















ORIGINAL ARTICLE

Dermatological patients with itch report more stress, stigmatization experience, anxiety and depression compared to patients without itch: Results from a European multi-centre study

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Abstract

Background: Itch as the most common symptom in dermatology has been shown to be related to psychological factors such as stress, anxiety and depression. Moreover, associations were found between perceived stigmatization and itch. However, studies investigating the differences between patients with dermatoses with and without itch regarding perceived stress, stigmatization, anxiety and depression are missing. Therefore, one of the aims of the second study of the European Society for Dermatology and Psychiatry (ESDaP study II) was to investigate these relationships in a large cohort of patients with different itchy dermatoses.

Results: 3399 patients with 14 different itchy dermatoses were recruited at 22 centres in 17 European countries. They filled in questionnaires to assess perceived stigmatization, stress, signs of clinically relevant anxiety or depression, itch-related quality of life, the overall health status, itch duration, frequency and intensity. The most significant association between the severity of itching and the perception of stress was observed among individuals with rosacea (correlation coefficient $r = 0.314$). Similarly, the strongest links between itch intensity and experiences of stigmatization, anxiety, and depression were found in patients with seborrheic dermatitis (correlation coefficients $r = 0.317$, $r = 0.356$, and $r = 0.400$, respectively). Utilizing a stepwise linear regression analysis, it was determined that within the entire patient cohort, 9.3% of the variation in itch intensity could be accounted for by factors including gender, levels of anxiety, depression, and perceived stigmatization. Females and individuals with elevated anxiety, depression, and perceived stigmatization scores reported more pronounced itch intensities compared to those with contrary attributes.

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Conclusion: This study underscores the connection between experiencing itch and its intensity and the psychological strain it places on individuals. Consequently, psychological interventions should encompass both addressing the itch itself and the interconnected psychological factors. In specific cases, it becomes imperative for dermatologists to direct individuals towards suitable healthcare resources to undergo further psychological assessment.

INTRODUCTION

Itch is the most common symptom in dermatology. It is estimated that 1/3 of all patients who attend a dermatological office suffer from it.¹ Chronic pruritus, which is, itching longer than 6 weeks,² affects almost one-fifth of the general population.³ The Global Burden of Disease project listed itch as one of the 50 most common interdisciplinary symptoms associated with a high burden.⁴ According to recently published data, the occurrence and intensity of itch in dermatoses such as psoriasis, atopic dermatitis⁵ and urticaria⁶ is a major factor contributing to a decrease in quality of life. A previous cross-sectional multi-centre study of the European Society for Dermatology and Psychology (ESDaP study I) investigated the occurrence of clinically relevant symptoms of anxiety, depression and suicidal ideations in more than 3500 patients with dermatological diseases. It was shown that patients with itch significantly more often reported clinical signs of depression and suicidal ideations than patients without itch.⁷

Besides, having an itchy dermatosis is associated with stigmatization and increased stress. In keeping with more general psychosocial models of stigmatization,⁸⁻¹⁰ a more recent macro model of stigmatization in patients with visible skin diseases postulates that stigmatization can arise from outside the person ('external stigma') as well as from self-imposed prejudices of the patient him/herself ('self-stigma').¹¹ Indeed, perceived stigmatization from others has been shown to be related to itch intensity and scratch frequency in patients with chronic itchy diseases.¹²⁻¹⁴

Perceived stress refers to an individual's subjective evaluation or interpretation of the stressors one encounters in life. It is associated with personal beliefs, attitudes, experiences and individual coping mechanisms. Perceived stress thus varies from person to person. Regarding the relationship between perceived stress and itch, it is not only known that the stress level of patients suffering from pruritic dermatoses such as psoriasis, urticaria and atopic dermatitis is higher than in healthy controls,¹⁵ but also that the intensity of itch is positively associated with perceived stress.¹⁶ A recent paper, for example, found that students with high stress levels compared to students with low stress levels more often reported to have itch.¹⁷ In this context, a physiological stress reaction is discussed as trigger of itch.^{7,18,19}

However, knowledge of these relationships arose from studies investigating small samples, usually only including one group of skin patients. A deeper understanding of the link between itch, perceived stigmatization, perceived stress,

and mental health is crucial for improving patient care, reducing stigma, and promoting well-being. By considering the psychological aspects alongside physical symptoms, healthcare professionals can provide comprehensive care and support to individuals experiencing itch and related mental health challenges. Initial analyses of the ESDaP Study II data revealed that itch is a significant predictor of stigmatization.¹⁴ However, the relationship between itch and stigmatization was only investigated in the whole group of dermatological patients, but not in patients with different itchy dermatoses separately and without considering the occurrence of itch as important grouping variable. Therefore, one of the aims of this analysis was to investigate, in a large cross-national cohort of patients with and without itch, whether stigmatization is associated with the occurrence of acute and chronic itch and its intensity. Similarly, the relationship between itch and stress, depression and anxiety was analysed. We hypothesize that patients with itchy skin conditions display higher stress and stigmatization levels as well as more often clinically relevant signs of anxiety and depression than patients without itch.

