM scale scores from baseline to week 24 and P-GIC and C-GIC at week 24; correlations greater than 0.30 are recommended for anchors used to establish thresholds for meaningful change.³⁴ In addition, we calculated mean changes in U-AIM scores from baseline to week 24 separately for each possible rating on the P-GIC and C-GIC at week 24, and we used ordinary least squares regression analysis to regress P-GIC and C-GIC ratings at week 24 on changes in U-AIM scores from baseline to week 24, controlling for baseline U-AIM score.

To establish clinically meaningful change thresholds, we integrated distribution- and anchor-based estimates. Following the recommendations of Revicki et al,³⁵ we based the thresholds for clinically meaningful change primarily on patient-based and clinical anchors that are correlated with U-AIM outcome; namely, P-GIC and C-GIC ratings of severity. Distribution-based information on U-AIM

Table 3
Urticaria Activity and Impact Measure Item and Score Descriptive Summary

Item	Baseline		Week 12		Week 24	
	No.	Mean (SD)	No.	Mean (SD)	No.	Mean (SD)
Itch severity (range, 0–3)	205	2.5 (0.6)	193	0.9 (0.9)	170	0.6 (0.8)
Itch bother (range, 0–4)	204	3.2 (0.7)	129	1.4 (1.0)	82	1.3 (1.0)
No. of hives (range, 0–3)	205	2.6 (0.6)	193	0.9 (1.0)	170	0.6 (0.9)
Hive bother (range, 0–4)	205	3.2 (0.7)	122	1.3 (1.1)	85	1.0 (1.2)
Swelling (range, 0–4)	205	1.2 (1.3)	192	0.3 (0.8)	169	0.2 (0.6)
Swelling bother (range, 0–4)	135	2.4 (1.3)	63	1.1 (1.3)	30	1.0 (1.2)
Interfere with daily activities (range, 0–4)	205	2.5 (1.0)	193	0.5 (1.0)	170	0.4 (0.8)
Interfere with sleep (range, 0–4)	206	2.5 (1.0)	193	0.7 (0.9)	170	0.4 (0.8)
Urticaria control (range, 0–4)	205	3.1 (0.8)	193	1.0 (1.0)	169	0.7 (1.0)
UAS7 proxy ^a (range, 0–42)	205	35.8 (6.5)	193	12.7 (13.0)	170	8.0 (11.0)

Abbreviation: UAS, Urticaria Activity Score.

^aCalculated as (itch severity and number of hives) × 7.

scales, including 1.0 and 1.96 SEM; 0.20, 0.30, 0.50, and 0.80 Cohen *d*; and 0.20, 0.50, and 0.80 Guyatt statistic, were used as supportive information for establishing the thresholds for clinically meaningful change. The SEM was considered the primary distribution-based estimate because it takes into account the reliability of the measure and thus estimates the precision of the instrument.³⁴ However, other distribution-based measures (ie, Cohen *d* and Guyatt statistic) were also considered.

Results

Baseline Assessments

Mean (SD) scores for weekly number of hives, weekly itch severity, and UAS7 were 16.8 (4.5), 15.4 (3.6), and 32.2 (7.0), respectively (Table 1). Mean (SD) scores for DLQI, UCT, ISI, and IC-UAS were 14.8 (6.9), 2.5 (2.5), 15.9 (6.9), and 4.9 (1.2), respectively. Table 3 gives the mean (SD) values for U-AIM item characteristics at baseline, week 12, and week 24. Ceiling effects at baseline ranged

from 10.2% (swelling bother) to 67.0% (number of hives), whereas floor effects at week 24 ranged from 8.2% (swelling bother) to 89.4% (swelling number of days). Several U-AIM items (eg, itch severity, number of hives, hive bother, interference with daily activities) showed substantial negative skew at baseline and positive skew at week 24. Exploratory factor analysis was considered and attempted, but it was unable to produce clinically relevant factors. Therefore, other than the calculation of the UAS7 proxy score, items from the U-AIM were scored individually.

