

Assessment of Pruritus in Patients With Psoriasis and Atopic Dermatitis: Subjective and Objective Tools

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Pruritus is a major symptom of skin disease. The quest to identify a valid and reliable method to assess this important symptom has led to the development of a myriad of measurement tools. Some clinical trials using subjective measurements of itch intensity have reported itch intensity levels in psoriasis that are close to severity levels found in atopic dermatitis. Although it is possible that we have previously underestimated the severity of pruritus in psoriasis, these unexpected findings prompted us to review and evaluate these subjective methodologies. We provide an overview of the current tools available to measure itch severity, including subjective rating scales and questionnaires and objective measures of scratch activity through videotape observation and wrist actigraphy. We discuss the advantages and limitations of these methods and encourage consideration of a novel objective method of evaluation.

Pruritus is a major symptom of skin disease. Assessing the intensity and course of pruritus is essential in evaluating the relative efficacy of therapeutic interventions and the impact of pruritic skin disease on quality of life. The quest to identify a valid and reliable method to assess this important symptom has led to the development of a myriad of measurement tools.

Samuel Hafenreffer, a German physician, in 1660 defined itch as “an unpleasant sensation that provokes the desire to scratch.”^{1,2} The definition provides 2 approaches to measurement, that of itch itself and the behavioral response, scratch. Subjective measurement of the sensation has been attempted through various patient self-reported rating scales of itch intensity and multidimensional questionnaires that assess its emotional and psychosocial impact. Actigraphy, or the measure of body movement over time by a wrist-worn device with a microaccelerometer, has recently been used to measure the objective correlate of itch, scratch.

The definition of itch provides a straightforward framework to characterize the symptom. Yet, in 2013, a special interest group of the International Forum for the Study of Itch (IFSI) concluded that there is no universally accepted and fully validated method to assess itch in clinical trials and clinical practice.³ Consequently, subjective evaluation techniques have been validated by correlation with other subjective tools. Yet, recent evidence suggests that these validated subjective measures of itch may not correlate with

objective assessment of scratching using actigraphic devices.^{4–9} Moreover, subjective itch rating scales and questionnaires have not been adequately validated in patients with atopic dermatitis (AD) or psoriasis, raising questions about their applicability in these patient populations. They are, however, used in clinical trials to validate emerging therapies and have been incorporated in a myriad of tools used to measure the severity of AD and psoriasis, such as Scoring Atopic Dermatitis (SCORAD) and Psoriasis Symptom Inventory.^{10,11}

For centuries, dermatologic textbooks and prevailing thought have not regarded pruritus as a major symptom of psoriasis, but recent studies suggest that the prevalence and level of itch intensity in psoriasis may approach that of AD.^{12–18} Itch scores in patients with moderate to severe psoriasis and AD have been reported to be approximately 6 to 7 out of 10, demonstrating near parity.^{19–21} A questionnaire-based study demonstrated only small differences in itch intensity between the 2 disease states.²² A critical reevaluation of our methods of evaluation of pruritus is warranted for accurate assessment of this important symptom in future studies evaluating therapeutic interventions.

This article provides an overview of the current tools available to measure the severity of pruritus. Our aim is to critically analyze the limitations of current methodologies available to assess itch and to stimulate consideration of novel valid and objective methods of evaluation.

SUBJECTIVE MEASURES OF ITCH

Scales

Various unidimensional rating scales have been used to study itch, including the visual analog scale (VAS), numerical rating scale (NRS), and verbal rating scale (VRS) (Table 1). These monodimensional

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TABLE 1. Referenced Assessment of Pruritus: Rating Scales for Measuring Itch Intensity