MATERIALS AND METHODS

Study design

Data for this study were gathered in an observational cross-sectional multi-centre study (ESDaP-study II) in 17 European countries. The study protocol and data on body dysmorphic disorder (BDD) as well as on stigmatization from this study have already been published.^{14,20,21} Before consecutive recruiting the participating centres were trained and all study material was forward and back translated. Patients were recruited in 22 dermatological outpatient clinics from September 2017 to December 2019. In spring 2020, four dermatologists established a more extensive classification of dermatological conditions for analytical purposes. This classification, derived from the previous ESDaP study and ICD-10 categorization, was introduced to allow statistical analyses by ensuring an adequate number of patients in each group. In the current study, a subsample of 3399 patients with 14 different skin conditions associated with itch was selected by an expert team of dermatologists. This team of experts routinely provides care to patients with chronic itch and has a wealth of experience over which dermatoses are associated with itch. After the pre-selection of 14 skin conditions which are associated with itch, this list

was further discussed by the authors and no changes were made.

Ethics

The study protocol was approved by the Institutional Review Board of the Department of Medicine at the University of Giessen, Germany (Protocol Number 87/17) and each ethic committee at all participating sites/countries. The study was conducted in accordance with the Declaration of Helsinki and was registered at the German registry for clinical studies (DRKS00012745). All patients provided written informed consent before participation in the study.

Patient reported outcome measurements (PROMs)

Patients were asked to complete several patient-reported outcome measures (PROMs).^{20,21}

Itch specific PROMs

Prevalence

The prevalence of itch was investigated by the question: 'Have you suffered from itch in the last 24h?' with the answer categories yes/no.

Intensity

The itch numerical rating scale (NRS; ranging from 0 (no itch) to 10 (worst imaginable itch)) was used to record the intensity of itch.

Chronicity

The duration of itch was assessed by asking if the itch lasted at least 6 weeks (=chronic itch) or less than 6 weeks (=acute itch).

Itch quality of life

The 5-Pruritus Life Quality (5PLQ) assessed aspects of quality of life related to itch during the last 7 days using five items: the frequency of itch (Item 1), the extent of impairment in daily life (Item 2), in social life (Item 3), impact on sleep (Item 4) and enjoyment of life and mood (Item 5). The answer categories range from 0 ('never'/'not at all') to 4 ('always'/'very much').

Perceived stress

Perceived stress was measured by the Perceived Stress Scale-10 (PSS),²² a 10 item PROM, which measures self-rated stress during the last month. An example item is 'In the last

month, how often have you found that you could not cope with all the things that you had to do?' Answers need to be given on a 5-point Likert scale with the answer categories 'never', 'almost never', 'sometimes', 'fairly often', 'very often'. The total score can range from 0 to 40 with higher scores indicating higher perceived stress.

Perceived stigmatization

The 21-item Perceived Stigmatization Questionnaire (PSQ)²³ was used to measure perceived stigmatization. The patients indicated how often other people behaved towards them in a certain way in the past year 'never' (1) to "always" (5).

Overall health status

Overall health status was assessed by self-report using the visual analogue scale part of the EQ-3D-3L ranging from 0 (worst state of health) to 100 (best imaginable state of health).²⁴

Depression and anxiety

The Patient Health Questionnaire (PHQ-4), a questionnaire consisting of two parts (one part depression: PHQ-2; one part anxiety: General Anxiety Disorder Assessment (GAD)-2), was used to screen for depression or anxiety. Each total score can range from 0 to 6. Values ≥ 3 indicate a positive screening for depression or anxiety, respectively.²⁵

A version of all items which were included in ESDaP-Study II is available at <https://bmjopen.bmj.com/content/8/12/e024877>.²⁰

Statistical analyses

Data were analysed using SPSS 26/29. In case of categorical variables, numbers and percentages are reported. For stigmatization, stress, overall health status and itch intensities means \pm SD are reported. As in most patient groups data were not normally distributed, non-parametric Mann-Whitney *U*-tests were conducted in order to compare groups with and without itch. One missing item was allowed per scale of the PSS and PSQ as described in the article on the epidemiology of body dysmorphic concerns.²¹ The scale scores were extrapolated. Relationships between itch intensities and stress, stigmatization, appearance-related concerns and the overall health status were determined by Spearman rank correlations for the whole group of patients and for each patient group separately. The strength of association between the continuous variable itch intensity and the dichotomous variables depression and anxiety (yes in case of values ≥ 3) was assessed with the point-biserial correlation. Hereby, a correlation of $r \geq 0.1$ refers to a small effect, of $r \geq 0.3$ to a moderate

effect and of $r \geq 0.5$ to a large effect. In addition, a stepwise linear regression analysis was performed for the whole group of patients in order to test whether the psychological variables (stress, stigmatization, anxiety and depression) were significant predictors of itch intensity in addition to age and sex. In this analysis, age and sex were entered in the first step of the analysis and the psychological variables were entered in the second step.