Convergent Validity

The pattern of correlations provides strong support for convergent validity of the U-AIM scores. Generally, correlations were weakest at baseline (Table 4) and stronger at weeks 12 and 24. Specifically, the U-AIM itch severity score correlated strongly with both the UPDD Weekly Itch (range, 0.634–0.806) and the IC-UAS Pruritus rating (range, 0.503–0.731); the U-AIM number of hives scores

Table 4
Convergent Validity: Spearman Correlations Between U-AIM Scores and Collateral Measures at Baseline

Measure	No. of patients	Spearman correlation coefficient		
		U-AIM itch severity	U-AIM no. of hives	U-AIM UAS7 proxy
UPDD weekly itch	202	0.634 ^a	0.303 ^a	0.589 ^a
UPDD weekly hives	202	0.260 ^a	0.735 ^a	0.644 ^a
UPDD UAS7	202	0.481 ^a	0.637 ^a	0.724 ^a
UPDD swelling	204	0.280 ^a	0.128	0.289 ^a
UPDD sleep	205	0.365 ^a	0.151 ^b	0.291 ^a
UPDD daily activities	205	0.425 ^a	0.178 ^b	0.291 ^a
DLQI overall	205	0.395 ^a	0.265 ^a	0.437 ^a
DLQI symptoms and feelings	205	0.496 ^a	0.353 ^a	0.549 ^a
DLQI daily activities	205	0.360 ^a	0.280 ^a	0.417 ^a
DLQI leisure	205	0.328 ^a	0.195 ^c	0.347 ^a
DLQI personal relationships	205	0.186 ^c	0.169 ^b	0.241 ^c
DLQI treatment	205	0.248 ^a	0.066	0.211 ^c
DLQI work and school	205	0.199	0.054	0.130
UCT total score	205	−0.545 ^a	−0.369 ^a	−0.585 ^a
ISI total score	205	0.452 ^a	0.142 ^b	0.384 ^a
WPAI absenteeism	162	0.272 ^a	0.070	0.244 ^c
WPAI presenteeism	163	0.409 ^a	0.196 ^b	0.407 ^a
WPAI work productivity loss	161	0.403 ^a	0.188 ^b	0.401 ^a
WPAI activity impairment	202	0.363 ^a	0.220 ^c	0.390 ^a
IC-UAS composite score	204	0.346 ^a	0.517 ^a	0.558 ^a
IC-UAS pruritus	205	0.503 ^a	0.180 ^b	0.435 ^a
IC-UAS hives	205	0.079	0.642 ^a	0.455 ^a

Abbreviations: DLQI, Dermatology Life Quality Index; IC-UAS, In-clinic Urticaria Activity Score; ISI, Insomnia Severity Index; U-AIM, Urticaria Activity and Impact Measure; UAS, Urticaria Activity Score; UCT, Urticaria Control Test; UPDD, Urticaria Patient Daily Diary; WPAI, Work Productivity and Activity Index.

^a*P* < .001.

^b*P* < .05.

^c*P* < .01.

correlated strongly with both the UPDD weekly hives score (range, 0.735–0.843) and the IC-UAS hives rating (range, 0.642–0.717). Finally, the UAS7 proxy scores correlated strongly with both the UPDD UAS7 score (range, 0.724–0.852) and the IC-UAS composite score (range, 0.558–0.781).

Known-Groups Validity

Significant differences between IC-UAS groups were found on all U-AIM scores at both baseline and week 24, with one exception (U-AIM itch severity at baseline for IC-UAS hives). Differences between groups were generally very large, providing strong support for the known-groups validity of the U-AIM scores. Patients who received a rating of 0 on the IC-UAS itch or hive ratings consistently had significantly lower (ie, less impairment) U-AIM scores than those receiving a rating of 1 or higher. Differences between those groups varied, depending on the IC-UAS measure and assessment point (data not shown).

Longitudinal Construct Validity of U-AIM Scores

U-AIM scores showed improvement at both week 12 and week 24. We observed strong correlations between changes in U-AIM scores and changes in UPDD weekly itch, weekly hives, and UAS7 scores (all correlations >0.55). Moderate correlations (all correlations >0.33) were also obtained between changes in U-AIM scores and changes in scores from the DLQI, including overall, symptoms

and feelings, and daily activities. These findings provide strong support for longitudinal construct validity of the U-AIM scores. The correlations between the U-AIM and collateral measures increased from baseline to week 24 as the variability in disease activity increased.

