

## INVESTIGATIVE REPORT

**Itch Severity and Quality of Life in Patients with Pruritus: Preliminary Validity of a Danish Adaptation of the Itch Severity Scale**Robert ZACHARIAE<sup>1</sup>, Ulrikke LEI<sup>2</sup>, Merete HAEDERSDAL<sup>3</sup> and Claus ZACHARIAE<sup>2</sup><sup>1</sup>Psychooncology, Aarhus University Hospital, Aarhus, Departments of Dermatology, <sup>2</sup>Copenhagen University Hospital Gentofte, and <sup>3</sup>Copenhagen University Hospital Bispebjerg, Copenhagen, Denmark

**The aim of this study was to examine the validity of a Danish adaptation of the Itch Severity Scale (ISS) by exploring the associations between pruritus severity, psychological symptoms, and quality of life in a consecutively recruited sample of 20 patients with atopic dermatitis, 20 with psoriasis, 20 with urticaria, 12 with genital pruritus, 11 with nephrogenic pruritus, and 20 controls with vascular malformations. Convergent and discriminative validity was explored by analysing the associations of the ISS total score and the individual ISS component scores with age, sex, diagnosis, disease severity, sleep quality, depressive symptoms, anxiety, non-specific somatic symptoms, and pruritus-related quality of life impairment. Patients with urticaria reported significantly ( $p < 0.05$ ) greater pruritus severity scores than the remaining patient groups, and pruritus severity was significantly associated with impaired sleep quality, more depressive symptoms, higher levels of anxiety, more non-specific somatic symptoms, and impaired quality of life. The results also confirmed the multidimensional nature of pruritus, with the affective dimension of pruritus being a better predictor of depressive symptoms, anxiety, and quality of life impairment than the sensory dimension. Finally, our results confirmed previous findings that the associations between pruritus severity and depressive symptoms and somatic symptoms were partly mediated by the effect of pruritus on sleep quality. *Key words: pruritus; quality of life; depression; anxiety; sleep impairment.***

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Pruritus is a common symptom in dermatological diseases such as atopic dermatitis, psoriasis, and urticaria (1, 2), and is associated with a number of systemic diseases, e.g. systemic nephrogenic fibrosis (3). Pruritus can be a very unpleasant symptom and has been associated with considerable reduction in health-related quality of life (QoL) (1). Psychiatric comorbidity, e.g. depression, in patients with chronic pruritus is common,

and psychosomatic factors and psychiatric comorbidity may have an impact on both the perception of pruritus, coping with pruritus, and on scratching behaviour (4, 5). So far, most studies have provided information only on the intensity of the sensation of itch, and data are lacking on the quality of the sensation (6), how it is experienced by the patients, and the effects on daily life. The reason for this may, until recently, have been the general lack of standardized instruments to assess pruritus severity.

The sensations of itch and pain have a lot in common, and there appears to be a considerable overlap between pain- and itch-related peripheral mediators and receptors (7). Based on a list of sensory and affective descriptors taken from the McGill Pain Questionnaire (8), Yosipovitch et al. (6) therefore developed a pruritus severity questionnaire that measured both the sensory and affective dimensions of pruritus. This instrument has so far been validated in uraemic, atopic dermatitis (9), and psoriasis patients (10). However, this instrument was designed to be administered by an interviewer, which is a considerable practical limitation, and does not assess the patient burden associated with pruritus severity. Majeski et al. (11) therefore further developed the instrument into the Itch Severity Scale (ISS), a practical questionnaire to quantify pruritus severity and the associated patient burden. Based on our previous Danish adaptation of the original instrument constructed by Yosipovitch et al. (10), we aimed at developing a Danish version of the ISS and to examine aspects of its construct, convergent, discriminant, and discriminative validity by exploring the associations between the different dimensions of pruritus and psychological symptoms and impairment of QoL in patients with pruritus with dermatological and systemic disease and patients with vascular malformations without pruritus. Pruritus is known to be associated with impaired sleep quality (1), and psychological symptoms, such as negative mood (12) and depression (13), have been linked to sleep disturbances. To further explore the validity of the ISS, we also attempted to replicate our previous findings of sleep impairment as an important mediator of the association between pruritus severity and psychological symptoms (10), but not between pruritus severity and impairment of QoL.