RESULTS

Sample characteristics

3399 patients were included in this analysis. 56% of the total sample were female. The mean age was 48.2 ± 16.5 years. The median was 17 for the PSS score and 16 for the PSQ score. Clinical signs of depression were reported by 29.1% of the patients, clinical signs of anxiety by 28.4% of the patients. Overall health status was reported at a median of 70.

A total of 1401 of the 3399 patients had psoriasis, 352 atopic dermatitis, 71 hand eczema, 173 urticaria, 145 bullous disorders, 142 hidradenitis suppurativa, 127 chronic prurigo, 114 chronic pruritus on non-lesional skin, 221 connective tissue disorders, 257 other dermatitis/eczema, 118 'allergies or hypersensitive reactions', 90 rosacea and 123 scaly conditions.

For more detailed information see [Table 1](#).

Prevalence of itch

In total, 73.8% of the patients reported having itch in the last 24 h (h) before the assessment ([Table 1](#)). The prevalence of itch during the last 24 h was highest (>90%) in patients with atopic dermatitis, chronic prurigo and pruritus on non-lesional skin. Itch during the last 24 h was least prevalent in patients with connective tissue disorders (40.5%). Itch occurring for six weeks or longer was reported most often in patients with the diagnosis chronic pruritus on non-lesional skin (ICD-code 29.9; 87.4%), while the group of patients with 'allergies or hypersensitive reactions' least often reported having chronic itch (33.7%). Itch intensity was highest in patients with chronic pruritus on non-lesional skin (Md=7; IQR: 5–8) and lowest in patients with hidradenitis suppurativa (Md=4; IQR: 2–6). For more itch-related characteristics of the sample, see [Table 2](#).

Psychological characteristics in patients with and without itch

The highest stress score was reported by patients suffering from hidradenitis suppurativa accompanied with itch, while the group with the lowest stress score was the group of patients with hand eczema without having itch. Patients with bullous disorders and itch during the last 24 h felt most

stigmatized, followed by patients suffering from psoriasis and chronic pruritus. The majority of patients with values suggesting anxiety were in the group of patients with hidradenitis suppurativa accompanied with itch, while the majority of patients with values for suggesting depression were seen in the group of patients with allergies or hypersensitive reactions and with itch lasting longer than six weeks. The lowest overall health status was reported by patients with bullous disorders who had itch during the last 24 h and with chronic itch due to scaly conditions. For more detailed information see [Table 1](#).

Correlation between itch intensity and psychological variables

In the whole group, itch intensity was significantly positively related to perceived stress, stigmatization, anxiety, depression and itch-related quality of life ([Table 3](#)). The highest correlation between itch intensity and perceived stress was seen in patients with rosacea ($r=0.314$), and the highest correlation between itch intensity and stigmatization, anxiety or depression was seen in patients with seborrheic dermatitis ($r=0.317$, $r=0.356$; $r=0.400$). The highest negative correlation with overall health status was seen in patients with chronic prurigo ($r=-0.421$).

Stepwise linear regression analysis revealed that in the whole group of patients, 9.3% of itch intensity could be predicted by sex, anxiety, depression and perceived stigmatization. Females and patients with higher anxiety, depression and perceived stigmatization scores reported higher itch intensities than persons with the opposite characteristics ([Table 4](#)).

DISCUSSION

This study has demonstrated that among patients with itchy skin conditions having itch is associated with perceived stigmatization, perceived stress and poorer health status.

Patients with psoriasis, atopic dermatitis, urticaria and chronic prurigo who reported chronic itch had higher scores in the PSQ and PSS and a higher prevalence of clinically relevant signs of anxiety, and depression than patients with the same diagnoses who reported that their itch was not chronic.

These data are consistent with results from other studies, which showed that atopic dermatitis, chronic pruritus on non-lesional skin and chronic prurigo are conditions in which itch is a very prominent symptom, often associated with impairment in quality of life and sleep.^{26,27} Also, in a sample of 838 German students, it was shown that itch intensity was significantly related to perceived stress.¹⁷ However, our data also show that in patients with diagnoses that were previously not regarded as typical pruritic dermatoses, such as rosacea, chronic itch occurs in more than half of the patients and is associated with psychological factors.

