

Approach to the Assessment and Management of Adult Patients With Atopic Dermatitis: A Consensus Document.

Section II: Tools for Assessing the Severity of Atopic Dermatitis

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Abstract

Clinicians rely on clinical measures to define the severity of atopic dermatitis and assess outcomes of therapy. These measures can be objective (ie, physician assessments of disease severity) or subjective (ie, patient-reported symptoms and quality of life outcomes). In this review, the most commonly used tools for assessing atopic dermatitis severity in adult patients are presented and compared. These include Eczema Area and Severity Index (EASI); SCORing Atopic Dermatitis (SCORAD); Physician Global Assessment (PGA); body surface area (BSA); Atopic Dermatitis Severity Index (ADSI); Six Area, Six Sign Atopic Dermatitis (SASSAD); Patient Oriented Eczema Measure (POEM); Dermatology Life Quality Index (DLQI); and pruritus Numerical Rating Scale (NRS). Available severity strata for the tools are summarized, although the use of severity strata in clinical practice is not recommended. Since both objective and subjective assessments of disease severity are important to assess, consideration of clinical characteristics such as disease recurrence or persistence, as well as location of the affected areas, should be considered in the overall judgement of disease severity and consideration of therapy choice.

Keywords

atopic dermatitis, assessment tools, severity, patient-reported outcomes, investigator-reported outcomes

There are no specific diagnostic tests to define atopic dermatitis (AD) severity. Therefore, clinicians rely on clinical measures to define severity of disease and assess outcomes of therapy. These measures can be objective (ie, physician assessments of disease severity) or subjective (ie, patient-reported symptoms and quality of life [QoL] outcomes).¹ There are many outcome measures being used in the literature; however, most have never been validated and are largely heterogeneous in nature, making comparisons between clinical trials difficult.² Importantly, there is no gold standard for defining a mild, moderate, or severe patient; however, it is important to define these patient groups both for clinical trials and for practical management considerations.

A systematic review of randomized controlled trials (RCTs) conducted on patients with AD between 2010 and 2015 found 62 different disease severity measures and 28 different QoL measures, with most published QoL measures having been used only once.³ This reflects a rapid increase compared to a previous review, which found 20 disease severity measures and 14 QoL measures between 382 RCTs

conducted in the 15 years prior.⁴ In an effort to standardize outcome measures for AD, the Harmonising Outcome Measures for Eczema (HOME) initiative is an international group whose primary objective is to determine core outcome measures for AD research that are valid, sensitive to change, and feasible.⁵ We provide here an overview of the commonly used assessment tools and provide clinical guidance on the practical utilization of these assessments in the clinic.

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An overview of the most commonly used physician assessment tools is found in Table 1. Of these, HOME and other groups have found that Eczema Area and Severity Index (EASI) and SCORing Atopic Dermatitis (SCORAD) are the only AD-specific physician outcome measures that have been validated enough to be used in both clinical trials and in a clinic setting.^{1,2}

EASI assesses disease extent in 4 defined body regions (head and neck, torso, arms, and legs), evaluating severity of 4 clinical signs (erythema, induration/papulation, excoriation, and lichenification) on a 4-point scale and weights these factors based on the size of the anatomic area being evaluated.⁶ Extent is measured from 0 (0% involvement) to 6 (90%-100% involvement), and severity is measured from 0 (clear) to 3 (severe) for each sign. This provides a range of EASI scores from 0 to a maximum score of 72. HOME provides practical resources to help physicians calculate EASI (available at <http://www.homeforeczema.org/research/easi-for-clinical-signs.aspx>).

The assessment is well validated and assesses both disease extent and severity, and while it does not account for any patient-reported symptoms, there is good correlation of EASI with relevant QoL index measures.⁷ It is a commonly used outcome measure in clinical trials for AD.

SCORAD is a composite score that takes into account the body surface area of involvement in AD and the severity of 6 clinical signs on a 4-point scale (erythema, edema/papulation, oozing/crusting, excoriation, lichenification, and dryness), and it incorporates a patient-reported component assessing pruritus and sleep loss.⁸ Extent is measured by percent disease involvement (A), and severity is measured from 0 to 3 (B) for each sign. Subjective symptoms are scored by the patient on a visual analog scale for each of pruritus and sleep loss (C). The total score is calculated as $A/5 + 7B/2 + C$ to a maximum score of 103. A web tool to help physicians calculate SCORAD is available at <http://scorad.corti.li/>.