## METHODS

### Patients

A total of 103 patients attending the outpatient dermatology clinic at the University Hospital of Copenhagen in Gentofte or Bispebjerg and the nephrology department at the University Hospital of Copenhagen at Rigshospitalet between March 2007 and March 2008 were invited to participate in the study. Recruitment continued until we had a sample of 20 patients with each of the diagnoses of psoriasis, atopic dermatitis, and chronic urticaria, as well as 12 patients with chronic genital pruritus and 11 patients with pruritus related to chronic renal failure. Twenty patients with non-itching vascular malformations (e.g. birthmarks) served as controls. All patients approached agreed to participate, and the study was conducted in accordance with the requirements of the local ethics committee.

### Measures

**Itch.** The Itch Severity Scale (ISS) (11) is a modified version of an instrument developed by Yosipovitch et al. (6), which has previously been translated into Danish and subjected to a preliminary validation (10). The ISS consists of 24 individual items forming 7 components: frequency, itch description, affected body surface area, intensity, effect on sleep, effect on mood, and effect on sexual desire/function. A standardized score for each component is calculated by dividing the actual score of each component with the maximum score of this component, yielding scores ranging from 0.0 to 1.0. The total ISS score is obtained by adding the scores and multiplying by 3, yielding total scores ranging from 0 to 21. The translation was conducted following the recommendations for cultural adaptation of questionnaires and other instruments (14). Two independent translations into Danish of the English items were discussed and a preliminary version was agreed upon. This version was back-translated, and a final version was prepared, taking any discrepancies between the two versions into consideration. No major translational issues emerged. For more details concerning the individual items and the development of the individual components, see (11).

**Depressive symptoms.** Depressive symptoms were assessed with the 13-item version of Beck Depression Inventory (BDI-13) (15, 16). The full 21-item has been used previously with Danish dermatology patients and healthy matched controls (17), and the BDI-13 version has been used in a previous sample of psoriasis patients with pruritus (10). Internal consistency (Cronbach's alpha) of the BDI-13 was 0.90 in the sample of psoriasis patients with pruritus and 0.88 in the present sample. Total scores range from 0 to 39. A cut-off of 9 has shown both high sensitivity (98.6%) and specificity (94.6%) for identifying participants characterized as having moderate-severe depressive symptoms on the full 21-item BDI (18).

**Anxiety and non-specific somatic symptoms.** Symptoms such as pain, nausea, numbness, and dizziness, were assessed with the Anxiety and Somatization subscales of the 18-item Brief Symptom Inventory (BSI-18) (19). The two subscales have previously been found to have acceptable internal consistencies in a sample of dermatology patients (0.79 and 0.81) (17) and in a previous sample of psoriasis patients with pruritus (0.81 and 0.87). The internal consistencies in the present sample were 0.80 and 0.77. The total score for each subscale ranges from 0 to 24.

**Quality of life.** A modified version of the Dermatology Life Quality Index (DLQI) (20, 21) was used to measure impairment of pruritus-related QoL. Items 1, 2, and 10, which referred either directly to pain or itch, embarrassment, or problems re-

lated to the treatment of the skin condition, were excluded, and the remaining items, e.g. influence on work, social activities, physical activities etc., were rephrased to refer to difficulties due to pruritus. The total pruritus-related QoL impairment score ranges from 0 to 21. The modified version had acceptable internal consistency (Cronbach's alpha: 0.85) in a previous sample of psoriasis patients with pruritus (10) and 0.81 in the present sample.

**Sleep quality.** This was assessed with three modified items from the Pittsburg Sleep Quality Index (PSQI) (22), asking patients to rate the past week with respect to: (i) how much their pruritus had made it difficult to sleep; (ii) how well they had generally slept (reversely scored); and (iii) their use of sleep medication. Total scores range from 0 to 9. The patients were also asked to estimate their average number of hours of sleep per night during the past week. The PSQI has been used previously in a sample of healthy elderly Danes (12).

**Disease severity.** This was assessed by a dermatologist with the Psoriasis Area and Severity Index (PASI) for psoriasis patients (23), and the SCORAD (SCORing Atopic Dermatitis) for patients with atopic dermatitis (24).

**Other.** Additional questions included age, pruritus duration, comorbidity, and general self-reported health rated on a scale from 1 (poor) to 5 (excellent).

