

The Urticaria Activity Score—Validity, Reliability, and Responsiveness



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What is already known about this topic? The urticaria activity score (UAS) is an established instrument to measure the activity of chronic spontaneous urticaria. Two versions of this tool exist. For one of them, critical clinimetric data are still missing.

What does this article add to our knowledge? We show that both UAS tools have good clinimetric properties. We define the minimal important difference and the smallest detectable change for both instruments.

How does this study impact current management guidelines? The guideline-recommended version of the UAS with once-daily documentation of symptoms is valid, reliable, and sensitive to change. Validity, reliability and responsiveness of the UAS version that requires twice-daily documentation are confirmed.

BACKGROUND: Chronic spontaneous urticaria is characterized by fluctuating symptoms. Its activity is assessed with the urticaria activity score (UAS). Two versions of the urticaria activity score used for 7 consecutive days (UAS7) are available: (1) The guideline-recommended UAS7, with once-daily documentation, and (2) the UAS7_{TD}, with twice-daily documentation.

OBJECTIVE: To better characterize both UAS7 versions with regard to their validity, reliability, sensitivity to change, minimal important difference (MID), and smallest detectable change (SDC).

METHODS: One hundred thirty adult patients with chronic spontaneous urticaria completed both UAS7 versions, the

Patients Global Assessment (PatGA) of disease activity, the Urticaria Control Test (UCT), the Chronic Urticaria Quality of Life Questionnaire, and the Dermatology Life Quality Index before and after the initiation of omalizumab therapy. Physicians completed a Physician Global Assessment of disease activity.

RESULTS: The UAS7 and the UAS7_{TD} showed high correlation with the activity anchor PatGA ($r = 0.568$, $P < .001$ and $r = 0.605$, $P < .001$) and the UCT ($r = -0.580$, $P < .001$ and $r = -0.585$, $P < .001$). The wheal and pruritus scores of the UAS7 and the UAS7_{TD} exhibited respectable internal consistency and, in each UAS7 version, correlated well with each other (Cronbach $\alpha = 0.78$, $r = 0.640$, $P < .001$, and Cronbach $\alpha = 0.77$, $r = 0.626$, $P < .001$). Changes in the UAS7 and UAS7_{TD} correlated well with PatGA changes ($r = 0.639$, $P < .001$, and $r = 0.763$, $P < .001$) and with UCT changes ($r = -0.642$, $P < .001$, and $r = -0.703$, $P < .001$). The MID was 11 for the UAS7 (SDC = 12) and 12 for the UAS7_{TD} (SDC = 11).

CONCLUSIONS: The UAS7 and UAS7_{TD} show good and comparable clinimetric properties, including good sensitivity to change, and similar MIDs. © 2017 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2018;6:1185-90)

Key words: Disease activity; Chronic spontaneous urticaria; Chronic inducible urticaria; Urticaria Activity Score; Quality of life; Validity; Reliability; Reproducibility; Responsiveness; Minimal important difference; Smallest detectable change; Patient-reported outcome

Chronic spontaneous urticaria (CSU) is a highly prevalent disease¹ with a strong negative impact on patients' health-related quality of life (HRQOL).²⁻⁵ CSU is characterized by the recurrent formation of itchy hives, angioedema, or both for longer than 6 weeks.^{1,2} Individual hives usually do not persist for longer than 24 hours. Urticaria symptoms can fluctuate considerably on a daily basis. As of now, reliable diagnostic and activity markers

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Abbreviations used

CIndU- Chronic inducible urticaria
CSU- Chronic spontaneous urticaria
CU-Q2oL- Chronic Urticaria Quality of Life Questionnaire
DLQI- Dermatology Life Quality Index
HRQOL- Health-related quality of life
ICC- Intraclass correlation coefficient
MID- Minimal important difference
PatGA- Patient Global Assessment
PhyGA- Physician Global Assessment
ROC- Receiver operating characteristic
SDC- Smallest detectable change
SEM- Standard error of measurement
UAS- Urticaria activity score
UAS7- Urticaria activity score used for 7 consecutive days
UAS7_{TD}- UAS7 with twice-daily documentation
UCT- Urticaria Control Test

of CSU are missing.^{6,7} Therefore, urticaria activity can currently be measured only by the use of patient-reported outcome measures.