The composite nature allows for incorporation of both physician and patient observations. It is important to note that because of the composite scoring system, SCORAD values of greater than zero may be found in clear skin due to measures of pruritus and sleeplessness, which are not disease specific.⁹ Accordingly, the objective SCORAD (oSCORAD) measures extent and severity items only, to a maximum score of 83.

Overall, SCORAD has high inter-rater reliability and correlates well with both objective assessments such as EASI and Investigator Global Assessment (IGA), as well as with QoL measures such as the Dermatology Life Quality Index (DLQI).^{10,11} It is also supported by HOME as a validated assessment for clinical trial and clinical use. However, EASI may simply be more practical than SCORAD due to its broader adoption.

The Physician Global Assessment (PGA), also referred to as IGA in clinical trials, assesses overall disease severity at a given timepoint on a 5- or 6-point severity scale from clear to very severe disease.⁴ Clinical characteristics of erythema,

infiltration, papulation, oozing, and crusting are used as guidelines for the overall severity assessment. Most IGA scales were never validated as an outcome measure, and the Investigators' Global Atopic Dermatitis Assessment (IGADA) was the first variant of IGA that provided clear definitions to rate severity.^{2,12} In addition, multiple IGA scales exist that can make studies using this outcome difficult to interpret. Despite this, the PGA/IGA remains one of the most commonly used assessments, largely due to ease of use in the clinic and requirements by authorities for labeling.^{1,4} In fact, it is commonly used to validate other outcome measures and is considered a gold-standard clinical assessment tool.

Finally, the body surface area (BSA) measurement is a simple measure of percent body surface area involved with atopic dermatitis that does not incorporate disease severity. The lack of clear lesion borders can make this assessment challenging and variable. However, despite the lack of standardization of this tool, it is very practical and commonly used in clinic, and it has been widely used as an inclusion criterion in AD clinical trials.¹³ Furthermore, this assessment sufficiently complements the PGA in providing an accurate representation of disease extent and severity, as both are relatively quick and easy to complete in a clinic setting. This is further evidenced by the psoriasis literature, in which $BSA \times PGA$ has been shown to be a practical alternative to more complicated outcome measures and correlates well with validated assessment tools.¹⁴

Other physician assessments include the Atopic Dermatitis Severity Index (ADSI) and the Six Area, Six Sign Atopic Dermatitis (SASSAD) severity score.⁶ Both assessments incorporate disease extent and severity and are sometimes used as outcome measures in clinical trials. However, these provide no additional benefit to other objective assessments used in clinical trials such as EASI and SCORAD, nor do they provide any practical benefit over PGA and BSA.

AD affects patient QoL proportionate with disease severity.^{7,15,16} Of note, health-related QoL in AD is worse than in the general population,¹⁷ and common patient-reported symptoms in AD, including pruritus and sleep disturbance, are predictors of overall QoL.¹⁸ In addition, health-related QoL is worse if face and anogenital areas are involved.¹⁸ Therefore, proper assessment of patient QoL is important to understand overall disease impact and to assess treatment efficacy.

Patient-reported outcomes (PROs) are increasingly important in the development of new therapies. They assess the subjective impact of an intervention and, as such, are core outcome measures when evaluating efficacy.¹⁹ The addition of subjective measures corroborates objective evidence of efficacy and, for AD, includes measures of patient-reported itch, sleep disturbance, depression, anxiety, and overall QoL.^{6,20} An overview of the most commonly used PRO assessments is represented in Table 2. It is important to note that no single PRO captures all elements of disease, but

Table 1. Comparison of Relevant Physician Assessment Tools for AD.