### Analytical strategy

Internal consistency was analysed by calculating Cronbach's alpha. **Discriminative** validity was assessed by exploring whether ISS scores could discriminate between pruritus patient groups and controls. **Construct (convergent) validity** was explored by investigating associations between pruritus severity and a number of outcomes expected to be associated with pruritus severity, including sleep quality impairment, depressive symptoms, anxiety, non-specific somatic symptoms, and pruritus-related QoL impairment. Furthermore, based on previous results (10), we expected sleep quality to partially mediate the association between pruritus severity and depressive symptoms, anxiety, and somatic symptoms (**construct validity**), but not the association between pruritus severity and QoL impairment (**discriminant validity**). To explore the possible underlying dimensions of the descriptors (ISS component 2), a principal component analysis was conducted (**construct validity**).

### Statistical analysis

Between-diagnosis group comparisons of categorical and ordinal variables were conducted with  $\chi^2$  and Kruskal-Wallis non-parametric tests, while between-diagnosis group comparisons of continuous variables were conducted with univariate analyses of variance (ANOVAs) and Scheffe *post-hoc* tests. Non-normally distributed variables were log-transformed prior to analysis with parametric statistics. Parametric and non-parametric correlations were calculated between continuous and ordinal variables as appropriate. The associations of pruritus severity with depressive symptoms, anxiety, somatic symptoms, and pruritus-related QoL impairment were analysed with multiple, hierarchical linear regression analyses, adjusting for any variables shown to correlate with either the dependent variables or pruritus severity. Logistic regression was used to test the associations between pruritus and the risk of being classified as having moderate-severe depressive symptoms. Finally, the possible mediating effects of sleep quality on these associations were explored using the methods described by Baron & Kenny (25). The Sobel bootstrap test (with 10,000 re-samples) was used as a direct test of mediation (26, 27).

## RESULTS

## Scale characteristics

In the total sample of patients, the mean total ISS score was 9.7 (standard deviation (SD) 3.9), while the mean score in controls was 0.2 (SD 0.5). The mean standardized scores of the individual components in the patient group ranged from 0.41 (Effect on sleep) to 0.60 (Frequency). An average of 10.1% missing responses per item was found in the sample as a whole, with most missing responses found for the item “effect on sexual desire” (16.2%). In the patient group, the average percent missing items was 4.9%. ISS-total scores were normally distributed, and the internal consistency of the total scale, based on the standardized scores of the seven components, was high for the sample as a whole (Cronbach’s alpha 0.88). The ISS component to ISS-total correlations ranged from 0.78 (component 1: Frequency) to 0.55 (component 3: Area). The six items of component 2 (Descriptors) were analysed with a Principal Components Analysis with Varimax rotation. The rotation converged in three iterations and the results suggested two independent sub-components, a sensory pruritus component including the descriptors of “stinging”, “stabbing”, and “burning” (factors loadings 0.68–0.86) and an affective pruritus component, which included the descriptors of “annoying”, “unbearable”, and “worrisome” (factor loadings of 0.78–0.92). While the majority of descriptors showed differences in loadings on the two factors of 0.30 or more, “burning” only showed a difference of 0.15. On theoretical grounds it was decided to include this descriptor in the sensory dimension, for which it showed the highest factor loading (0.68).

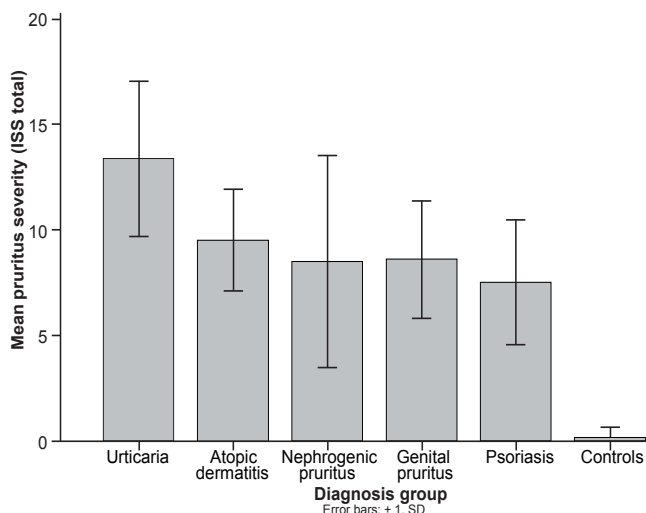


Fig. 1. Mean Itch Severity Scale (ISS) scores of pruritus patients ( $n=83$ ) and controls ( $n=20$ ).