The urticaria activity score (UAS), used for 7 consecutive days (UAS7), is an established and widely accepted patient-reported outcome tool to prospectively measure CSU activity.⁸ It has been used in most clinical trials in CSU in the recent years as a main outcome parameter.⁹⁻¹¹ The UAS entails the assessment of the 2 key urticaria signs and symptoms wheals and itch. Two versions of this tool exist. These versions differ in 2 aspects: first, their categories of wheal numbers, and, second, their mode of documentation, once daily for the UAS7 and twice daily for the UAS7_{TD}.^{8,12} The international EAACI/GA²LEN/EDF/WAO guideline for urticaria recommends to use the former, the UAS7, in medical practice and in clinical trials.⁷ However, some critical data on the validity, reliability, and responsiveness of this patient-reported outcome measure are still missing.

The aim of this work was to better characterize and compare both available UAS7 versions and to determine their clinimetric properties, including validity, reliability, sensitivity to change, minimal important difference (MID), and smallest detectable change (SDC).

METHODS**Patient population**

We included 130 consecutive adult patients referred to the urticaria specialty outpatient clinics of the Department of Dermatology and Allergy of the Charité—Universitätsmedizin Berlin and the Department of Dermatology in Mainz. All patients had difficult-to-treat CSU (ie, they had not responded to increased doses of second-generation antihistamines) and were eligible for omalizumab therapy. Some of the patients, in addition to their CSU, had chronic inducible urticaria (CIndU), but it was not predominant. The study was approved by the local ethics committees.

Study design and outcome tools

All patients were intended to be treated with omalizumab. During the 2 weeks before the planned start of omalizumab therapy and the 4 weeks thereafter, patients were asked to prospectively document their disease activity by using both the UAS7 and the UAS7_{TD}.^{7,12} Patients who postponed their visit for omalizumab injection for no longer than 5 days were asked to continue to complete their UAS and UAS7_{TD}. In those

patients, the UASs from the first 2 weeks were used for reliability analyses, whereas the UASs obtained in the last 7 days preceding omalizumab injection were used for validity and responsiveness analyses, that is, to determine the sensitivity to change, the SDC, and the MID.

In addition, patients and physicians globally assessed urticaria activity independently with a 4-item Likert scale (none, mild, moderate, or severe). The Patients' Global Assessment (PatGA) of disease activity and the Physicians' Global Assessment (PhyGA) of disease activity, as well as the Urticaria Control Test (UCT), the Chronic Urticaria Quality of Life Questionnaire (CU-Q2oL), and the Dermatology Life Quality Index (DLQI), were administered twice: before the initiation of therapy with omalizumab and 4 weeks thereafter.¹³⁻¹⁵ In the 2 weeks before the first omalizumab administration, patients were asked to keep and not change their treatment.

Analysis of convergent validity

To determine the convergent validity of both UAS7 instruments, we correlated (Spearman correlation) their values with those of the above-mentioned anchors of disease activity (PatGA and PhyGA), disease control (UCT), and HRQOL (CU-Q2oL and DLQI). For these analyses, baseline data obtained before the initiation of omalizumab therapy were used. We hypothesized that the correlation coefficient should be highest for the correlation between the UAS7 and the conceptually closest related anchors for disease activity.

Reliability analyses

Correlations between baseline wheal and pruritus scores of each UAS7 version and Cronbach alpha coefficients were computed to characterize internal consistency reliability. Cronbach alpha above 0.7 was considered as respectable.¹⁴ To investigate test-retest reliability, the UAS7 values obtained during the first week of baseline documentation were compared with the values obtained in the subsequent week (the week before the first injection of omalizumab) by computing the intraclass correlation coefficient (ICC). A 2-way mixed-effect and absolute agreement model has been used.¹⁶ An ICC above 0.7 is considered to reflect excellent agreement.^{14,17}

Analysis of sensitivity to change

Sensitivity to change was analyzed by computing the correlation (Spearman correlation) of changes from baseline to 4 weeks after the start of treatment with omalizumab, between both UAS and anchor instruments.