Category	Name	Description	Validation Method
Manual rating scales	VAS*	100-mm Horizontal line with descriptive anchors “no itch” and “worst imaginable itch” at the extremes. Scored by measuring the distance in millimeters from one end of the scale to a vertical mark placed on the line that indicates the intensity of itch ²³	Concurrent validity demonstrated by high correlation with NRS ($r > 0.8$, $P < 0.01$) and VRS ($r > 0.7$, $P < 0.01$) ^{23,28}
			Histamine-induced itch studies demonstrated a dose-response relationship between itch severity and increasing transdermal histamine iontophoretic stimulation ^{26,27}
			Skin prick tests with histamine and codeine showed coherent variation in itch scores over time, with highly significant differences from controls ²⁵
	NRS†	Scale ranges from 0 (no pruritus) to 10 (the worst imaginable pruritus). Subjects assign a numerical score to represent the intensity of itch ²³	Concurrent validity demonstrated by high correlation with VAS and VRS ($r > 0.8$, $P < 0.01$) ^{23,28}
	VRS‡	Severity descriptions are associated with numerical values, eg, 0 = none, 1 = mild, 2 = moderate, and 3 = severe/intense. Subjects choose 1 of 4 levels of itch intensity ²³	Concurrent validity demonstrated by high correlation with VAS ($r > 0.7$, $P < 0.01$) and NRS ($r > 0.8$, $P < 0.01$) ^{23,28}
	6-Point Pruritus Assessment Tool	Severity descriptions are associated with numerical values at the extremes, eg, 0 = none and 5 = severe. Intermediate steps of the scale defined by numbers 1–4 without any associated verbal descriptors. Subjects select 1 of 6 levels of itch intensity ⁴²	Construct validity demonstrated by correlation between PASI scores and pruritus assessment intensity in patients treated with etanercept (weeks 2-4, $0.25 \leq r \leq 0.46$; weeks 8-12, $0.56 \leq r \leq 0.67$; $P < 0.001$ for all time points) ⁴²
Mechanical rating scales	SymTrack	Portable VAS data-logger device with a lever for rating itch intensity along a 100-mm VAS scale, a switch for indicating “awake” vs “sleep” mode, compliance button to indicate the presence of the subject, “event” marker to indicate intake of medications or other relevant events. In “awake” mode, a signal occurs every hour to remind patient to rate itch intensity. Allows continuous recording of VAS score from 11 d to 16 wk, depending on the sampling rate (adjustable). Weight 350 g, including a 9-V battery; size $142 \times 90 \times 25$ mm ³⁴	Concurrent validity demonstrated by correlation between daily continuous SymTrack itch scores and retrospective VAS itch scores ($r = 0.8$) ^{34,35}
	ActiWatch Score	Wristwatch that combines standard activity monitoring with an NRS for the patient to record subjective inputs on a user-adjustable scale from 0 (no pruritus) to 15 (the worst pruritus imaginable). Includes an automated alarm to prompt patient to enter numerical rating score at predetermined intervals. Allows continuous recording of NRS score for 21 d. Weight 25 g (with band); size $37 \times 35 \times 12$ mm. ³⁸	Unknown

*Component of the SCORAD and Patient-Oriented SCORAD.

†Component of the Skin Detective Questionnaire.

‡Component of the Self-administered EASI, Psoriasis-Symptom Inventory, and National Psoriasis Foundation Psoriasis Score.

scales represent a simple and rapid estimation of itch intensity and are therefore widely used in clinical trials. They also exist in ambulatory electronic formats such as the ActiWatch Score (Philips Respironics, Murrysville, PA) and SymTrack (Autenta AB, Uppsala, Sweden), although these instruments are rarely used to assess itch severity.

The VAS is the most frequently used instrument in clinical and experimental pruritus research. In contrast to other graphic rating scales, no labels or numbers are used to define the intermediate steps of the scales, although the extremes are defined as “no itch” and “worst itch imaginable.”²³ Yet the validity of VAS for rating of itch has been only partially supported by research studies on experimentally induced itch in healthy subjects. The VAS has been used to support the efficacy of topical strontium in decreasing the duration and intensity of cowhage-induced itch.²⁴ In addition, randomized prick testing with histamine and codeine demonstrated coherent variation in VAS itch scores.²⁵ However, VAS itch scores decreased on repeat skin prick testing, raising concerns that familiarity with the testing procedure may lessen anxiety levels and influence the precision of VAS scoring.²⁵ In 2 studies by Magerl et al^{26,27} and Wahlgren et al,^{26,27} a dose-response relationship between increasing transdermal histamine iontophoretic stimulation and itch severity was demonstrated. In both studies, subjects were cued to estimate itch severity in response to transdermal histamine iontophoretic stimulation of increasing intensities.^{26,27} However, when histamine stimuli were presented in the reverse order, the study by Wahlgren et al^{26,27} found there was no dose-response relationship, highlighting the challenges in subjective reporting of perceived itch.²⁷ Nonetheless, a high correlation between VAS, NRS, and VRS in patients with chronic itch due to a variety of medical conditions²³ as well as pruritic dermatoses²⁸ has been used to support the convergent validity of these subjective scales.

Evidence suggests that some patients may have difficulty translating the subjective symptom of pruritus into a specific point on a blank line. In a prospective study assessing the validity and reliability of self-reported pruritus intensity on rating scales, 471 patients with chronic pruritus due to a variety of medical conditions were asked to complete the VAS, NRS, and VRS on 3 separate occasions.²³ The number of missing values, or incomplete scales, was highest with the VAS assessment, suggesting that the VAS is more difficult to use than other graphic rating tools.²³ Another study evaluating the reliability and validity of the VAS instrument in patients with pruritic dermatoses found that patients who stated that they did not itch still recorded a VAS itch level other than 0, indicating that some patients may not grasp how to document their itch level on a VAS.²⁸ Studies have also shown that subjects tend to cluster their ratings at the midpoint and the extremes of the VAS, raising concerns about the sensitivity and reliability of this purportedly continuous scale.^{29,30} A recent consensus statement raised questions regarding whether daily or weekly VAS assessments are more accurate, if VAS scores reflect daytime or both day- and night-time itch, and if subjects should be blinded from their previous VAS score before rating current itch intensity.³¹ While horizontal VAS has been shown to produce a more uniform distribution of scores than a vertical VAS³²

and lines greater than or equal to 100 mm have been found to yield the least error variance,³³ a standardized graphic representation of the instrument does not exist.³¹