TABLE 1 Sample characteristics of 3,365 patients with and without itch in the last 24 h and with acute and chronic itch regarding sex-, age-, psychological- and health-related variables (if itch was present in the last 24 h, the duration of itch was assessed in order to classify acute and chronic itch).

Diagnosis	Itch in the last 24 h	Sex female/total number (%)	Age (x ± STD)	Perceived stress Md (IQR)	Perceived stigmatization Md (IQR)	Anxiety n/N (%)	Depression n/N (%)	Overall health status Md (IQR)
Psoriasis N=1390	Yes	529/1015 (52.1%)	47.4 ± 14.8	18 (13–22)	20 (11–31)	327/1006 (32.5%)	306/1015 (30.1%)	65 (50–80)
	No	366/1390	51.2 ± 15.4	15 (10–19)	15 (9–25)	63/358 (17.6%)	64/358 (17.9%)	75 (60–85)
Atopic dermatitis N=350	Chronic itch was present in the last 24 h	338/628 (53.8%)	47.6 ± 14.5	18.4 (13–23)	21 (12–32)	220/624 (35.3%)	201/631 (31.9%)	60 (50–75)
	Acute itch	152/295 (51.5%)	46.9 ± 15.0	17 (13–22)	16 (10–27)	88/290 (30.3%)	79/293 (27%)	70 (53.8–80)
Other dermatosis N=257	Yes	174/319 (54.5%)	39.0 ± 15.8	18.9 (14–22)	17.5 (10–28)	109/319 (34.2%)	130/318 (40.9%)	70 (50–80)
	No	29/350	40.2 ± 18.0	16 (10–20.5)	14 (7.4–18.5)	5/29 (17.2%)	9/29 (31%)	80 (70–90)
Connective tissue disorders N=215	Chronic itch was present in the last 24 h	117/217 (53.9%)	37.9 ± 16.0	19 (14–23)	20 (10–30.5)	83/217 (38.2%)	92/216 (42.6%)	65 (50–75)
	Acute itch	52/94 (55.3%)	40.8 ± 14.7	18 (15–21)	14 (9.3–23)	25/95 (26.3%)	37/95 (38.9%)	74 (65–80)
Urticaria N=171	Yes	107/195 (54.9%)	49.7 ± 17.3	16.3 (11–21)	15 (8.8–24.3)	54/193 (28%)	55/192 (28.6%)	70 (50–80)
	No	60/257	50.9 ± 17.6	13.5 (10–17)	11 (7–19.5)	7/57 (12.3%)	8/56 (14.3%)	80 (60–90)
Chronic itch was present in the last 24 h	Chronic itch	71/127 (55.9%)	49.9 ± 16.8	16 (10.3–22)	15 (9–25)	35/125 (28%)	37/125 (29.6%)	65 (50–80)
	Acute itch	28/53 (52.8%)	47.5 ± 19.0	16.8 (10–20.3)	16 (8–24.3)	14/52 (26.9%)	14/51 (27.5%)	70 (50–80)
Acute itch	Yes	69/86 (80.2%)	55.1 ± 14.5	18 (13–22)	13 (7–23)	31/87 (35.6%)	24/86 (27.9%)	60 (50–80)
	No	128/215	52.5 ± 16.9	16 (12–20)	13 (8–20)	21/125 (16.8%)	22/124 (17.7%)	70 (50–80)
Chronic itch was present in the last 24 h	Chronic itch	34/46 (73.9%)	55.3 ± 14.9	18 (14–22)	12.8 (7.8–24.3)	17/46 (37%)	13/45 (28.9%)	60 (50–80)
	Acute itch	46/77 (59.7%)	51.3 ± 13.3	18 (13–22)	13.5 (6.8–22.3)	10/31 (32.3%)	8/31 (25.8%)	70 (50–80)
Itch in the last 24 h	Yes	92/132 (69.7%)	42.6 ± 15.4	18.9 (15–22)	13.5 (9–23)	44/132 (33.3%)	53/130 (40.8%)	70 (50–80)
	No	38/171	43.1 ± 14.9	17 (12–19)	11 (6–16.6)	5/36 (13.9%)	6/37 (16.2%)	81 (70–90.8)
Chronic itch was present in the last 24 h	Chronic itch	50/67 (74.6%)	43.7 ± 15.8	19 (15–22)	17.5 (10.1–27)	30/68 (44.1%)	26/67 (38.8%)	65 (40–75)
	Acute itch	34/53 (64.2%)	41.6 ± 15.4	18 (16–21)	10 (8–14.8)	9/52 (17.3%)	24/52 (46.2%)	80 (65–85)

(Continues)

TABLE 1 (Continued)