Physician Evaluation Tools	Brief Description of Assessment	Validation Performed ^a	Inclusion of Patient-Reported Symptoms	Inclusion of Body Surface Area Involved in Rating	Inclusion of Lesion Severity in Rating	Resource	Comments
EASI	Assesses disease extent on a 7-point scale in 4 defined body regions, based on severity of 4 clinical signs on a 4-point scale, to a maximum score of 72	Y	N	Y	Y	http://www.easicalc.uk/	Less sensitive for patients with very low body surface area
SCORAD	Assesses disease extent, severity of 6 clinical signs on a 4-point scale, and patient-reported pruritus and sleep loss, to a maximum score of 103	Y	Y	Y	Y	http://scorad.corti.li/	Intraevaluator reliability is fair to good ³⁰ Interevaluator variability lies in the dimension of induration/papulation ⁴ Pruritus and especially sleep loss can be influenced by factors other than AD
PGA	Assesses overall disease severity at a given time point on a 6-point severity scale	Y ^b	N	N ^c	Y		PGA scales often use different descriptors; 5-grade and 6-grade scales exist
BSA	Assesses disease extent as a percentage of total body surface area	N	N	Y	N		Difficult to evaluate in patients with less severe lesions, especially in the presence of xerosis
ADSI	The sum of 5 items rated on a 4-point scale (0-3): erythema, excoriation, exudation, lichenification, and pruritus	N ^d	N	Y	Y		Only evaluates I area affected by AD; only usable for patients with antecubital AD Dimension of antecubital lesion may be difficult to measure in patients with more extensive AD
SASSAD	Six clinical signs are scored from 0 to 3 at each of 6 sites on the body	Y	N	Y	Y	Berth-Jones ³¹	

Abbreviations: AD, atopic dermatitis; ADSI, Atopic Dermatitis Severity Index; BSA, body surface area; EASI, Eczema Area and Severity Index; N, no; PGA, Physician Global Assessment; SASSAD, Six Area, Six Sign Atopic Dermatitis; SCORAD, SCORing Atopic Dermatitis; Y, yes.

^aAt least construct validity, interrater reliability, and intrarater reliability.

^bPerformed for some scales.¹⁰ At the time of this writing, validated Investigator Global Assessment Scale for Atopic Dermatitis (vIGA-AD) had been validated but results were not yet published.

^cSome IGA scales, such as the vIGA-AD, include some notion of BSA involved.

^dOnly construct validity and interobserver reliability.

Table 2. Comparison of Relevant Patient-Reported Outcome Assessments for AD.

Patient-Reported Outcome	Brief Description of Assessment	Validation ^a	Developed Specifically for Dermatitis Evaluation	> 1 Aspect of Disease Evaluated	Resource	Comments
POEM	Assesses severity and duration of 7 symptoms experienced over the preceding week on a 5-point scale	Y	Y	Y	https://www.nottingham.ac.uk/research/groups/cebd/resources/poem.aspx	- Validated in AD populations and in a few languages - Increasingly used in AD studies and clinical trials - Scores are correlated with disease severity - Appropriate to assess clinical trial populations - Readily incorporated into a general dermatology clinic - Utility is high in clinical studies but low in a dermatology clinic
DLQI	10-item questionnaire assessing impact on daily activities and overall quality of life	Y ^b	N	Y	http://sites.cardiff.ac.uk/dermatology/quality-of-life/dermatology-quality-of-life-index-dlqi/	- Validated in many populations and in many languages - Widely used in dermatology studies and clinical trials - Scores are correlated with disease severity - Appropriate to assess clinical trial populations - Readily incorporated into a general dermatology clinic - May be required by drug insurance plans - Utility is high in clinical studies and in dermatology clinics
Pruritus NRS	0-10 scale of patient-reported itch	Y	N	N	Ständer et al ³² http://www.pruritussymposium.de/numerical-rating-scale.html	- Validated in many populations and in many languages - Widely used in AD studies and clinical trials - Scores are correlated with disease severity - Appropriate to assess clinical trial populations - Readily incorporated into a general dermatology clinic - Utility is high in clinical studies but low in a dermatology clinic

Abbreviations: AD, atopic dermatitis; DLQI, Dermatology Life Quality Index; N, no; NRS, Numerical Rating Scale; POEM, Patient Oriented Eczema Measure; Y, yes.

^aAt least construct validity and test-retest reliability.

^bTest-retest reliability validated for Spanish version.

the addition of a PRO to an objective assessment may provide a better representation of overall disease impact.

The Patient Oriented Eczema Measure (POEM) was constructed to assess symptom severity and duration in patients

with AD, evaluating 7 symptoms experienced over the preceding week on a 5-point scale.²¹ The 7 symptoms (itch, sleep, bleeding, weeping/oozing, cracking, flaking, and dryness/roughness) were seen to be the most sensitive in a list of 10

Table 3. Proposed Severity Strata for Physician Assessment Tools and Patient-Reported Outcome Assessments in AD.