SymTrack is a computerized ambulatory version of VAS for the continuous recording of subjective symptom intensity (Table 1).² When the VAS recording on the data-logger device is completed, the data are transferred into a computer for evaluation. The data are displayed graphically, and the software computes select variables such as median and average itch intensity and the percentage of time without itching. While this ambulatory method of itch assessment provides a detailed and graphic recording of itch severity over an extended period, the device is cumbersome to wear, limiting its usability.³⁴

Validity of the SymTrack has been supported by demonstrating a positive correlation with conventional VAS data. Evidence suggests that patients can rate itch retrospectively and adequately for periods up to 72 hours.^{34,35} However, SymTrack recordings were not found to be consistent with global retrospective assessments of diurnal itch fluctuations, illustrating the difficulty of using rating scales to recall itch over longer periods.³⁴ Nonetheless, studies have demonstrated that this ambulatory method for recording itch may be a useful tool to assess clinical itch and antipruritic effect of drugs in short-term trials. In 2 double-blind crossover studies, SymTrack recorded itch intensity was significantly lower in AD patients during active treatment with topical betamethasone dipropionate and oral cyclosporine A.^{36,37} The SymTrack ambulatory computerized system may reduce memory bias associated with VAS and have the capacity to more reliably record treatment response. Compliance with this potentially cumbersome device may limit its use in longer-term trials.

The NRS and VRS are also commonly used to assess itch intensity (Table 1). For the NRS, patients are asked to assign a numerical score representing the intensity of itch on a scale from 0 (no pruritus) to 10 (the worst imaginable pruritus). Similar to the SymTrack for VAS, ActiWatch Score wristwatch provides an ambulatory recording of NRS and may reduce memory bias associated with the paper format of NRS.³⁸ The VRS attempts to associate severity descriptions with a numerical value (eg, 0 = none, 1 = mild, 2 = moderate, and 3 = severe/intense). The VRS and NRS have been validated in patients with chronic itch because of a variety of medical conditions as well as pruritic dermatoses by demonstrating a high correlation with VAS.^{23,28} With regard to interscale validation, Reich and colleagues²⁸ have demonstrated that patients rated their pruritus significantly higher on NRS than with VAS.

A hybrid of the NRS and VRS rating scales was recently used to create the 6-point pruritus assessment tool for patients with psoriasis (Table 1). The 6-point pruritus assessment tool has been utilized in several phase III, randomized controlled trials of etanercept for the treatment of psoriasis.^{39–41} Using data from one of the trials, the 6-point pruritus assessment tool was shown to be a valid determinant of pruritus intensity in patients with moderate to severe plaque psoriasis.^{39,42} Improvements in pruritus assessment scores correlated with expected improvements in Psoriasis

Area Severity Index (PASI) for patients on active treatment with etanercept, providing evidence of construct validity. The test-retest reliability of the instrument was also determined to be high. However, the 6-point pruritus assessment tool has limited applicability, because to date it has not been validated in other pruritic skin diseases.⁴²

The aforementioned assessment scales are the most commonly used tools for measurement of pruritus intensity in clinical and behavioral studies. A combination of rating scales may be used in a clinical setting in order to internally test the consistency of data.⁴³ The VAS or NRS should be used in combination with the VRS.³ The itch rating scales may be supplemented by supportive scales that assess quality of life, anxiety, depression, and sleep quality.³ Prior to administering these scales, clinicians should train subjects on their proper use.²³ Although rarely used, the electronic rating scales (SymTrack and ActiWatch Score) may be preferable to paper-based scales, as they are ambulatory and allow for itch intensity to be recorded in real time. Therefore, they are less dependent on memory bias associated with recalling itch intensity retrospectively. Moreover, these electronic ambulatory tools can report greater fluctuations in itch intensity.

The rating scales are simple to administer and sensitive, but the applicability of these scales is challenged by a number of observations. They may be dependent on patient recall, are not suitable for people with motor or cognitive impairments, and may be susceptible to memory recall bias. The subjective nature of these scales makes them prone to psychological, sociodemographic, and cultural influences, which may or may not be related to dermatologic pathology.^{12,44} Variations in itch severity comparing metrics of sex and ethnicity have also been reported.^{28,45} Moreover, whereas studies have demonstrated reliability and concurrent validity of the VAS with other subjective scales,^{23,28} others have shown dissociation with objective actigraph scores.⁴⁻⁹

Nonetheless, VAS for itch intensity has been incorporated into several disease-specific measures for AD, including SCORAD, Patient-Oriented SCORAD, and Self-administered Eczema Area and Severity Index.^{11,46,47} It has been suggested that the objective SCORAD index be used in clinical trials, because social and cultural factors may influence the grading of itch using the VAS component of the scoring system.^{11,48,49} The NRS has also been incorporated in the Skin Detective questionnaire to assess itch severity in patients with AD.⁵⁰ The VRS has been incorporated in the Psoriasis Symptom Inventory and the National Psoriasis Foundation Psoriasis Score to evaluate itch severity in patients with psoriasis.^{10,51}