Identification of the SDC

The SDC or the minimal detectable change, both of which are used interchangeably, is a measure of the variation in a scale due to measurement error.^{18,19} A change in the score that is bigger than the SDC is considered to reflect a real change and not just a measurement error. Different methods of calculation of the SDC exist, and we used 2 of them.¹⁹ According to the Bland and Altman method, the SDC, defined as a change beyond the limits of agreement, was calculated as $1.96 \times \text{SD of the UAS change between the first week and the second week of the baseline phase}$.^{20,21} Another method of calculation of the SDC is based on the standard error of measurement (SEM). According to this approach, the SDC is calculated by using the formula $1.96 \times \sqrt{2} \times \text{SEM}$ and the SEM is calculated by using the formula $\text{SD} \times \sqrt{(1 - \text{reliability coefficient})}$.^{19,22,23} Here also the longitudinal changes between the first week and the second week of the baseline phase were considered; therefore, the ICC as a test-retest reliability coefficient has been used.^{19,22,23}

TABLE I. Clinical characteristics of the patient population

Characteristic	Baseline (before omalizumab injection)	Follow-up (4 wk after omalizumab injection)	Change from baseline to follow-up
No. of patients	130	84	84
UAS7, mean $\pm$ SD, median	24.1 $\pm$ 10.3, 26 (n = 130)	11.3 $\pm$ 11.9, 7 (n = 84)	-13.7 $\pm$ 12.1, -14 (n = 84)
UAS7 _{TD} , mean $\pm$ SD, median	25.7 $\pm$ 10.7, 28 (n = 130)	11.6 $\pm$ 12.8, 6 (n = 84)	-15.5 $\pm$ 13.2, -14.5 (n = 84)
PatGA disease activity			
Missing	n = 7 (5.4%)	n = 4 (4.8%)	—
None	n = 2 (1.5%)	n = 29 (34.5%)	
Mild	n = 18 (13.8%)	n = 28 (33.3%)	
Moderate	n = 61 (46.9%)	n = 16 (19.0%)	
Severe	n = 42 (32.3%)	n = 7 (8.3%)	
PhyGA disease activity			
Missing	n = 0	n = 0	—
None	n = 2 (1.5%)	n = 32 (38.1%)	
Mild	n = 4 (3.1%)	n = 25 (29.7%)	
Moderate	n = 36 (27.7%)	n = 14 (16.7%)	
Severe	n = 88 (67.7%)	n = 13 (15.5%)	
UCT score, ¹⁴ mean $\pm$ SD, median	4.8 $\pm$ 3.3, 4.5 (n = 122)	11.1 $\pm$ 4.1, 12 (n = 81)	6.4 $\pm$ 4.2, 6 (n = 79)
CU-Q2oL total score, ¹³ mean $\pm$ SD, median	52.8 $\pm$ 18.5, 53.3 (n = 108)	25.5 $\pm$ 18.7, 23.9 (n = 66)	-26.5 $\pm$ 19.9, -23.9 (n = 59)
DLQI score, ¹⁵ mean $\pm$ SD, median	13.1 $\pm$ 6.9, 12 (n = 123)	5.2 $\pm$ 5.6, 3.5 (n = 80)	-7.6 $\pm$ 6.4, -7 (n = 78)

TABLE II. Nonparametric correlations of the UAS7 and UAS7_{TD} with measures of disease activity, disease control, and HRQOL impairment

UAS	PatGA disease activity	PhyGA disease activity	UCT score	CU-Q2oL total score	DLQI score
UAS7	0.568* (n = 123)	0.459* (n = 130)	-0.580* (n = 122)	0.321† (n = 108)	0.416* (n = 123)
UAS7 _{TD}	0.605* (n = 123)	0.492* (n = 130)	-0.585* (n = 122)	0.362* (n = 108)	0.422* (n = 123)

* $P < .001$.

† $P < .01$.