Diagnosis		Sex female/total number (%)	Age (x±STD)	Perceived stress Md (IQR)	Perceived stigmatization Md (IQR)	Anxiety n/N (%)	Depression n/N (%)	Overall health status Md (IQR)
Bullous disorders N=144	Itch in the last 24h	Yes 89/144 (61.8%)	62.6±16.5	18 (13-22)	19 (10-31)	32/87 (36.8%)	31/88 (35.2%)	60 (40-75)
		No 55/144	59.3±13.9	15 (7.3-19)	14 (6.5-24)	10/52 (19.2%)	7/53 (13.2%)	70 (50-80)
	Duration of itch (if itch was present in the last 24h)	Chronic itch 65/82 (79.3%)	61.4±16.9	18 (13.5-22)	20 (11.3-31.8)	26/64 (40.6%)	24/65 (36.9%)	60 (40-70)
		Acute itch 17/82	67.0±14.2	17 (11.5-21.5)	22 (9.5-28.5)	5/17 (29.4%)	6/17 (35.3%)	50 (42.5-67.5)
Hidradenitis suppurativa N=142	Itch in the last 24h	Yes 94/142 (66.2%)	38.4±11.8	20 (16-25)	18.5 (12-30.9)	49/94 (52.1%)	39/92 (42.4%)	60 (45-70)
		No 48/142	38.0±11.9	16 (11.5-26)	12 (8-21)	17/48 (35.4%)	14/48 (29.2%)	67.5 (50-80)
	Duration of itch (if itch was present in the last 24h)	Chronic itch 60/88 (68.2%)	38.9±11.9	20 (15.75-25)	18 (10-29.4)	28/60 (46.7%)	24/59 (40.7%)	60 (45-75)
		Acute itch 28/88	39.0±11.5	10 (16.3-26)	21.5 (13.2-30.6)	17/28 (60.7%)	12/27 (44.4%)	60 (36-70)
Chronic prurigo N=127	Itch in the last 24h	Yes 119/127 (93.7%)	54.5±15.0	18 (12.6-21.1)	12 (8-23.6)	38/119 (31.9%)	48/116 (41.4%)	70 (50-80)
		No 8/127	58.0±15.3	12.2 (7.3-18)	9.5 (6-18)	2/8 (25%)	1/8 (12.5%)	80 (58.8-83.8)
	Duration of itch (if itch was present in the last 24h)	Chronic itch 85/115 (73.9%)	56.5±13.6	18 (12.1-22)	14.5 (8-26)	30/85 (35.3%)	34/82 (41.5%)	60 (50-77.5)
		Acute itch 30/115	50.8±16.3	17 (15.5-18.9)	11 (7.5-12.5)	8/30 (26.7%)	14/30 (46.7%)	80 (70-86.5)
Scaly conditions N=119	Itch in the last 24h	Yes 81/119 (68.1%)	53.2±17.1	17 (13-22.8)	15 (9-22)	23/78 (29.5%)	26/78 (33.3%)	60 (50-80)
	Duration of itch (if itch was present in the last 24h)	No 38/119	51.5±15.5	14 (9-18.3)	12 (8-20)	5/38 (13.2%)	6/38 (15.8%)	80 (60-90)
		Chronic itch 43/75 (57.3%)	54.7±14.1	17 (11.6-23)	15 (9-22)	9/42 (21.4%)	15/42 (35.7%)	50 (50-80)
		Acute itch 32/75	49.2±19.7	17 (15.8-22.5)	16.3 (8.6-22.5)	12/31 (38.7%)	9/30 (30%)	63 (50-81.3)
Allergies_ hypersensitive reactions N=116	Itch in the last 24h	Yes 86/116 (74.1%)	50.3±17.3	17 (15-20)	10.5 (7.3-20)	27/86 (31.4%)	39/86 (45.3%)	70.5 (51-80)
		No 30/116	45.9±16.2	17 (15-18.5)	10 (4-16)	23/30 (23.3%)	9/30 (30%)	79 (59.5-90)
	Duration of itch (if itch was present in the last 24h)	Chronic itch 28/83 (33.7%)	53.2±17.4	17 (15-25)	10 (6-26.3)	9/28 (32.1%)	16/28 (57.1%)	70 (50-80)
		Acute itch 55/83	49.1±17.5	17 (15-20)	11 (7.8-19.3)	18/55 (32.7%)	22/55 (40%)	71.5 (55-81)

TABLE 1 (Continued)