In the validation study for the 6-point pruritus self-assessment tool, the correlation between PASI and itch scores enhanced over time. Earlier time points demonstrated low to moderate correlation.⁴² Time was an unexpected variable influencing the power of the correlation between PASI and itch scores. Whereas some studies have demonstrated a correlation between VAS and PASI,^{18,52} others have shown that VAS,^{17,53-56} a 10-point pruritus self-assessment tool,¹² and other itch metrics¹⁶ do not correlate with psoriasis

severity assessed by PASI. This suggests that subjective reporting of itch severity may be independent of objective clinical disease severity measures for psoriasis. Further investigation is needed to evaluate the scientific quality and construct validity of itch rating scales.

The itch scores obtained from subjective rating scales challenge accepted thought regarding the intensity of itch in psoriasis versus AD. Whereas pruritus is regarded as the predominant feature of AD,⁵⁷ the frequency and intensity of itch in psoriasis can vary and do not consistently correlate with disease severity.^{56,58,59} The physical manifestation of psoriasis adversely influences self-esteem and social interaction and oftentimes has a greater negative impact on patient well-being and quality of life than itching.⁶⁰⁻⁶² Early seminal manuscripts on biologic therapies for psoriasis make no mention of itch or pruritus.⁶³⁻⁶⁵ Yet, in a recent study evaluating itch severity in moderate to severe psoriasis, 70% of psoriasis patients reported having high levels of itch intensity.⁵⁵ Three randomized controlled trials evaluating the efficacy of adalimumab in patients with moderate to severe psoriasis reported baseline VAS scores ranging from 7.3 to 7.8 out of 10.²¹ In addition, 79% of patients with psoriasis receiving etanercept in the 12-week trial reported baseline itch in the range of 3 to 5 (moderate to severe) on the 6-point pruritus assessment tool.³⁹ These itch intensity ratings are similar to or greater than ratings reported by patients with moderate to severe AD.^{14,15} These findings are inconsistent with the results from studies by Evers et al^{22,66} and O'Neill et al^{22,66} in which patients with AD reported significantly higher levels of itching and greater likelihood to experience itch than patients with psoriasis. Although it is possible that there are distinct subpopulations of psoriasis patients with variable itch frequency and severity,^{58,59} these conflicting results raise questions regarding the validity of our current measurement tools.

Further investigation of these subjective rating scales is warranted, because they influence our therapeutic decisions and understanding of the role of pruritus in psoriasis and other skin diseases.

Questionnaires

Structured questionnaires are often used to measure itch and evaluate its impact on functional and psychosocial dimensions. They also serve as an important tool to aid in the differential diagnosis of pruritic skin disease.⁶⁷

Pruritus-specific quality-of-life instrument (ItchyQoL) is a questionnaire that evaluates impairment in quality of life in patients with chronic pruritus, irrespective of underlying disease (Table 2).⁶⁸ Construct validity was demonstrated by comparing the subscale scores for symptoms, functioning, and emotion with self-reported pruritus severity and pruritus frequency.⁶⁸ Discriminant validity was shown by comparing differences in the number of insensitive items (ie, those where >50% of participants chose "never" as their response) in the pruritus-specific quality-of-life instrument compared with the Skindex 29 and Skindex 16.⁶⁸ High internal consistency and reproducibility were also

TABLE 2. Referenced Assessment of Pruritus: Questionnaires for Measuring Itch Intensity