Tool	Severity Strata				κ^a
	Clear	Mild	Moderate	Severe	
EASI ^{b,13}	0	0.1-5.9	6.0-22.9	23.0-72	0.69
EASI ^{c,33}	0 0.1-1.0 ^d	1.1-7.0	7.1-21.0	21.1-50.0 50.1-72.0 ^e	0.75
mEASI ¹³	0-0.9	1-8.9	9.0-29.9	30.0-90	0.71
oSCORAD ¹³	0-7.9	8.0-23.9	24.0-37.9	38.0-83	0.70
SCORAD ¹³	0-9.9	10.0-28.9	29.0-48.9	49.0-103	0.68
PGA	0	1 ^d -2	3	4-5 ^e	Not reported
BSA ¹³	0	0.1-15.9	16.0-39.9	40.0-100	0.66
POEM ⁹	NA	0-7	8-16	17-28	0.440
DLQI ⁹	NA	0-5	6-10	11-30	0.398
Pruritus NRS ⁹	NA	0-3	4-6	7-10	0.499

Abbreviations: AD, atopic dermatitis; BSA, body surface area; DLQI, Dermatology Life Quality Index; EASI, Eczema Area and Severity Index; mEASI, modified EASI; NA, not applicable; NRS, Numerical Rating Scale; oSCORAD, objective SCORAD; PGA, Physician Global Assessment; POEM, Patient Oriented Eczema Measure; SCORAD, SCORing Atopic Dermatitis.

^aCohen's κ coefficient, a statistical measure of inter-rater agreement.

^bChopra et al.¹³

^cLeshem et al.³³

^dAlmost clear.

^eVery severe.

identified by patients as significant disease characteristics. This assessment is validated in AD and is available in several languages, correlates well with disease severity, and is readily incorporated into dermatology clinics. It demonstrates excellent psychometric properties, including internal consistency, reliability, and sensitivity to change.⁹ Importantly, this tool is being increasingly used in clinical trials and is recommended by the HOME group as the core outcome instrument for measuring patient-reported symptoms in clinical trials.⁵ However, as it does not capture all clinical signs and symptoms of AD, it should be used in conjunction with an objective assessment.

Developed in the early 1990s, the Dermatology Life Quality Index (DLQI) was designed to be a robust and easily implemented assessment of skin disease-related QoL impact.²² Each of 10 items is scored on a 4-point scale and largely assesses impact on daily activities, including work, social activities, and intimacy. The DLQI is the most commonly used QoL assessment measure in AD, is validated in several formats and languages and across many dermatologic conditions, and has good psychometric properties.^{3,22,23} The DLQI is already in clinical use for other conditions, therefore making incorporation feasible and potentially requested by payors.²³ Notwithstanding, the DLQI was designed for use in clinical trials and not for routine practice.²² In addition, it is not disease specific and may miss important features specific to AD.

Pruritus is a very important symptom of AD that has a significant impact on overall patient QoL.²⁴ Of the instruments used to quantify pruritus, the Numerical Rating Scale (NRS) is the simplest and most commonly used.^{25,26} This assessment consists of a simple rating of itch from 0 to 10, with 0 representing "no itch" and 10 representing "worst

imaginable itch." This instrument is well validated and widely used in clinical trials but not validated for clinical use.¹ It correlates well with disease severity, is easy to administer, and is practical for use in a clinic setting. Similarly, the pruritus visual analog scale (VAS) measures itch on a continuum of values by asking patients to score their itch, typically by marking a hash on a horizontal line 10 cm in length. This tool has the added advantage of capturing itch across a continuum as opposed to discrete values.^{25,26} However, there are more missed data with VAS compared to NRS, especially when these are completed by patients older than 60 years.²⁵

In order for clinicians to use these assessments effectively, it is important to understand how each scoring result reflects disease severity. Severity strata help interpret the assessments properly; however, they are not intended for routine clinical practice and as such are not recommended for the diagnosis and assessment of AD.²⁷ Table 3 represents the proposed severity strata for commonly used physician assessment tools and PRO assessments. Of note, there is some minor variation between published severity strata, particularly for EASI. In addition, a recent publication of severity strata for various PROs in AD reported a low to marginal Cohen's coefficient for proposed severity strata and self-reported AD severity, suggesting modest concordance.^{9,28} Given the proliferation of clinical studies in AD and the equally prolific appearance of outcomes measures used to assess QoL, the available data suggest a need for standardization of both objective and subjective outcomes measures.³ Overall, the available literature does not present a unified view on strata for the severity of disease.