Characterization of the MID

The MID is the smallest change that can be considered to be clinically relevant. Two anchor-based approaches to determine the MID were applied: the “mean change” method and a receiver operating characteristic (ROC)-curve analysis.^{24,25} The PatGA was used as an anchor. For the “mean change” method, we used the mean change in UAS in patients who reported a 1-step change in PatGA activity ratings between baseline and follow-up (4 weeks after the first omalizumab administration). For the ROC-curve approach, patients were dichotomized, on the basis of results of PatGA, into those who improved under the therapy (defined as at least 1-step improvement) and those who did not improve (defined by an unchanged or worsened PatGA). An alternative, distributional-criterion approach was also applied, by dividing the baseline UAS7 SD by 2.²⁶ In the performed analyses, P value of .05 or less was considered as statistically significant.

RESULTS

Patient population

The 130 antihistamine-refractory patients with CSU included in this analysis had a mean age of 44.6 ± 16.2 years, and most (73%) was women. The clinical characteristics of the patient population are presented in Table I.

Both UAS show good convergent validity

Both the UAS7 and the UAS7_{TD} correlated well with anchors for disease activity, disease control, and HRQOL impairment.

Accordingly, both tools exhibited good levels of convergent validity. As hypothesized, the correlations of the UAS7 and UAS7_{TD} were highest with the PatGA disease activity (Table II). Notably, the correlations with the UCT were comparably high.

Both UAS show respectable internal consistency and excellent test-retest reliability

The wheal scores and pruritus scores of the UAS7 ($r = 0.640$; $P < .001$) and of the UAS7_{TD} ($r = 0.626$; $P < .001$) correlated well with each other. Cronbach alpha coefficient was found to be 0.78 and 0.77 for the UAS7 and UAS7_{TD}, respectively, indicating a respectable internal consistency of both measures.

The mean UAS7 values of the first week and the second week of the baseline phase were 25.3 ± 10.4 (median, 25) points and 24.7 ± 10.3 (median, 26) points, respectively. The mean UAS7_{TD} values of the first week and the second week of the baseline phase were 27.0 ± 10.2 (median, 28.5) points and 26.7 ± 10.6 (median, 28) points, respectively. The ICC was 0.91 (95% CI, 0.86-0.94) for the UAS7 and 0.93 (95% CI, 0.89-0.95) for the UAS7_{TD}, indicating excellent test-retest reliability for both measures.

Both UASs are sensitive to change

Changes in the UAS7 and UAS7_{TD} correlated well with anchors for changes in disease activity, disease control, and HRQOL impairment. The correlations of the UAS7 and

TABLE III. Nonparametric correlations of changes in the UAS7 and UAS7_{TD} with changes in disease activity, disease control, and HRQOL impairment

Change	PatGA disease activity change	PhyGA disease activity change	UCT score change	CU-Q ₂ oL total score change	DLQI score change
UAS7 change	0.639* (n = 78)	0.653* (n = 84)	−0.642* (n = 79)	0.612* (n = 59)	0.460* (n = 78)
UAS7 _{TD} change	0.763* (n = 78)	0.758* (n = 84)	−0.703* (n = 79)	0.643* (n = 59)	0.533* (n = 78)

**P* < .001.

UAS7_{TD} changes were highest with changes in the PatGA disease activity and UCT scores (Table III).

The MID is similar for the UAS7 and the UAS7_{TD}

UAS7 and UAS7_{TD} values decreased with improved PatGA disease activity. The correlation of the UAS7 and UAS7_{TD} changes with changes in the PatGA disease activity was $r > 0.5$ for both (Table III), indicating that PatGA disease activity is a suitable anchor for the computation of the MID of the UAS7 and the UAS7_{TD}.

The mean UAS7 and UAS7_{TD} change for the smallest possible improvement in PatGA disease activity (improvements by 1 step on the Likert scale rating, eg, from “moderate” to “mild”) was a decrease by 13.0 ± 8.5 (median, 15) points and by 13.5 ± 9.3 (median, 12.5) points, respectively. In contrast, the mean UAS7 and UAS7_{TD} decreased by only 4.7 ± 8.3 (median, 3.5) points and 4.6 ± 6.8 (median, 3.25) points, respectively, when the PatGA disease activity rating did not change. Accordingly, the mean change method suggests an MID of 13 points for the UAS7 and of 13.5 points for the UAS7_{TD}.