## Group comparisons

Results of group comparisons are shown in Fig. 1 and Tables I and II. Urticaria patients experienced greater pruritus severity (ISS-total) than all other patient groups, which in turn reported greater severity than controls. With a few exceptions, urticaria patients also generally experienced greater impairment of sleep, more depressive symptoms, higher levels of anxiety, and more non-specific somatic symptoms than other patients. Female pruritus patients had significantly higher ISS-total scores (mean 10.9; SD 3.6) than male patients (7.9; SD 3.6) ( $t=3.7$ ;  $p=0.001$ ). When including controls, the difference between women and men did not reach statistical significance (8.1; SD 5.7 vs. 7.2; SD 4.1;  $p=0.40$ ). As an indicator of the magnitude of the differences found, the effect size correlations (ESr) (28) are presented in Tables I and II for each of the comparisons.

The mean scores of each patient group were then compared for each of the seven ISS components, the total ISS score, and the calculated standardized scores (0.0–1.0) of the sensory and affective sub-components. As seen in Table II, there were significant group differences for all of the seven original components except component 1 (Frequency), with *post-hoc* tests generally showing urticaria patients to have higher scores than the remaining groups. Significant group differences were also found for the affective subcomponent, again with urticaria patients showing the largest scores. The sensory component, however, did not differ between pruritus patient groups.

## Bivariate associations

Several statistically significant ( $p<0.05$ ) correlations were found between ISS total scores and scores on the individual ISS components and the remaining variables investigated (data not shown). Self-reported health and hours of sleep were all negatively correlated with ISS total and ISS component scores ( $r: -0.31$  to  $-0.53$ ), while PSQI difficulties falling asleep and sleep quality impairment, depressive symptoms, anxiety, somatic symptoms, and pruritus-related QoL impairment were positively associated with ISS scores ( $r: 0.23$ – $0.64$ ). Generally, there were no significant associations with age and pruritus duration. When correlating ISS-total scores with disease severity (PASI or SCORAD), the correlation reached statistical significance for psoriasis patients ( $r=0.51$ ;  $p<0.05$ ) but not for atopic dermatitis patients ( $r=0.24$ ;  $p=0.30$ ). Women had significantly higher levels of depressive symptoms, anxiety, somatic symptoms, and impaired pruritus-related QoL than men ( $t$ -tests:  $p=0.018$ – $0.046$ ).

Table I. Sample characteristics, pruritus severity, sleep quality, depressive symptoms, anxiety, somatic symptoms, and pruritus-related quality of life (QoL) impairment