Importantly, as both objective and subjective assessments of disease severity are important to assess, consideration of clinical characteristics such as disease recurrence or persistence, as well as location of the affected areas, should be considered in the overall judgement of disease severity and consideration of therapy choice. Boguniewicz et al²⁹ have consensus recommendations for defining moderate-to-severe AD in clinical practice, which include $\geq 10\%$ BSA or, regardless of BSA, moderate-to-severe lesions, involvement of special sites, or significant QoL impact.

In terms of practical application of these assessments, it is our expert opinion that PGA and BSA are the most practical tools for use in clinic that accurately capture the important objective elements of disease. As EASI also may be required by payors for reimbursement, health care providers should understand how to administer this assessment.

When assessing patient-reported symptoms, we recommend the use of POEM, as it captures symptoms for AD such as pruritus and sleep disturbance, which significantly affect QoL in patients with AD. DLQI or NRS may be considered, but these measures may miss some of these important features of disease. However, considering that DLQI is already in use in dermatology clinics for other conditions and that pruritus NRS is a quick and easy-to-adopt tool for use in a clinical setting, these may be considered alternatives to POEM. We recommend that if PRO instruments are not used, health care providers should ask patients about itch, sleep, and activities of daily living as these are important measures of disease severity, patient QoL, and treatment success.

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References

- Chalmers JR, Simpson E, Apfelbacher CJ, et al. Report from the fourth international consensus meeting to harmonize core outcome measures for atopic eczema/dermatitis clinical trials (HOME initiative). *Br J Dermatol*. 2016;175(1):69-79.
- Schmitt J, Langan S, Williams HC, Network E. What are the best outcome measurements for atopic eczema? A systematic review. *J Allergy Clin Immunol*. 2007;120(6):1389-1398.
- Hill MK, Pishkenari A, Braunberger TL, Armstrong AW, Dunnick CA. Recent trends in disease severity and quality of life instruments for patients with atopic dermatitis: a systematic review. *J Am Acad Dermatol*. 2016;75(5):906-917.
- Rehal B, Armstrong AW. Health outcome measures in atopic dermatitis: a systematic review of trends in disease severity and quality-of-life instruments 1985-2010. *PLoS One*. 2011;6(4):e17520.
- Schmitt J, Spuls P, Boers M, et al. Towards global consensus on outcome measures for atopic eczema research: results of the HOME II meeting. *Allergy*. 2012;67(9):1111-1117.
- Charman C, Williams H. Outcome measures of disease severity in atopic eczema. *Arch Dermatol*. 2000;136(6):763-769.
- Maksimović N, Janković S, Marinković J, Sekulović LK, Zivković Z, Spirić VT. Health-related quality of life in patients with atopic dermatitis. *J Dermatol*. 2012;39(1):42-47.
- Schallreuter KU, Levenig C, Berger J, et al. Severity scoring of atopic dermatitis: the SCORAD index. Consensus Report of the European Task Force on Atopic Dermatitis. *Dermatology*. 1993;186(1):23-31.
- Vakharia PP, Chopra R, Sacotte R, et al. Severity strata for five patient-reported outcomes in adults with atopic dermatitis. *Br J Dermatol*. 2018;178(4):925-930.
- Božek A, Reich A. Assessment of intra- and inter-rater reliability of three methods for measuring atopic dermatitis severity: EASI, objective SCORAD, and IGA. *Dermatology*. 2017;233(1):16-22.
- Kim D, Li K, Seo S, et al. Quality of life and disease severity are correlated in patients with atopic dermatitis. *J Korean Med Sci*. 2012;27(11):1327-1332.
- Schachner LA, Lamerson C, Sheehan MP, et al. Tacrolimus ointment 0.03% is safe and effective for the treatment of mild to moderate atopic dermatitis in pediatric patients: results from a randomized, double-blind, vehicle-controlled study. *Pediatrics*. 2005;116(3):e334-e342.
- Chopra R, Vakharia PP, Sacotte R, et al. Severity strata for Eczema Area and Severity Index (EASI), modified EASI, Scoring Atopic Dermatitis (SCORAD), objective SCORAD, Atopic Dermatitis Severity Index and body surface area in adolescents and adults with atopic dermatitis. *Br J Dermatol*. 2017;177(5):1316-1321.
- Walsh JA, Tan H, Valdez H, Duffin K. Comparative assessment of PASI and variations of PGA $\times$ BSA as measures of psoriasis severity. *J Psoriasis Psoriatic Arthritis*. 2017;2(4):113-118.
- Alzolibani AA. Impact of atopic dermatitis on the quality of life of Saudi children. *Saudi Med J*. 2014;35(4):391-396.
- Torreloa A, Ortizb J, Alomarc A, Rosc S, Pedrosad E, Cuervo J. Health-related quality of life, patient satisfaction, and adherence to treatment in patients with moderate or severe atopic dermatitis on maintenance therapy: the CONDA-SAT study. *Actas Dermosifiliogr*. 2013;104(5):409-417.
- Blome C, Radtke MA, Eissing L, Augustin M. Quality of life in patients with atopic dermatitis: disease burden, measurement, and treatment benefit. *Am J Clin Dermatol*. 2016;17(2):163-169.
- Beikert F, Langenbruch A, Radtke M, Kornek T, Purwins S, Augustin M. Willingness to pay and quality of life in patients with atopic dermatitis. *Arch Dermatol Res*. 2014;306(3):279-286.
- Calvert M, Blazeby J, Altman DG, Revicki DA, Moher D, Brundage MD. Reporting of patient-reported outcomes in randomized trials: the CONSORT PRO extension. *JAMA*. 2013;309(8):814-822.
- Savovic J, Jones HE, Altman DG, et al. Influence of reported study design characteristics on intervention effect estimates from randomized, controlled trials. *Ann Intern Med*. 2012;157(6):429-438.
- Charman CR, Venn AJ, Williams HC. The patient-oriented eczema measure: development and initial validation of a new