A second anchor-based method, an ROC-curve analysis, showed cutoff points of 11 points for the UAS7 (Figure 1; see Table E1 in this article's Online Repository at www.jaci-inpractice.org) and of 12 points for the UAS7_{TD} (Figure 2; see Table E2 in this article's Online Repository at www.jaci-inpractice.org), to have the best balance of sensitivity and specificity for a meaningful (true) improvement in disease activity. At these cutoff points, the sum of the proportion of patients misclassified as disease activity “improved” or “not improved” was lowest. Accordingly, the ROC-curve analysis suggests an MID of 11 points for the UAS7 and of 12 points for the UAS7_{TD}.

The indirect distributional-criterion approach suggests an MID of 5.2 (5 points) points for the UAS7 and of 5.4 points for the UAS7_{TD}, which are the SDs of the UAS7 and UAS7_{TD} baseline scores (10.3 and 10.7) divided by 2.

The SDC is similar for the UAS7 and the UAS7_{TD}

The mean UAS7 and UAS7_{TD} difference between the first week and the second week of the baseline phase was 0.3 ± 6.0 and 0.1 ± 5.3 points, respectively. According to the Bland and Altman method, the SDC of the UAS7 was 11.8 points and the SDC of the UAS7_{TD} was 10.5 points. According to the SEM-based method, the SDC was 5.0 points for the UAS7 and 4.1 points for the UAS7_{TD}.

DISCUSSION

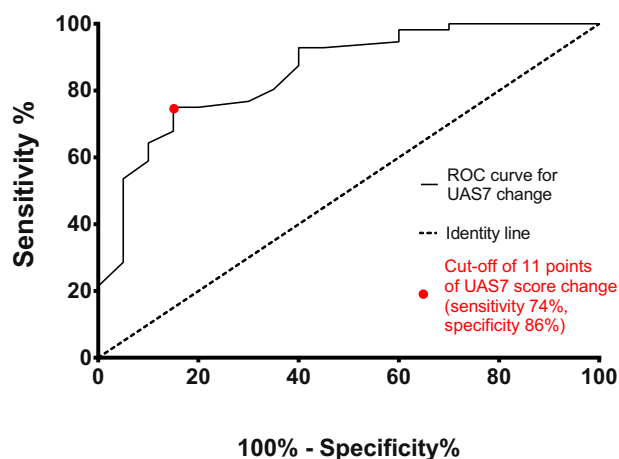
The results of our study provide evidence that both available variants of the UAS are appropriate and valid tools to measure disease activity in patients with CSU.

The UAS7 and the UAS7_{TD} showed good levels of convergent validity, correlating moderately to strongly with other measures of disease activity and control. Previously, an even stronger

correlation between the UCT and the UAS7 was reported ($r = -0.750$).¹⁴ This may be explained by the fact that in the UCT validation study of Weller et al,¹⁴ the UAS was recorded over 28 days to cover the whole 4-week recall period of the UCT, whereas in this study, only 1-week UAS documentation was used. The correlation between UAS7 and HRQOL instruments was only moderate. This is in line with previous studies²⁷⁻³⁰ and suggests that factors other than disease activity may influence HRQOL, as has already been shown for psychiatric comorbidities in CSU³¹ and for psychosocial variables in other chronic skin diseases, for example, psoriasis.³²⁻³⁴

The internal consistency reliability of both UAS instruments is supported by the Cronbach alpha coefficient exceeding 0.7. Test-retest reliability analyses were performed using UASs of the first 2 subsequent weeks of the baseline phase to minimize the influence of a possible fluctuation in CSU activity over a longer period. Both UAS versions showed excellent test-retest reliability, the UAS7 with an ICC of 0.91 and the UAS7_{TD} with an ICC of 0.93. These values are higher than the ICC of 0.659 previously reported for the UAS7_{TD}.¹² The differences between the ICCs obtained in both studies may be explained by differences between the examined patient populations.¹² It is possible that CSU in our patients was more stable during the observation period of 2 weeks.