Diagnosis	Itch in the last 24h	Sex female/total number (%)	Age (x±STD)	Perceived stress Md (IQR)	Perceived stigmatization Md (IQR)	Anxiety n/N (%)	Depression n/N (%)	Overall health status Md (IQR)
Pruritus on non-lesional skin N=113	Yes	52/104 (50%)	58.7±16.4	16 (11–20)	14 (9–22)	32/103 (31.1%)	30/101 (29.7%)	60 (40–70)
	104/113 (92%)							
	No	7/9 (77.8%)	52.0±15.9	15.6 (15–18.5)	14 (9.5–14)	0/9 (0%)	2/9 (22.2%)	80 (65–87.5)
Rosacea N=90	Yes	47/90 (52.2%)	60.5±15.4	16 (11–20)	14 (9–21.8)	28/89 (31.5%)	28/87 (32.2%)	55 (40–70)
	90/103 (87.4%)							
	No	5/13 (38.5%)	48.2±18.3	16 (14–18.25)	13.5 (9.3–24.3)	4/13 (30.8%)	2/13 (15.4%)	62.5 (42.5–80)
Hand eczema N=71	Yes	32/49 (65.3%)	45.6±13.6	17 (14–20.8)	13 (9–18)	15/48 (31.3%)	18/48 (37.5%)	71 (50–85)
	49/90 (54.4%)							
	No	23/41 (56.1%)	53.6±16.1	16 (11.3–19.8)	12 (7–23)	8/38 (21.1%)	9/38 (23.7%)	80 (50–90)
Seborrheic dermatitis N=60	Yes	11/18 (61.1%)	39.7±10.2	17.3 (12.5–29)	13 (7.5–26)	7/18 (38.9%)	10/18 (55.6%)	65 (40–85)
	18/43 (41.9%)							
	No	17/25 (68%)	46.6±13.4	17 (14–19.5)	15 (8.5–17.5)	7/25 (28%)	7/25 (28%)	75 (58–85)
All patients with skin conditions associated with itch N=3365	Yes	39/57 (68.4%)	40.0±16.5	16 (13–21)	14 (8.5–21)	17/57 (29.8%)	17/57 (29.8%)	76 (60–90)
	57/71 (65.4%)							
	No	7/14 (50%)	43.4±15.9	13.1 (9.8–15)	11 (6–16.6)	1/14 (7.1%)	1/14 (7.1%)	90 (72.5–97)
All patients with skin conditions associated with itch N=3365	Yes	25/34 (73.5%)	39.9±16.4	16.5 (12.8–21)	14.5 (8.5–21.5)	9/34 (26.5%)	9/34 (26.5%)	75 (55–89.5)
	34/52 (80.3%)							
	No	12/18 (66.7%)	41.2±17.2	17 (14–20)	12.5 (8–21.5)	6/18 (33.3%)	5/18 (27.5%)	82.5 (63.8–89.3)
All patients with skin conditions associated with itch N=3365	Yes	19/44 (43.2%)	43.8±18.2	16.5 (10.8–20)	16 (9–22)	9/40 (22.5%)	8/42 (19%)	80 (60–90)
	44/60 (73.3%)							
	No	10/16 (62.5%)	44.4±15.4	15.5 (10.3–18.3)	12.6 (2–19.5)	4/14 (28.6%)	1/13 (7.7%)	90 (70–90)
All patients with skin conditions associated with itch N=3365	Yes	11/24 (45.8%)	43.4±16.9	15.5 (10.3–22.3)	18.9 (8–29)	6/23 (26.1%)	7/23 (30.4%)	77.5 (59.5–90)
	24/41 (58.5%)							
	No	8/17 (47.1%)	42.9±20.0	20 (15–20)	15 (11–18.5)	3/14 (21.4%)	1/16 (6.3%)	80 (70–90)
All patients with skin conditions associated with itch N=3365	Yes	1392/2467 (56.4%)	47.5±16.5	18 (13–22)	17 (10–28)	807/2449 (33%)	824/2449 (33.6%)	70 (50–80)
	2485/3365 (73.8%)							
	No	477/872 (54.7%)	50.2±16.3	15 (10–19)	13 (8–21)	155/856 (18.1%)	159/855 (18.6%)	75 (60–85.8)
All patients with skin conditions associated with itch N=3365	Yes	873/1530 (57.1%)	47.9±16.5	18 (13–23)	18 (10–30)	537/1523 (35.3%)	536/1522 (35.2%)	60 (50–75.8)
	1541/2303 (66.9%)							
	No	428/760 (56.3%)	46.3±16.3	17 (14–21)	14 (9–23.2)	226/751 (30.1%)	249/753 (31.9%)	70 (58–80)

Note: Significant group differences ($p < 0.05$; results of the Mann–Whitney U -test) between patients with and without chronic itch and between patients with or without acute itch respectively are highlighted in pink. Abbreviations: IQR, interquartile range; Md, median; PSQ, Perceived Stigmatization Questionnaire; PSS, Perceived Stress Scale; STD, standard deviation; x, mean.

TABLE 2 Assessment of itch intensity and itch-related quality of life for each diagnose group in the study sample (N=3365).