Longitudinal Known-Groups Validity of U-AIM Scores

Significant changes in U-AIM scores from baseline to week 24 by P-GIC and C-GIC groups were found on all U-AIM scores (all $P < .001$), with large differences between groups (all η^2 coefficients >0.30). However, few patients were rated as experiencing no change or worsening.

Responsiveness to Change

The pattern of results generally provides strong support for the responsiveness of the U-AIM scores. U-AIM score decreases (ie, improvements) were largest for patients rated as very much improved and progressively smaller for those rated as much improved, minimally improved, and no change (Table 5). For itch severity and number of hives, U-AIM scores decreased approximately 3 to 5 points for those very much improved, 2 to 3 points for those much improved, and 0 to 2 points for those minimally improved. Improvements in the UAS7 proxy were generally much larger but still followed the same pattern across P-GIC and C-GIC ratings.

Table 5
Responsiveness of U-AIM Scores From Baseline to Week 24

U-AIM score	Week 24 P-GIC/C-GIC group		No. of patients	SES	SRM	Responsiveness statistic
Itch severity	P-GIC rating	Very much improved	125	−3.79	−2.26	−3.05
		Much improved	25	−2.88	−1.71	−2.32
		Minimally improved	7	−1.25	−0.75	−1.01
		No change	5	0	0	0
		Minimally worse	0			
		Much worse	0			
No. of hives	P-GIC rating	Very much improved	125	−3.65	−2.37	−5.15
		Much improved	25	−2.79	−1.81	−3.94
		Minimally improved	7	−0.90	−0.59	−1.28
		No change	5	−0.32	−0.21	−0.45
		Minimally worse	0			
		Much worse	0			
UAS7 proxy	P-GIC rating	Very much improved	125	−32.55	−17.99	−37.38
		Much improved	25	−24.78	−13.72	−28.42
		Minimally improved	7	−9.38	−5.18	−10.78
		No change	5	−1.47	−0.84	−1.68
		Minimally worse	0			
		Much worse	0			
Itch severity	C-GIC rating	Very much improved	117	−4.04	−2.34	−2.98
		Much improved	29	−2.78	−1.61	−2.05
		Minimally improved	10	−1.43	−0.83	−1.06
		No change	7	−0.51	−0.30	−0.38
		Minimally worse	1	0	0	0
		Much worse	1	0	0	0
No. of hives	C-GIC rating	Very much improved	117	−3.73	−2.41	−2.99
		Much improved	29	−2.84	−1.84	−2.28
		Minimally improved	10	−1.11	−0.72	−0.89
		No change	7	−0.91	−0.59	−0.73
		Minimally worse	1	0	0	0
		Much worse	1	0	0	0
UAS7 proxy	C-GIC rating	Very much improved	117	−34.23	−18.48	−26.53
		Much improved	29	−24.85	−13.37	−19.25
		Minimally improved	10	−11.13	−6.02	−8.61
		No change	7	−6.37	−3.43	−4.97
		Minimally worse	1	0	0	0
		Much worse	1	0	0	0

Abbreviations: C-GIC, Clinician Global Impression of Change; P-GIC, Patient Global Impression of Change; SES, standardized effect size; SRM, standardized response mean; U-AIM, Urticaria Activity and Impact Measure; UAS, Urticaria Activity Score.

Table 6
Thresholds for Clinically Meaningful Change in U-AIM Scores

U-AIM score	Range
Itch severity	0.8–1.0
No. of Hives	0.8–1.0
UAS7 proxy	10.5–12.5

Abbreviations: U-AIM, Urticaria Activity and Impact Measure; UAS, Urticaria Activity Score.

Clinically Meaningful Change

The U-AIM itch and hives scores produced similar distribution-based estimates, with 1.0 SEM coefficients ranging from 0.430 to 0.720, 0.5 Cohen *d* values ranging from 0.283 to 0.517, and 0.50 Guyatt statistics ranging from 0.224 to 0.652. These results suggest a minimal detectable change (MDC) for the U-AIM itch and hives scores that can be reliably distinguished from random fluctuations of 0.5 to 0.7. A similar comparison of the distribution-based measures suggests that the MDC for the UAS7 proxy score that can be reliably distinguished from random fluctuations is in the range of 7.0 to 9.3.