Name	Description	Validation Method
Pruritus-Specific Quality of Life Instrument (ItchyQoL)	22-Item questionnaire that queries 3 dimensions: symptoms, functioning, and emotions. Frequency and impact of symptoms on quality of life are each ranked on 5-point scales ⁶³	Construct validity demonstrated by comparing the subscale scores with self-reported pruritus severity and pruritus frequency levels ($P < 0.05$). Discriminant validity demonstrated by fewer insensitive items than Skindex 29 and Skindex 16 ⁶³
Questionnaire for Assessment of Pruritus	9-Item questionnaire that includes medical and pruritus history, antipruritic medications, impact of pruritus on sleep and daily activities/habits, coping and quality-of-life measures, itch sensation and affective descriptors, VAS assessment of itch intensity at various times, and extent of body surface area involvement ⁶⁴	Construct validity demonstrated by correlating the affective score with the VAS during maximal itch intensity ($r = 0.58$, $P < 0.001$) ⁶⁴
Itch Severity Scale	7-Item questionnaire that assesses itch frequency, itch sensation and affective descriptors, body surface area involved, itch intensity at various times using the Likert scale, and impact of pruritus on sleep, mood, sexual desire, and sexual function ⁶⁵	Construct validity demonstrated by correlation with DLQI scores ($r = 0.219$ - 0.546) and RAND-36 Health Status Inventory score (mental health composite, $r = -0.102$ to -0.414 ; physical health composite, $r = -0.102$ to 0.414) ⁶⁵
Eppendorf Itch Questionnaire	Form 1 presents 80 randomized descriptors. Sensory items are grouped on the left side, and more affective or emotional items of different intensity values are found on the right side. Every item is scored within a range of 0 ("not true") to 4 ("describes exactly my itch sensation"). Form 2 assesses itch frequency and localization, scratching behavior, anti-itch measures, and VAS assessment of itch intensity ⁶⁷	Construct validity demonstrated by comparing components of the questionnaire that assess extent of "suffering" and "phasic intensity" with disease severity as determined by the SCORAD index ("suffering," $r = 0.59$; "phasic intensity" = 0.38) ⁶⁷
Pruritus Grading System	4-Item questionnaire that rates symptoms and objective skin findings. Includes an assessment of various itch parameters, including distribution, frequency, severity of itch, and quality of sleep. Scores range from 0 (no pruritus) to 19 (most severe pruritus) ⁶⁸	Unknown
Patient Benefit Index for Pruritus	Two-part questionnaire consisting of "Patient Needs Questionnaire" and "Patient Benefit Questionnaire." Prior to therapy, patient rates the importance of 27 predefined treatment goals, and during or following therapy, the patient rates the extent to which these goals have been achieved on a Likert scale ranging from 0 to 4 ⁷⁰	Convergent validity with change in pruritus intensity as measured by NRS ($r = 0.57$, $P < 0.001$) and DLQI after therapy ($r = 0.41$, $P < 0.05$). ⁷⁰
5-D Itch Scale	Brief, single-page instrument that evaluates 5 itch dimensions, including degree, duration, progression, disability, and distribution. Scores range between 5 (no pruritus) and 25 (most severe pruritus) ⁷¹	Convergent validity with VAS on 3 separate occasions, including baseline, 3-d repeat, and 6 wk ($r > 0.7$, $P < 0.001$) ⁷¹

demonstrated.⁶⁸ However, a statistically significant increase in total scores with self-reported worsening of pruritus was not found.⁶⁸ The value of the ItchyQoL has not yet been conclusively evaluated.³

The Questionnaire for the Assessment of Pruritus and Itch Severity Scale are multidimensional questionnaires that assess itch based on descriptor scales that attempt to quantify the frequency, duration, quality, extent, severity of itching, and its effect on mental and physical functioning, appetite, psychosocial state, and sexual desire (Table 2). These instruments have been assessed for internal consistency and retest reliability and validated against the VAS

for pruritus intensity and RAND-36/Dermatology Life Quality Index (DLQI), respectively.^{69,70} Whereas the Itch Severity Scale was validated in patients with chronic plaque psoriasis,⁷⁰ the Questionnaire for the Assessment of Pruritus was validated only in patients with chronic kidney disease.⁶⁹

The Eppendorf Itch Questionnaire (EIQ) is a multidimensional questionnaire that collects detailed information on the patient's subjective assessment of pruritus by using a comprehensive list of 80 sensory and affective descriptors (Table 2).⁷¹ The German and English versions have been used to analyze the subjective itch assessment in patients with acute exacerbation of atopic eczema.⁷²

Components of the questionnaire that assess extent of “suffering” (eg, unbearable, terrible, excruciating, etc) and “phasic intensity” (eg, sharp, stinging, and burning qualities of sensation) weakly correlated with disease severity as determined by the SCORAD index, with $r = 0.47$ and $r = 0.38$, respectively. Of note, the Spearman correlation coefficient for SCORAD and the questionnaire’s VAS itch score was low ($r = 0.33$), but statistically significant.⁷²

Szepietowski⁷³ proposed the Pruritus Grading System (PGS) questionnaire for the evaluation of pruritus in uremic patients (Table 2). PGS is a 4-item questionnaire that assesses itch severity, frequency, distribution, and sleep quality. Although to our knowledge it has not been formally validated against other scales or questionnaires, PGS has been used to characterize pruritus in patients with AD, psoriasis, and end-stage renal disease.^{18,74}

In 2009, Blome and colleagues⁷⁵ introduced the Patient Benefit Index for Pruritus PBI-P questionnaire for assessment of pruritus in clinical practice and trials (Table 2). Prior to therapy, the patient rates the importance of predefined treatment goals, and during or after therapy, the patient rates the extent to which these goals have been achieved.⁷⁵ PBI-P has been evaluated for feasibility and validated by demonstrating a highly significant correlation with the NRS rating for pruritus intensity and DLQI.⁷⁵ The instrument has been validated in patients with chronic pruritus from unspecified dermatological, systemic, neurologic, and multifactorial diseases, of unknown origin.⁷⁵ According to the International Working Group on Pruritus Research and the IFSI, the PBI-P is an indispensable tool in clinical trials and can be highly valuable for setting therapy goals in clinical practice.^{3,43}