	Atopic dermatitis n=20	Psoriasis n=20	Urticaria n=20	Genital pruritus n=12	Nephrogenic pruritus n=11	Control n=20s	Statistics	p	ESr
Sex, % female	60	35	68	67	55	80	$\chi^2=9.5$	0.09	0.30
Age, years, mean (SD)	31.4 (12.7)	51.6 (17.0)	44.5 (17.0)	48.8 (12.5)	60.2 (20.6)	41.2 (15.0)	F(5,101)=6.0	<b>0.001</b>	0.49
Disease severity, mean (SD)	40.4 (13.1)	13.0 (10.7)	-	-	-	-	-	-	-
	SCORAD		PASI						
Pruritus duration (months), mean (SD)	351 (183)	180 (134)	47 (69)	71 (73)	182 (198)	42.6 (108.2)	F(5,92)=15.9	<b>0.001</b>	0.69
Comorbidity, %	55	42	42	40	100	20	$\chi^2=19.3$	<b>0.002</b>	0.43
General self-reported health (1-5), median (range) <sup>a</sup>	3 (1-5)	3 (1-5)	4 (1-5)	4 (2-5)	3 (2-4)	4 (3-5)	$\chi^2=24.1$	<b>0.001</b>	0.48
Pruritus severity (ISS total score, mean (SD)) <sup>b</sup>	9.5 (2.4)	7.5 (2.9)	13.4 (3.7)	8.6 (2.8)	8.5 (5.0)	0.2 (0.5)	F(5,102)=41.5	<b>0.001</b>	0.83
							F(5,91)=47.0*	<b>0.001</b>	
PSQI Hours of sleep/night, mean (SD)	7.0 (1.4)	6.3 (1.0)	5.6 (1.6)	7.1 (1.2)	5.6 (1.5)	6.9 (1.3)	F(5,96)=4.1	<b>0.002</b>	0.43
PSQI Difficulties falling asleep (0-3), median (range) <sup>c</sup>	2 (0-3)	2 (0-3)	3 (0-3)	2 (0-3)	2 (0-3)	0.5 (0-3)	$\chi^2=9.3$	0.10	0.30
PSQI General sleep quality (0-3), median (range) <sup>d</sup>	1 (0-3)	1 (0-3)	2 (0-3)	1 (0-3)	2 (0-2)	1 (0-2)	$\chi^2=15.9$	<b>0.007</b>	0.39
PSQI Sleep medication (0-3), median (range) <sup>e</sup>	0 (0-1)	0 (0-3)	0 (0-3)	0 (0-0)	3 (0-3)	0 (0-2)	$\chi^2=20.8$	<b>0.001</b>	0.45
Depressive symptoms (BDI-13), mean (SD) <sup>f</sup>	6.5 (5.2)	9.0 (6.3)	10.3 (6.6)	5.3 (5.5)	7.5 (6.5)	1.0 (1.6)	F(5,100)=8.7	<b>0.001</b>	0.56
Moderate-severe depression (BDI-13), % <sup>f</sup>	30	45	65	25	46	0	$\chi^2=19.6$	<b>0.001</b>	0.44
Anxiety (BSI-18 subscale), mean (SD) <sup>g</sup>	3.9 (2.7)	3.6 (4.8)	5.3 (5.0)	3.3 (3.7)	2.2 (2.6)	1.1 (1.6)	F(5,100)=2.7	<b>0.02</b>	0.36
Somatic symptoms (BSI-18 subscale), mean (SD) <sup>g</sup>	4.4 (3.8)	4.9 (5.2)	5.7 (4.4)	2.5 (1.8)	6.0 (3.8)	1.1 (2.0)	F(5,100)=4.0	<b>0.002</b>	0.42
Pruritus-related QoL impairment, mean (SD) <sup>h</sup>	6.3 (4.9)	4.7 (3.4)	9.6 (5.7)	4.8 (3.4)	4.3 (4.7)	0.0 (0.0)	F(5,98)=9.8	<b>0.001</b>	0.59

\*Adjusted for age and pruritus duration; *post-hoc* group comparisons, controlled for multiple comparisons (Scheffe tests); Age, *post-hoc* tests ( $p < 0.05$ ): nephrogenic pruritus, psoriasis > atopic dermatitis; Duration: *post-hoc* tests: Atopic dermatitis > general pruritus, urticaria, controls; ISS: *post-hoc* tests: Urticaria > atopic dermatitis, genital pruritus, nephrogenic pruritus, psoriasis > controls; Hours of sleep: *post-hoc* tests: No sign. Differences (Scheffe test); General pruritus, atopic dermatitis, controls > urticaria and nephrogenic pruritus (Newman-Keuls test); BDI: *post-hoc* tests: Urticaria, psoriasis > nephrogenic pruritus, atopic dermatitis, genital pruritus > controls; BSI anxiety: *post-hoc* tests: No sign differences (Scheffe test); Urticaria > remaining groups (Newman-Keuls test); BSI somatic symptoms: *post-hoc* tests: nephrogenic pruritus > remaining groups. QoL: *post-hoc* tests: Urticaria > Atopic dermatitis > genital pruritus, psoriasis, nephrogenic pruritus, controls.  
<sup>a</sup>5=excellent, <sup>b</sup>min: 0; max: 21, <sup>c</sup>3=3 or more nights/week, <sup>d</sup>3=severely impaired, <sup>e</sup>min: 0; max: 52, <sup>f</sup>Cut-off: 9, <sup>g</sup>min: 0; max: 24, <sup>h</sup>min: 0; max: 22. Significant values are shown in bold. ESr: effect size correlation; ISS: Itch Severity Scale; PSQI: Pittsburgh Sleep Quality Index; BDI: Beck Depression Inventory; BSI: Brief Symptom Inventory; SD: standard deviation.