- tool for measuring atopic eczema severity from the patients' perspective. *Arch Dermatol*. 2004;140(12):1513-1519.
22. Lewis V, Finlay AY. 10 Years experience of the Dermatology Life Quality Index (DLQI). *J Invest Dermatol Symp Proc*. 2004;9(2):169-180.
23. Hehl D, Prinsen CA, Deckert S, et al. Measurement properties of adult quality-of-life measurement instruments for eczema: a systematic review. *Allergy*. 2016;71(3):358-370.
24. Chrostowska-Plak D, Reich A, Szepietowski JC. Relationship between itch and psychological status of patients with atopic dermatitis. *J Eur Acad Dermatol Venereol*. 2013;27(2):e239-e242.
25. Phan N, Blome C, Fritz F, et al. Assessment of pruritus intensity: prospective study on validity and reliability of the visual analogue scale, numerical rating scale and verbal rating scale in 471 patients with chronic pruritus. *Acta Derm Venereol*. 2012;92(5):502-507.
26. Ständer S, Augustin M, Reich A, et al. Pruritus assessment in clinical trials: consensus recommendations from the International Forum for the Study of Itch (IFSI) Special Interest Group Scoring Itch in Clinical Trials. *Acta Derm Venereol*. 2013;93(5):509-514.
27. Eichenfield LF, Tom WL, Berger TG, et al. Guidelines of care for the management of atopic dermatitis: Section 2. Management and treatment of atopic dermatitis with topical therapies. *J Am Acad Dermatol*. 2014;71(1):116-132.
28. Landis JR, Koch GG. The measurement of observer agreement for categorical data. *Biometrics*. 1977;33(1):159-174.
29. Boguniewicz M, Alexis AF, Beck LA, et al. Expert perspectives on management of moderate-to-severe atopic dermatitis: a multidisciplinary consensus addressing current and emerging therapies. *J Allergy Clin Immunol Pract*. 2017;5(6):1519-1531.
30. Hanifin JM, Thurston M, Omoto M, Cherill R, Tofte SJ, Graeber M. The Eczema Area and Severity Index (EASI): assessment of reliability in atopic dermatitis. EASI Evaluator Group. *Exp Dermatol*. 2001;10(1):11-18.
31. Berth-Jones J. Six Area, Six Sign Atopic Dermatitis (SASSAD) severity score: a simple system for monitoring disease activity in atopic dermatitis. *Br J Dermatol*. 1996;135(suppl 48):25-30.
32. Ständer S, Augustin M, Reich A, et al. Pruritus assessment in clinical trials: consensus recommendations from the International Forum for the Study of Itch (IFSI) Special Interest Group Scoring Itch in Clinical Trials. *Acta Derm Venereol*. 2013;93(5):509-514.
33. Leshem YA, Hajar T, Hanifin JM, Simpson EL. What the Eczema Area and Severity Index score tells us about the severity of atopic dermatitis: an interpretability study. *Br J Dermatol*. 2015;172(5):1353-1357.