The 5-D itch scale is a multidimensional questionnaire that was developed to assess the therapeutic benefit of antipruritic therapies in clinical trials (Table 2). Elman and colleagues⁷⁶ demonstrated that 5-D was a reliable and valid measure of itch in patients with chronic pruritus, including those with unspecified primary dermatologic skin disease, burn wounds, HIV, hepatobiliary disease, or chronic kidney disease. The 5-D score was found to correlate strongly with VAS at baseline, 3-day repeat, and 6-week follow-up, providing evidence for convergent validity. In addition, the test-retest reliability was high between days 1 and 3 in untreated individuals. 5-D was also shown to be responsive to change, as the instrument detected significant changes in pruritus over the 6-week follow-up period. The correlation between 5-D and observed changes in VAS suggests that the 5-D itch scale may be useful to monitor the long-term course of pruritus. Yet, there are currently no randomized controlled trials that have used the 5-D itch scale. Therefore, the utility of the 5-D scale has yet to be determined.³

Subjective structured questionnaires play an important role in assessing the functional, psychosocial, and emotional impact of pruritus. Rating scales such as the VAS do not sufficiently capture the impact of a treatment regimen.⁶⁷ While structured questionnaires provide important multifaceted information about patient life experience with pruritus, the results are difficult to quantify. Furthermore, with the exception of components of the EIQ, they have not been shown to correlate to disease activity. In addition,

questionnaires may be influenced by sex, age, educational background, and social and psychological factors.^{44,77,78} Such instruments are often lengthy, require psychometric expertise, and are not suited for repeated assessments. In addition, many of these questionnaires, with the exception of the 5-D itch scale, have not been shown to detect changes in itch over time and therefore have limited application.⁶⁷ Moreover, these instruments have yet to be validated in clinical studies and because of their heterogeneity may be difficult to compare. In addition, these questionnaires require further validation in patients with AD and psoriasis before they can be recommended in these patient populations. Consequently, there is currently no internationally accepted questionnaire for assessing itch severity and its contingent psychosocial and emotional impact.³ According to the special interest group of the IFSI, future studies should focus on disease- and population-specific questionnaire validation.⁶⁷

Objective Measurements of Itch

Although itch sensation is an inherently subjective phenomenon, recent advances in technology have allowed for the quantification of itch through measurement of itch threshold. The measurement of scratching through physical manifestations of scratching, video surveillance, actigraphy, and acoustic devices also provides valuable objective data about itch intensity.

Skin Manifestations

Scratching can result in physical signs such as excoriations and lichenification, which can provide valuable objective evidence of itch severity. These skin manifestations are included in several scoring systems for AD, including SCORAD, EASI, Six Area Six Sign Atopic Dermatitis, and Three-Item Severity.⁷⁹ In these scoring systems, a 4-point VRS (0 = absent, 1 = mild, 2 = moderate, 3 = severe) is used to grade the severity of lichenification and excoriation. The SCORAD has been shown to correlate with transepidermal water loss, skin hydration, and stratum corneum integrity as well as global assessments of disease severity, providing evidence of construct and criterion validity.^{80,81} The SCORAD has been used to validate various other scoring systems for AD, including the EASI and Three-Item Severity.^{82,83} However, several studies using the SCORAD and the Six Area Six Sign Atopic Dermatitis have shown significant interobserver variability in the grading of lichenification and excoriation.^{11,84–88} A recent systematic review concluded that EASI and SCORAD are the best instruments to assess the clinical signs of AD and are recommended for use in future clinical trials.⁷⁹ A validated scoring system for assessment of physical signs associated with pruritus in patients with psoriasis does not currently exist.

Video Surveillance

Video recording of subjects with pruritic skin disease enables direct observation of scratch activity, allowing for the calculation of total scratching time (TST) or the sum of the duration of all the

scratching bouts. Ebata et al^{89,90} defined an observed bout of scratching as an apparent action of rubbing or scratching to any part of the body with a rhythmical movement using hands, fingers, or feet lasting longer than 5 seconds. Scratching bouts with intervals between them of less than 3 seconds were also considered a single bout.^{89,90} The ratio of TST divided by total recording time (TST%) can be used as objective index of scratch activity. Ebata et al⁸⁹ demonstrated that nocturnal videotape observation could be used to differentiate scratch activity in patients with mildly itchy skin disease versus healthy volunteers. In addition, the authors found that clinical improvement correlated with reduction in TST following anti-itch therapy, supporting the validity of this modality in assessing itch severity. However, video surveillance is time consuming and not practical for direct use in clinical trials and longitudinal assessment of itch.

Wrist Actigraphy

A wrist actigraph is a portable compact device, similar to the early prurimeter scratch detection device that uses microaccelerometers to detect scratch activity.⁹¹ Using actigraphy to detect scratching affords several advantages for the evaluation of itch. The devices are lightweight, allow for longitudinal recording, and are usable in the patient's natural home environment. Signal output can be easily transmitted digitally, opening up the possibility of home monitoring of disease activity and possible anticipation of disease exacerbation.