Multivariate analyses

To test the association between pruritus severity and distress and QoL, a series of hierarchical linear regressions were conducted with depressive symptoms, anxiety, somatic symptoms, and pruritus-related QoL impairment as dependent variables and pruritus severity (ISS-total scores) entered at step 1 as the independent variable. As sex and sleep quality had been found to be correlated with both the dependent variables and pruritus severity, sex and total impairment of sleep quality were entered as covariates at step 2 and 3. At step 1, ISS-scores significantly predicted depressive symptoms, anxiety, somatic symptoms, and QoL (Betas: 0.31 to 0.77;  $p < 0.001$ ). When entering sex as covariate, the magnitudes of the association of ISS-scores with the dependent variables of depressive symptoms, anxiety, and somatic symptoms were only slightly reduced, and continued to be statistically significant (Betas: 0.25 to 0.72;  $p < 0.001$ ). With the exception of QoL-impairment (Beta: 0.59;  $p < 0.001$ ), ISS-scores no longer were statistically significantly associated with any of the independent variables (Betas: 0.01–0.32;  $p$ : 0.923–0.09) when entering sleep quality impairment at step 3. For pruritus-related QoL impairment, none of the covariates were statistically significant predictors, and the magnitude of the association between ISS-scores and QoL was unchanged from step 1 to 3. The association of pruritus severity with moderate-severe depressive symptoms (BDI-13 cut-off = 9) was analysed with a hierarchical logistic regression. Pruritus severity was a significant predictor of having moderate-to-severe depressive symptoms both alone and when controlling for sex, but not when controlling for both sex and impaired sleep quality (OR: 1.19;  $p < 0.06$ ). In the final models, ISS-total scores, sex, and sleep impairment explained between 16% and 36% of the variation in the dependent variables. For further details, see Table SI (available at <http://www.medicaljournals.se/acta/content/?doi=10.2340/00015555-1221>).

Multiple linear regressions showed the affective pruritus component to be a significant predictor of all three dependent variables when entered at the first step (Betas 0.68–0.53;  $p = 0.001$ ), explaining

Table II. Mean scores and standard deviations (SD) of the Itch Severity Scale (ISS) components and ISS total scores for patients with atopic dermatitis, psoriasis, urticaria, genital pruritus, and nephrogenic pruritus patients

Pruritus severity component	Atopic dermatitis	Psoriasis	Urticaria	Genital pruritus	Nephrogenic pruritus	Statistics	<i>p</i>	ESr
	<i>n</i> =20 Mean (SD)	<i>n</i> =20 Mean (SD)	<i>n</i> =20 Mean (SD)	<i>n</i> =12 Mean (SD)	<i>n</i> =11 Mean (SD)			
ISS1 Frequency (min: 0; max: 1)	0.55 (0.15)	0.56 (0.22)	0.71 (0.24)	0.52 (0.25)	0.60 (0.36)	F(4,80)=1.6	0.171	0.28
ISS2 Description (min: 0; max: 1)	0.51 (0.21)	0.41 (0.21)	0.63 (0.21)	0.53 (0.24)	0.40 (0.26)	F(4,80)=3.9	<b>0.007</b>	0.41
ISS3 Area (min: 0; max: 1)	0.29 (0.18)	0.21 (0.12)	0.43 (0.23)	0.07 (0.06)	0.37 (0.29)	F(4,79)=7.7	<b>0.001</b>	0.54
ISS4 Intensity (min: 0; max: 1)	0.57 (0.14)	0.55 (0.16)	0.70 (0.15)	0.57 (0.15)	0.52 (0.26)	F(4,81)=4.3	<b>0.003</b>	0.43
ISS5 Mood (min: 0; max: 1)	0.54 (0.29)	0.36 (0.15)	0.76 (0.22)	0.40 (0.26)	0.45 (0.33)	F(4,82)=8.8	<b>0.001</b>	0.56
ISS6 Effect on sexuality (min: 0; max: 1)	0.35 (0.33)	0.28 (0.31)	0.72 (0.41)	0.50 (0.43)	0.25 (0.38)	F(4,77)=5.1	<b>0.001</b>	0.47
ISS7 Sleep impairment (min: 0; max: 1)	0.38 (0.18)	0.33 (0.26)	0.55 (0.26)	0.28 (0.18)	0.48 (0.38)	F(4,82)=3.1	<b>0.020</b>	0.37
ISS Total with area (min: 0; max: 21)	9.5 (2.4)	7.5 (2.9)	13.4 (3.7)	8.6 (2.8)	8.5 (5.0)	F(4,82)=8.9	<b>0.001</b>	0.56
ISS2a (sensory) (min: 0; max: 1)	0.43 (0.26)	0.39 (0.25)	0.49 (0.28)	0.42 (0.33)	0.30 (0.27)	F(4,63)=0.6	0.637	0.20
ISS2b (affective) (min: 0; max: 1)	0.59 (0.27)	0.54 (0.27)	0.83 (0.23)	0.71 (0.26)	0.44 (0.31)	F(4,67)=4.0	<b>0.006</b>	0.45