The UAS is used both in routine patient care and in clinical trials to determine disease activity and response to treatment.⁷ Therefore, it is important to assess its responsiveness and MID.³⁵ We found that changes in response to treatment for both instruments, the UAS7 and the UAS7_{TD}, showed strong and comparable correlations with changes in disease activity assessed

**FIGURE 1.** ROC curve. Area under the ROC curve for change in UAS7 from baseline to follow-up: 0.85 (95% CI, 0.76-0.95).

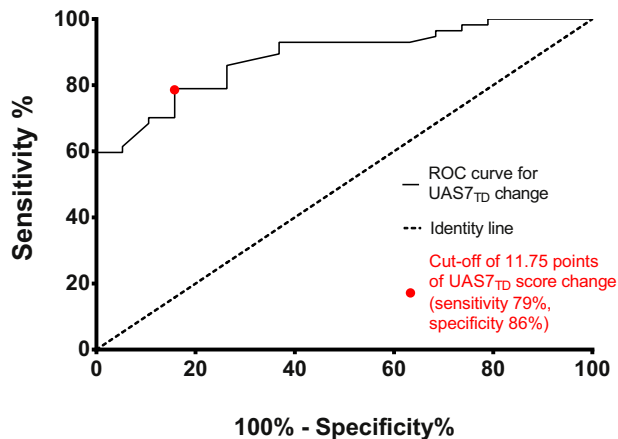


FIGURE 2. ROC curve. Area under the ROC curve for change in UAS7_{TD} from baseline to follow-up: 0.89 (95% CI, 0.81-0.96).

by patients and with disease control (UCT scores) as well as moderate to strong correlations with HRQOL measures (CU-Q2oL and DLQI scores). Thus, both UAS versions are responsive to changes in disease activity and comparable in their sensitivity to change.

The SDC was found to be 12 points for the UAS7 and 11 points for the UAS7_{TD} according to the Bland and Altman method, and 5.0 points for the UAS7 and 4.1 points for the UAS7_{TD} according to the SEM-based method. This implies that changes in urticaria activity that exceed these values may be considered with 95% of confidence to be real rather than due to a measurement error.

To determine which changes are actually important for patients, MID values were calculated using several methods. The lowest MID values were obtained using a distributional-criterion approach. This approach, however, does not take into account changes in disease activity; thus, anchor-based methods are preferred.³⁵ We applied 2 anchor-based approaches to determine the MID, the “mean change” method and the ROC-curve analysis. The “mean change” method yielded higher values as compared with the ROC-curve analysis. We recommend the use of the MID obtained from the ROC-curve analysis rather than from the “mean change” method, because the first approach also includes patients whose urticaria activity did not improve during the observation period. The MID value of 12 points for the UAS7_{TD}, obtained by using the ROC-curve analysis, exceeds the measurement error (SDC) of 11 obtained using the method of Bland and Altman.^{20,21} Thus, changes in the UAS7_{TD} between 11 and 12 points should be interpreted as real but not important to the patients. In contrast, the MID value of 11 points for the UAS7, obtained from the ROC-curve analysis, lies below its SDC value of 12. Thus, changes in the UAS7 above 12 points should be interpreted as real and important to the patients. The SDC values based on the SEM were lower than the MIDs for both the UAS7 and the UAS7_{TD}. The SEM-related SDC value of 4.1 for the UAS7_{TD} was similar to the values 3.5 to 4.0 obtained by Mathias et al¹² using the same method.¹² Our study, for the first time, delivers evidence for the MID of the UAS7. Our results obtained for the UAS7_{TD} are slightly higher than the MID range of 9.5 to 10.5 recommended by Mathias et al.¹²

Our study has several limitations, which should be mentioned. (1) The recruited patients may not be fully representative of the overall population of patients with CSU because all of them were German, refractory to antihistamine treatment, and were treated in a specialized, tertiary reference center of a university hospital. (2) Changes in disease activity were observed only in response to one type of treatment, and only few patients worsened under therapy, which prevented a reliable estimation of the MID for worsening of the symptoms. (3) Patients with CIndU were not excluded from the study as long as CSU was predominant because we aimed to test UAS validity under real-life conditions. As much as 36% of patients with CSU were recently reported to have comorbid CIndU.³⁶ In this group, activity of inducible urticaria may influence the UAS, because it may be difficult for the patients to differentiate to what extent their symptoms are due to CSU and to what extent due to CIndU. However, we believe, that in these patients, the UAS7 is still the best tool to measure disease activity. In contrast, if symptoms of physical urticaria prevail, monitoring of its activity should be in the first line on the basis of available physical testing. (4) A considerable dropout rate between the first visit and the second visit was observed, which resulted in a lower number of patients included in the analyses of sensitivity to change, SDC and MID, only.