ActiWatch Plus (Cambridge Neurotechnology, Cambridge, UK) and ActiTrac (IM Systems, Baltimore, Md) have been used to detect scratching activity in patients with AD.^{4,5,7,90} Both actigraphic devices are programmed to collect data in fixed epochs (time intervals). Equipped with 2-axial accelerometers, these devices can record physical motion in 2 planes (up-and-down and back-and-forth). Ebata et al^{4,90} and Benjamin et al⁴ found a high correlation between the accelerometer results and video analysis, validating the use of accelerometers as a measure of scratching activity in patients with AD. Ebata et al⁹⁰ defined scratching using the criteria described above, whereas Benjamin et al⁴ defined scratching as observed rhythmic movements greater than 1 Hz without accompanying movements. Moreover, accelerometer scores in AD patients were statistically significantly higher than scores in subjects without itchy skin disease, supporting the sensitivity of these devices in detecting scratch activity.

Another actigraphic device, the DigiTrac (IM Systems) is equipped with a triaxial accelerometer that allows for the detection of movement in all 3 planes and collects data in short epochs of 0.025 seconds. The DigiTrac provides qualitative information through fast-Fourier-transformation 3-dimensional contourgraphy and average spectral plots. The contour can be assessed to determine different patterns of wrist movements in patients with AD and other itchy conditions.⁹² DigiTrac results have been shown to correlate with other objective disease parameters of the SCORAD index in patients with AD, such as the lichenification and extent of disease.⁹ In another study, Hon and investigators⁹³ also found a correlation

between DigiTrac reduction in scratching activity and improvement in SCORAD score following treatment with tacrolimus in children with AD. Preliminary evidence supports the potential role of actigraphy in providing objective documentation of itch in therapeutic clinical trials.

While actigraphy shows potential for measuring scratching, the validity of the data obtained from actigraphic devices has been challenged by a number of observations. In studies validating actigraphy for itch severity, activities unassociated with itch or scratch confounded the actigraphic data.⁹⁴ Although several different methods were utilized to discriminate scratching activity from other movements, none was sufficiently sensitive to distinguish scratch from other activities.⁹⁴ The methods rely on the correlation between mean accelerometer activity and amount of scratching to estimate total scratch time and disease severity.⁹⁴ In addition, whereas some studies have shown strong correlations between actigraphy and the course of disease activity,^{6,9,89,90,93} other studies have failed to demonstrate a relationship.^{5,95} A multicenter randomized controlled trial of ion-exchange water softeners for the treatment of eczema in children found a low correlation between overnight actigraphy and Six Area Six Sign Score scores.⁹⁵ The discordance may be attributed to the device's inability to discriminate scratching from other movement, erroneously inflating accelerometer scores. In addition, using accelerometer data as an objective surrogate for disease activity may be complicated by broad interindividual variation in scratching. Itchy patients may not always respond with scratching, and nonitchy patients may scratch nevertheless. These findings may in part explain the recent evidence that objective assessment of scratching using actigraphic devices may not correlate with subjective measures of itch intensity.⁴⁻⁹

Recently, a novel approach to actigraphy-based scratch detection in the presence of confounding nighttime activity was developed and validated.⁹⁶ The approach was validated in 12 healthy volunteers who were instructed to scratch, simulate restless sleep, and to walk, with an actigraphic device (PAM-RL; Philips Respironics, Bend, Ore) placed on their wrists. A clustering technique (*k* means), which used 4 features derived from actigraphic data, was used to separate periods of scratching from restless sleep and walking, the 2 most prominent confounding nighttime activities.⁹⁶ The results were recently extended to use the same features as independent variables in a logistic regression model that allows for direct estimation of the conditional probability of scratching for each epoch.⁹⁴ The enhanced approach has both high sensitivity (0.96) and specificity (0.92) for identifying scratch, outperforming all competing actigraphy-based approaches. The proposed methodology for analysis of actigraphic data has yet to be validated in subjects with itchy skin diseases.

Acoustic Devices

A wrist-worn sound detector has also been recently developed to objectively quantify scratching behavior.⁹⁷ This novel device has

the ability to specifically detect bone-conducted scratching sounds, which are transmitted to a piezoelectric sensor on the wrist.⁹⁷ The data are automatically processed and evaluated to detect scratching movement using specific software based on the periodicity and energy of the signal. A high correlation ($r = 0.98$) was demonstrated between the sound-based scratching evaluation system and video-based analysis of nocturnal scratching in patients with AD and healthy volunteers.⁹⁷ Patients with AD were found to have significantly higher scratching rates compared with healthy volunteers, supporting the sensitivity of the acoustic device in detecting scratch activity.⁹⁷ Although the sensitivity and specificity of the device in detecting scratch were reportedly high, the device has yet to be tested in a clinical setting (Table 3).