SD: standard deviation; ESr: effects size correlation; *post-hoc* tests (Scheffe) controlled for multiple comparisons ( $p < 0.05$ ): Frequency: No sign. Differences; Description: Urticaria > remaining groups; Area: urticaria, nephrogenic pruritus, atopic dermatitis, psoriasis > genital pruritus; Intensity: Urticaria > remaining groups; Mood: Urticaria > remaining groups; Effect on sexuality: Urticaria > remaining groups; Effect on sleep: No sign. differences. ISS-total: Urticaria > remaining groups. ISS2a (sensory): No differences. ISS2b (affective): Urticaria > genital pruritus, atopic dermatitis, psoriasis > nephrogenic pruritus. Significant values are shown in bold.

between 27% and 46% of the variation. When entering the sensory component at the second step, it was also a significant predictor of all 3 outcomes (Betas: 0.20–0.37;  $p = 0.001–0.05$ ), but only explaining an additional 3–9% of the variation (no further data shown).

#### Mediation analysis

As sleep quality impairment appeared to reduce the association between ISS-scores and depressive symptoms, anxiety, and somatic symptoms, a further analysis of impaired sleep quality as a possible mediator of the association between ISS-total scores (omitting the sleep component) and the dependent variables of depressive symptoms, anxiety, and non-specific somatic symptoms was conducted. Baron (25) and Kenny et al. (29), have defined 4 analytical steps necessary to establish mediation: (i) the independent variable (IV) should be a significant predictor of the dependent variable (DV); (ii) the IV should predict the mediator; (iii) the mediator should predict the DV, when controlling for the IV; and (iv) the association between the IV and the DV should be reduced, when controlling for the mediator. Complete mediation of the IV–DV-association requires that the IV–DV association is reduced to zero when controlling for the mediator. Partial mediation requires the association to be reduced to a non-trivial amount, but not to zero. In addition, for each of the three DVs, the Sobel bootstrap test (26) was used as a direct test of mediation. The Sobel test examines whether the indirect effect of the IV on the DV via the mediator is significantly different from zero. The analyses revealed impairment of sleep quality to be a significant mediator of the association between ISS-scores and both depressive symptoms and non-specific somatic symptoms. In both cases, the IV–DV coefficient was reduced, and Sobel tests indicated that the indirect effect of the IV

on the DV via the mediator was significantly different from zero. In contrast, sleep quality did not appear to be a mediator of the association between ISS and anxiety. For further details, see Table SII (available from: <http://www.medicaljournals.se/acta/content/?doi=10.2340/00015555-1221>).

#### DISCUSSION

Taken together, our results provide preliminary support for the Danish adaptation of the ISS as a reliable and valid measure of pruritus severity. In addition, previous results (6, 9, 10), indicating that pruritus perception is a multidimensional phenomenon consisting of, at least, two independent dimensions of sensory and affective pruritus, were confirmed.

The total ISS scores appeared to be normally distributed and the total scale showed acceptable internal consistency (0.88), similar to the 0.81 reported for the original English version of the ISS. It had been tested in a group of 93 psoriasis patients, who reported a mean pruritus severity score of 7.4 (11). The mean score of 7.5 found among psoriasis patients in our study supports the validity of the Danish adaptation.

The differences found between patient groups and between patients and controls without pruritus support the *discriminative validity* of the scale. Urticaria patients thus reported significantly more severe pruritus than patients with atopic dermatitis, nephrogenic pruritus, genital pruritus, and psoriasis, while control participants with vascular malformations showed no indication of pruritus. When examining the individual component scores, one would perhaps expect that patients with genital pruritus would report greater effects on sexual desire and function than the remaining patients. This, however, was not the case, and could be taken to re-

flect that the influence of pruritus on sexuality involves more aspects than just the direct effects on the genital region in itself. Female patients generally reported more severe pruritus than men across diagnosis groups, and this difference applied to all components of the ISS, except component 7 (Effect on sleep). One explanation could be that women may generally be more focused on bodily sensations (30).