Spearman correlations between changes in U-AIM scores and week 24 P-GIC/C-GIC ratings exceeded 0.30, and changes in U-AIM scale scores by global ratings of change demonstrated large differences between groups, with all η^2 coefficients greater than 0.30 (data not shown); these findings suggest that the global ratings are adequate anchors.

For the U-AIM itch and hives scores, the slopes for change in U-AIM scores range from 0.736 to 0.803. Thus, the amount of change in U-AIM score associated with a 1-unit improvement in global rating (calculated as the inverse of the slope) ranges from 1.25 to 1.36. For the UAS7 proxy score, the slopes for change in U-AIM scores range from 0.061 to 0.063. Thus, the amount of change associated with a 1-unit improvement in global rating range from 15.87 to 16.39.

To establish clinically meaningful change estimates, we began with the distribution-based estimates, which suggest an MDC of 0.5 to 0.7 for the U-AIM itch and hives scores and an MDC of 7.0 to 9.3 for the UAS7 proxy score. These MDC estimates provide the practical lower bound for establishing a meaningful change threshold. After considering both the anchor-based and distribution-based results and considering that changes among patients rated in the minimally improved range of –0.57 to –0.80, it is appropriate to establish the lower range of the meaningful change threshold at the upper limit of observed change among patients who are only minimally improved. Consequently, it is proposed that the range for establishing meaningful change in the U-AIM itch and hives scores be set at 0.8 to 1.0. Similar deduction suggests that the range for establishing meaningful change in the UAS7 proxy score be set at 10.5 to 12.5 (Table 6). Meaningful change estimates were previously established for UAS7 and range from 9.5 to 10.5.³⁶ Another study found the minimal important difference of the UAS7 and the UASTD to be 11 and 12, respectively.³⁷

Discussion

The U-AIM can help clinicians assess disease activity and effect in their patients with CSU (also known as CIU) during routine clinical practice. Unlike the UAS7 or UAS7TD, the U-AIM requires only one assessment, using patient recall during the previous 7 days. Furthermore, the U-AIM allows for an assessment of angioedema. Our evaluation of its psychometric properties suggests that it is valid for use in patients with CSU.

There was strong support for construct validity based on both cross-sectional and longitudinal analyses, including high levels of convergence with collateral measures (correlations increased from

baseline to week 24 as the variability in disease severity increased), excellent known-groups differentiation, and strong responsiveness. We established meaningful change thresholds as 0.8 to 1.0 for the U-AIM itch severity and number of hives scores and a range of 10.5 to 12.5 for the U-AIM UAS7 proxy score.

The U-AIM represents a practical, retrospective tool to assess disease activity and effect of CSU that does not require daily assessments. The U-AIM also provides a proxy score for the UAS7, although daily assessment and documentation of disease activity as part of the UAS7 allow patients to actively deal with their disease and detect triggering factors. The U-AIM is available on request from the corresponding author.

The strengths of this study include the large, diverse sample of patients, the variety of collateral measures used in the evaluation, and the use of both anchor- and distribution-based methods to estimate clinically meaningful change. However, the results should be considered in light of the study's limitations. To begin, the current sample of patients is not likely to be representative of all patients with urticaria, particularly those with milder disease. In addition, some patients may not experience symptoms during the 7 days before their physician visit. Several U-AIM items skewed negatively at baseline and positively at week 24, although this was most likely attributable to the initiation of omalizumab therapy as part of the trial. In addition, this study lacks an assessment of test-retest reliability. Even though the U-AIM was administered multiple times, the interval between test and retest was too long (2 weeks), and patients experienced a change in disease activity during that period, preventing an adequate assessment of test-retest reliability. Finally, most patients experienced improvements or no change in condition during the study. Therefore, we were unable to establish a meaningful change threshold for a worsening of CSU.

The psychometric properties of the U-AIM have been demonstrated, including construct validity, convergent validity, known-groups validity, responsiveness, and what constitutes a meaningful change. In the future, the test-retest reliability of the U-AIM should be evaluated in patients with CSU (also known as CIU).

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