CONCLUSIONS

Patient-reported outcomes play an important role in the evaluation of therapies in randomized controlled trials as well as in the assessment of treatment efficacy in clinical practice.⁹⁸ However, the subjective nature of the sensation of itch makes it difficult to consistently and accurately quantify through patient self-report. The use of subjective questionnaires and rating scales relies on the assumption that the subject is able to relate their experience of itch accurately. However, itch and scratch may not be a conscious activity (eg, at night) and even when conscious may be poorly remembered. In addition, questionnaires and rating scales currently in use do not take into account the psychosocial, demographic, and cultural influences that impact one's self-report of pruritus intensity.^{28,45}

TABLE 3. Advantage(s) and Disadvantage(s) of Itch Assessment Methods

Category	Advantage(s)	Disadvantage(s)
Manual rating scales	Simple and rapid estimation of itch intensity	Standardized graphical representations and guidelines for methods of use have not yet been established Prone to psychological, sociodemographic, and cultural influences Dependent on patient recall Not suitable for people with motor or cognitive impairments VAS may be difficult for patients to understand Scales should be used in combination with other rating scales for accurate itch assessment
Mechanical rating scales	Ambulatory Reduces memory bias and allows for detection of greater fluctuations in itch intensity Allows itch intensity to be recorded in real time in natural home environment Enables continuous subjective scoring of itch intensity for extended period	SymTrack cumbersome to wear, limiting compliance and usability ActiWatch Score has not been validated in patients with itchy skin disease
Questionnaires	Provides multifaceted information about patient life experience with pruritus	Results are difficult to quantify May be influenced by sex, age, educational background, and social and psychological factors Lengthy and are not suited for repeated assessments Most have not been demonstrated to detect changes in itch over time and therefore have limited application
Video surveillance	Enables direct observation of scratch activity	Intrusive Time-consuming to analyze scratching activity May be influenced by inter-individual variation in scratch response to itch
Wrist actigraphy and acoustic devices	Ambulatory Allows for longitudinal recording of scratch activity in natural home environment Provides qualitative and quantitative information about scratch activity	Actigraphic algorithm for scratch detection has not been validated in patients with itchy skin disease May be influenced by interindividual variation in scratch response to itch

There are major limitations to the scientific quality of these subjective methods, and therefore, there is no widely accepted standardized and validated method for measuring pruritus.³ While it can be demonstrated that one subjective scale or questionnaire correlates with another, ultimately neither represents a criterion standard objective measurement of itch intensity.

Moreover, equivalent levels of reported itch in patients with psoriasis and AD create pause in our understanding of itch assessment in these disease states.^{12,14,17,20,21,55} Although it is possible that the intensity of itching in psoriasis has been greatly underestimated in the dermatology literature, the similarity of itch intensity levels in psoriasis and AD patients with comparable disease severity raises questions about the validity of these widely used tools. Nonetheless, these questionnaires and rating scales are commonly used in pharmaceutical research to authenticate the value of medications in treating pruritus associated with psoriasis, AD, and other skin diseases.

Scratching as a measurement of itch has also been challenged. Itchy patients may not always respond with scratching, and nonitchy patients may scratch nevertheless. To reflect this subtlety, Savin¹ proposed the adoption of a new definition of itch as “a sensation that, if sufficiently strong, will provoke scratching or the desire to scratch.” Several investigators have demonstrated that even patients with mild skin disease apparently scratched more in response to itch compared with healthy volunteers.^{4,5,89,90,99} The measurement of scratch represents an objective and sensitive method of evaluation of itch intensity that has recently been made feasible by actigraphy and acoustic devices. The recent advances in the analysis of actigraphic and acoustic data for detection of scratch pave the road for the development of a valid objective criterion against which other pruritus evaluation tools can be validated.

Many devices are able to provide data on the intensity of scratch in addition to scratch frequency, allowing for interesting avenues of research into the characterization of itch in different skin diseases. Moreover, the usability of actigraphic and acoustic data allows for longitudinal measurement of disease severity. This represents a major advantage over subjective scales, which were largely developed as point-in-time assessments. The sensitivity of subjective rating scale instruments in detecting clinically relevant changes over time has yet to be established.²³ The longitudinal recording of itch is essential, because the symptom severity fluctuates in response to many factors, such as time of day, mental state, and activity level. Home monitoring of itch severity would also provide a window into factors that lead to symptom exacerbation, permitting a personalized, targeted approach to treatment. Nonetheless, patient-reported outcomes play an indispensable role in the evaluation of itch intensity, and these subjective methods of itch assessment require further refinement and validation for use in drug testing and clinical practice.

Valid quantitative techniques for the assessment of itch are of considerable value for the evaluation of therapeutic regimens for inflammatory skin disease. Because of the subjective nature of itch and its unique and variable impact on an individual's quality of life,

a combination of subjective and objective tools may provide the best window into this important symptom of skin disease. Further exploration of the correlation between objective and subjective measures of pruritus is warranted to develop a validated set of instruments suitable for use in clinical trials.

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