Diagnosis	Itch intensity (NAS 0–10)* (Md (IQR))	Frequency (5PLQ1) (Md (IQR))	Impact on daily life (5PLQ2) (Md (IQR))	Impact on social life (5PLQ3) (Md (IQR))	Impact on sleep (5PLQ4) (Md (IQR))	Enjoyment impairment (5PLQ5) (Md (IQR))
Psoriasis	5 3–7	2 1–3	1 0–3	1 0–2	1 0–2	1 0–3
Atopic dermatitis	6 4–8	3 2–3	2 1–3	2 1–3	2 1–3	2 1–3
Dermatitis_eczema	6 4–8	3 2–3	2 1–3	1 0–2	1 0–3	1 0–3
Connective tissue disorders	4 3–6	1 0–2	0 0–1	0 0–1	0 0–1	0 0–1
Urticaria	6 4–8	2 1–3	2 1–3	1 0–3	2 1–3	2 1–3
Bullous disorders	6 3.25–8	2 0.5–3	1 0–3	1 0–2	1 0–3	1 0–3
Hidradenitis suppurativa	5 3–7	2 2–3	2 0–3	1 0–3	1 0–3	1 0–3
Chronic prurigo	6 3–8	3 2–4	2 1–3	2 1–3	2 1–3	2 1–3
Scaly conditions	5 3–7	2 1–3	1 0–3	1 0–2	1 0–2	1 0–2
Allergies – hypersensitive reactions	5 3–7	2 1–3	2 1–2	1 0–2	2 0–2	1 0–2
Pruritus on non-lesional skin	7 5–8	3 2–4	3 1–3	1 0–3	2.5 1–3	2 1–3
Rosacea	4 2–6	2 0–3	1 0–2	1 0–2	1 0–2	1 0–2
Hand eczema	5 3–7.5	2 1–3	1 0–3	1 0–2	1 0–2	1 0–2.25
Seborrheic dermatitis	5 2.25–7	2 1–3	1 0–2	1 0–2	1 0–2	1 0–2
All patients with skin conditions associated with itch	5 3–7	2 1–3	2 0–3	1 0–2	1 0–3	1 0–3

Note: 5PLQ 1: How often have you experienced an itching, burning, stinging, tingling sensation or pain on your skin? (0–4); 5PLQ 2: To what extent has the itching negatively affected you in your everyday life (e.g. if you must wear specific clothing) in your leisure time and/or at work?; 5PLQ 3: To what extent does the itching make you feel impaired when dealing with other people (e.g. feeling embarrassed and insecure)?; 5PLQ 4: To what extent does the itching have a negative impact on your sleep?; 5PLQ 5: To what extent has the itching influenced your enjoyment of life and your mood?

Abbreviations: Md, median; IQR, interquartile-range; n, affected persons; N, investigated patients.

In all dermatoses, with the exception of ‘allergies hypersensitive reactions’, there was an at least moderate correlation between the intensity of itch and the quality of life related to itch. In all patients, a higher itch intensity was accompanied with a lower overall health status. This confirms previous findings in which the highest ‘disability-adjusted life years’ were found in patients with itchy dermatoses in European countries.²⁸ In addition, in 10 out of 14 dermatoses the presence of clinically relevant signs of anxiety and/or depression significantly correlated with itch intensity. These results confirm previous work on the correlation between itch (intensity) and depression, suicidal ideation and anxiety in patients with psoriasis and atopic dermatitis.^{29,30} However, this work additionally shows that this connection also occurs in other skin diseases associated with itch

such as bullous disorders, scaly conditions and seborrheic dermatitis.

In the study cohort, patients with psoriasis who reported to have chronic itch most frequently suffered from perceived stigmatization. Further connections between perceived stigmatization and itch intensity were seen in patients with atopic dermatitis, urticaria, chronic prurigo, scaly conditions and seborrheic dermatitis. These results are in line with the results of a former study, which showed positive correlations between perceived stigmatization and self-reported scratching in patients with psoriasis.¹² This can be explained by itch being not only a very distressing symptom, but also associated with perceived stigmatization and, thus, is a precipitating factor for social fears and perceived negative attitudes particularly due to scratch marks visible for

TABLE 3 Correlation between itch intensity and perceived stress, perceived stigmatization, prevalence of depression and anxiety, overall health status and itch-related quality of life (5PLQ) across skin conditions in the sample $N=3,365$.