Construct validity, in specific *convergent validity*, was explored by analysing associations between pruritus severity and a number of variables hypothesized to be correlated with pruritus severity. As expected, pruritus severity scores were significantly associated with depressive symptoms, anxiety, non-specific somatic symptoms, and pruritus-related impairment of QoL. Furthermore, the prevalence of moderate-to-severe depressive symptoms was highest among urticaria patients (65%), who also exhibited the highest pruritus severity scores. These results confirm previous findings of psychological comorbidity in patients with pruritus (5) and in dermatological patients in general (17).

When we adjusted for sleep impairment, the associations between pruritus severity and psychological and somatic symptoms ceased to be statistically significant. This suggested that pruritus-related sleep impairment could be an important mediator of the association between pruritus severity and these symptoms. Furthermore, previous studies have shown that psoriasis patients often report that their itch becomes worse at night but is ameliorated by sleep (1), and that a large proportion of atopic dermatitis patients with pruritus report difficulties falling asleep (9). In addition, distressed patients often report sleep problems, including difficulties falling and staying asleep as well as poor subjective sleep quality; findings that have been confirmed by objective assessments with polysomnography (13, 31). We therefore conducted a number of mediation analyses to test whether sleep impairment would live up to the proposed criteria (25) for mediation of the association between pruritus severity and psychological symptoms. The results were confirmed for depressive and somatic symptoms, but not for anxiety. We have previously found support for sleep impairment as a possible mediator of the association between pruritus and depressive symptoms in patients with psoriasis (10), and the present results provide additional support for this hypothesis in pruritus patients with other dermatological illnesses and systemic disease for both depressive and non-specific somatic symptoms, further supporting the *construct validity* of the Danish adaptation of the ISS.

Although sleep impairment was significantly correlated with QoL impairment in a bivariate analysis, adjusting for sleep impairment in a multivariate analysis did not affect the association between pruritus severity and QoL impairment. We have previously found similar results in a sample of psoriasis patients (10), and the

findings could indicate that the impact of pruritus on daily activities is unrelated to its impact on sleep quality, thus supporting the *discriminant validity* of the ISS.

As previous research has found support for a distinction between a sensory and an affective dimension of pruritus (6, 9, 10), we had specifically planned to explore the possible underlying factor structure of the ISS component 2, which consists of six pruritus descriptors. Our results confirmed that this ISS component consists of two underlying sub-components: a sensory and an affective pruritus component. Furthermore, the affective pruritus dimension appeared to be a considerably stronger predictor of depressive symptoms, anxiety, and pruritus-related QoL impairment than the sensory dimension. In addition, significant between-diagnosis group differences were found for the affective pruritus sub-component, but not for the sensory component. Taken together, this supports the *construct validity* of a multidimensional pruritus severity measure, and suggests that a distinction between these two dimensions or sub-components should be taken into consideration in future adjustments of the ISS.

A few other instruments assessing pruritus perception have been published. The Eppendorf itch questionnaire (32) measures pruritus severity using a traditional visual analogue scale (VAS), 80 different descriptors, and 50 items concerning time course, topographic information, and scratch behaviour. While the multi-dimensional approach is similar to that of the ISS, the very large number of items and the 30 min required to complete the form makes it impractical for use in clinical settings. Another, recently published instrument is the brief 5-D itch scale (33), which measures duration, intensity, change over time, disability, and distribution. While brief and practical, and covering several aspects, this scale lacks the qualitative descriptors of the sensory and affective aspects of pruritus perception.

In conclusion, the results provide preliminary support for the Danish adaptation of the ISS as a reliable and valid measure of pruritus severity. However, a number of limitations of the present study should be noted. First, the study is based on a relatively small sample of convenience, limiting the generalizability of the results. Secondly, the study is cross-sectional, and the validity of the modified QoL measure used in lack of a designated pruritus-related QoL measure is unclear. Finally, the stability and sensitivity of the instrument remains to be investigated in larger representative samples assessing pruritus severity over time and in clinical trials.

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