This study provides, for the first time, validation data for the UAS7 and confirms as well as extends the previous US validation data for the UAS7_{TD} in German patients with CSU. Because of the very simple linguistic structure of the UAS and its straightforward questions, no significant cross-linguistic and cross-cultural differences are to be expected in different populations. It cannot be excluded, however, that the disease activity of the patients in the setting of this study (tertiary care) is higher as compared with other patient groups treated in a primary or secondary care setting. This may have an effect on the UAS values but rather not on the results of the UAS validity and reliability. Therefore, we believe that the results of this study can be applied to different populations and generalized, even though it was performed in a relatively homogenous population.

In conclusion, our results show good and comparable clinimetric properties of both instruments, including good levels of validity, reliability, and sensitivity to change, with a recommendable MID and an SDC of 12 and 11 for the UAS7_{TD} and of 11 and 12 for the UAS7, respectively.

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TABLE E1. Performance of UAS7 changes at various cutoff values in screening for patients with an “improved” or “not improved*” disease activity

Cutoff value* (UAS7 change)	Truly “improved”	Truly “not improved”	Sum of % misclassified†
	Sensitivity	Specificity	
≤ -14	63%	90%	46%
≤ -13	67%	86%	48%
≤ -12	72%	86%	42%
≤ -11	74%	86%	41%
≤ -10	74%	81%	45%
≤ -9	75%	71%	53%
≤ -8	79%	67%	54%
≤ -7	86%	62%	52%
≤ -6	88%	62%	50%
≤ -5	91%	62%	47%
≤ -4	91%	57%	52%
≤ -2	93%	43%	64%
≤ 0	95%	38%	67%

Bold indicates minimal important difference value, according to the ROC curve analysis.

*For this analysis of cutoff values, change in disease activity was categorized into “improved” (rating of disease activity was improved by at least 1 category from baseline to follow-up, eg, from “moderate” to “mild”) or “not improved” (rating of disease activity was unchanged or even worse at follow-up).

†Sum of misclassified = (100% – sensitivity%) + (100% – specificity%).

TABLE E2. Performance of UAS7_{TD} changes at various cutoff values in screening for patients with an “improved” or “not improved*” disease activity

Cutoff value* (UAS7 _{TD} change)	Truly “improved”	Truly “not improved”	Sum of % misclassified†
	Sensitivity	Specificity	
≤ -13.75	70%	90%	39%
≤ -13.00	70%	86%	44%
≤ -12.25	72%	86%	42%
≤ -11.75	79%	86%	35%
≤ -11.25	79%	81%	40%
≤ -10.50	79%	76%	45%
≤ -9.75	81%	76%	43%
≤ -9.00	82%	76%	41%
≤ -8.00	84%	76%	40%
≤ -7.25	86%	76%	38%
≤ -6.75	88%	71%	41%
≤ -5.25	89%	67%	44%
≤ -3.75	93%	67%	40%
≤ -3.25	93%	57%	50%
≤ -2.75	93%	48%	59%
≤ -2.00	93%	43%	64%
≤ -0.75	95%	38%	67%
≤ 0.50	95%	29%	77%

Bold indicates minimal important difference value, according to the ROC curve analysis.

*For this analysis of cutoff values, change in disease activity was categorized into “improved” (rating of disease activity was improved by at least 1 category from baseline to follow-up, eg, from “moderate” to “mild”) or “not improved” (rating of disease activity was unchanged or even worse at follow-up).

†Sum of misclassified = (100% – sensitivity%) + (100% – specificity%).

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