Itch intensity (NAS 0–10)	Perceived stress	Perceived Stigmatization	Anxiety	Depression	Overall health status	Frequency (5PLQ1)	Impact on daily life (5PLQ2)	Impact on social life (5PLQ3)	Impact on sleep (5PLQ4)	Enjoyment impairment (5PLQ5)
Psoriasis	0.279**	0.183**	0.286**	0.279**	-0.271**	0.618**	0.562**	0.483**	0.548**	0.533**
Atopic dermatitis	0.229**	0.176**	0.330**	0.274**	-0.394**	0.472**	0.451.451**	0.358**	0.437**	0.465**
Other dermatitis_eczema	0.163*	0.137	0.307**	0.357**	-0.379**	0.657**	0.545**	0.446**	0.640**	0.594**
Connective tissue disorders	0.115	0.040	0.127	0.094	-0.132	0.468*	0.461*	0.333*	0.509**	0.338**
Urticaria	0.041	0.300**	0.296**	0.087	-0.332**	0.493**	0.645**	0.422**	0.539**	0.532**
Bullous disorders	0.125	0.153	0.339**	0.249*	-0.341**	0.492**	0.611**	0.519**	0.628**	0.586**
Hidradenitis suppurativa	0.175	0.139	0.047	0.284**	-0.256**	0.468**	0.576**	0.436**	0.517**	0.429**
Chronic prurigo	0.128	0.199*	0.204*	0.110	-0.421**	0.546**	0.492**	0.418**	0.525**	0.528**
Scaly conditions	0.141	0.271*	0.047	0.368**	-0.180	0.688**	0.603**	0.596**	0.609**	0.557**
Allergies_hypersensitive reactions	0.081	0.215	0.187	-0.022	-0.270*	0.363**	0.302**	0.202	0.477**	0.400**
Pruritus on non-lesional skin	0.120	0.090	0.185	0.225*	-0.391**	0.459**	0.313**	0.402**	0.419**	0.432**
Rosacea	0.314*	0.073	0.192	0.285	-0.358*	0.490**	0.457**	0.385**	0.598**	0.376*
Hand eczema	-0.111	-0.075	0.010	0.214	-0.061	0.300*	0.444**	0.427**	0.401**	0.377**
Seborrheic dermatitis	0.288	0.317*	0.356*	0.400**	-0.299*	0.642**	0.593**	0.418**	0.506**	0.540**
All patients with skin conditions associated with itch	0.193**	0.152**	0.246**	0.246**	-0.299**	0.575**	0.537**	0.439**	0.553**	0.521**

** illustrates highly significant correlations ($p < 0.001$), * illustrates significant correlations ($p < 0.05$).

TABLE 4 Association between itch intensity and age, sex, perceived stress, perceived stigmatization, anxiety and depression. In all patients with skin conditions associated with itch $N=3.365$.

All patients with pruritic dermatoses (included variables in the regression; step 4)					
	Non-standardized coefficients		Standardized coefficients		
	Regression coefficient B	Standard-error	β	T	Significance
Sex	0.369	0.101	0.073	3.665	<0.001
Anxiety	0.756	0.126	0.142	5.991	<0.001
Depression	0.757	0.125	0.143	6.044	<0.001
Perceived Stigmatization	0.020	0.004	0.096	4.614	<0.001

others. Most patients showed perceived stress values indicative of moderate perceived stress. This result is important as perceived stress can trigger dermatoses such as psoriasis, atopic dermatitis or urticaria³¹ by modulating the activation of the hypothalamic–pituitary–adrenal axis via the activation of stress mediators, including cortisol, ACTH and CRH, which in turn lead to skin inflammation. In the skin itself, keratinocytes and fibroblasts produce hypothalamic and pituitary signalling peptides and express CRH receptors and melanocortin receptors, whereby upon activation corticosteroid secretion occurs.³² In addition, keratinocytes express receptors for neurotransmitters (e.g. adrenaline, noradrenaline, dopamine, histamine and acetylcholine), neurotrophins and neuropeptides (e.g. substance P and nerve growth factor), which in turn are linked to psychoneuroimmunological mechanisms.³³ Interestingly, patients with rosacea and showed the highest correlation between itch intensity and perceived stress. One reason for this could be that negative emotions also intensify the experience of itch and other symptoms. Conversely, a high itch intensity in these skin disorders which are normally located on the face or scalp can lead to high perceived stress.

Limitations

Analyses to detect the minimal clinical differences for the used instruments in a dermatological cohort are lacking.

CONCLUSIONS

These results underline that itch is associated with psychological burden and impairment in everyday life. Some of the dermatoses examined in this study have not yet been generally thought of as typically pruritic dermatoses, although patients report itch and associated psychological burden. This study demonstrates that it is important for physicians to be cognizant that psychological variables (such as stress, stigmatization, anxiety or depression) both accompany and exacerbate ‘itch’, and are also likely to affect scratching behaviour. As a consequence psychological interventions should target both itch and related psychological variables. In certain instances, it is crucial to refer individuals to an

appropriate healthcare service for additional psychological evaluation.

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DATA AVAILABILITY STATEMENT

The data that support the findings of the study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ETHICS STATEMENT

All participating centres completed in compliance with ethical board.

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