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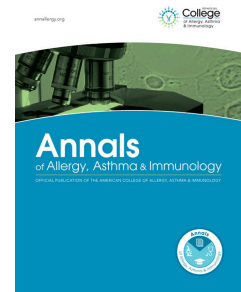
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Validation of four single-item patient-reported assessments of sleep in adult atopic dermatitis patients

Short title: Sleep in atopic dermatitis

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Background: The optimal approaches for monitoring sleep disturbances in adults with atopic dermatitis (AD) is not established. Multiple patient-reported outcome measures for AD and itch have sleep-related items. These items have not been validated previously.

Objective: Assess the measurement properties of sleep-related items from the Patient- Oriented Eczema Measure (POEM), SCORing AD (SCORAD), 5-dimensions of itch (5D) and ItchyQOL in adults with AD.

Methods: We performed a prospective dermatology practice-based study using questionnaires and evaluation by a dermatologist (n=115).

Results: There was modest overlap and weak-moderate concordance of responses to the different assessments. Regarding concurrent validity, POEM-sleep, SCORAD-sleep, 5D-sleep and ItchyQOL-sleep showed moderate correlations with each other. Regarding convergent validity, all items showed moderate correlation with total POEM, but weak correlations with Eczema Area and Severity Index (EASI), objective and total SCORAD, moderate to strong correlations with mean ItchyQOL and Dermatology Life Quality Index (DLQI), but poor or no significant correlation with Numeric Rating Scale (NRS) for worst or average itch. Regarding discriminant validity, all items showed significant and stepwise increases with increasing self-reported and physician-reported AD severity (Kruskal Wallis, $P < 0.01$ for all). Floor-effects were observed for POEM-sleep (n=53, 46.1%), SCORAD-sleep (n=28, 24.4%), 5D-sleep (n=41, 35.7%) and ItchyQOL-sleep (n=33, 28.7%); no ceiling-effects were observed.

Change in sleep-related item scores showed moderate-strong correlations with change in POEM, 5Ditch, mean ItchyQOL, DLQI, objective and total SCORAD, and EASI, but inconsistent correlations with change of itch severity.

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1 Introduction

2 Atopic dermatitis (AD) is a chronic inflammatory skin disease that greatly impacts
3 patient quality of life (QOL). AD is associated with numerous symptoms, including pruritus¹,
4 skin pain¹⁻³, blistering¹, oozing¹, anxiety⁴, and depression^{4, 5}. One particularly important
5 symptom is sleep disturbance. Sleep disturbance affects a large subset of adults with AD^{1, 6}, and
6 is associated with fatigue, impaired activities of daily living⁷, decreased performance and work
7 productivity⁸, and poor QOL^{7, 9}. It is also associated with poorer overall health^{8, 10}, increased
8 outpatient and inpatient healthcare utilization⁸, mental health and cardiovascular disorders^{5, 11-13},
9 injuries and fractures, motor vehicle accidents, and workplace injuries^{14, 15}. However, standard
10 practices or guidelines have yet to be established for screening or monitoring sleep disturbances
11 in clinical practice of AD patients.

12 Assessment of sleep disturbances in AD can be challenging in clinical practice. The gold
13 standard is polysomnography, which is costly and requires overnight assessment¹⁰. A rarely used
14 alternative is actigraphy, which uses accelerometry to measure movement during sleep. While
15 cheaper and more feasible than polysomnography, actigraphy is still fairly expensive, devices are
16 easily lost or damaged, and scoring is difficult¹⁶. Patient-reported outcome measurements
17 (PROMs) are the cheapest and most feasible options for assessing sleep disturbance in clinical
18 practice. For a measure to be clinically useful, it has to be simple to administer and score and
19 have good validity. Many existing PROMs developed for or used in AD include questions
20 related to sleep disturbance, including the Patient Oriented Eczema Measure (POEM), SCORing
21 Atopic Dermatitis (SCORAD), 5D-itch and ItchyQOL^{17, 18}. As single questions, all of the
22 abovementioned sleep-related questions are inherently very feasible. However, it is unclear
23 whether they are valid. We hypothesized that the sleep-related questions from POEM, SCORAD,

24 5D-itch and ItchyQOL all have sufficient validity and responsiveness to screen and monitor for
25 severity of sleep disturbances in adults with AD. In the present study, we sought to determine
26 their measurement properties in adults with AD.

Methods

Study Design

We performed a prospective, dermatology practice-based study of male and female adults (≥ 18 years) with AD diagnosed according to the Hanifin-Rajka criteria¹⁹. These were patients of the eczema clinic at an academic medical center who completed self-administered questionnaires prior to their visit between January, 2014 and April, 2019. Patients without a definitive diagnosis of AD or who did not complete questionnaires were excluded. Over 99% of patients who were invited participated in the surveys. Patients received standard of care follow-up and treatment. Treatment included emollients, prescription topical and systemic medications, or phototherapy when indicated. The study was approved by the institutional review boards of Northwestern University and informed consent was obtained electronically.

AD, itch and sleep assessments

Patients completed questionnaires at each encounter, including the Patient Oriented Eczema Measure (POEM) (7 questions, range 0-28)²⁰, Numeric Rating Scale (NRS) for average-itch or worst-itch in the past 7 days (single questions, range 0-10), 5D-Pruritus Scale (5 questions, range 5-25)²¹, ItchyQOL (22 questions, mean score range 1-5), Dermatology Quality of Life Index (DLQI) (10 questions, range 0-30)²² and patient-reported global AD severity (1 question, clear, almost clear, mild, moderate, severe)^{23, 24}.

Patients were also assessed with full body skin examinations by a dermatologist (JS) using the Clinician-Reported Outcomes (ClinROs) EASI (4 signs [erythema, excoriation, swelling, lichenification] on 4 body sites, range: 0–72), Scoring AD (SCORAD; 6 signs [erythema, excoriation, swelling, oozing/crusting, lichenification, dryness] on 8 body sites,

pruritus and sleeplessness; range: 0–103), and objective component of the SCORAD (O-SCORAD) (range: 0-83)^{25, 26}.

Sleep disturbance was assessed using the individual sleep-related questions from POEM, SCORAD, 5D and ItchyQOL. POEM-sleep asks how many days in the past week their sleep was disturbed by their eczema (0=no days/1=1-2 days/2=3-4 days/3=5-6 days/4=every day). SCORAD-sleep asks about sleep loss in the past 3 days on a scale of 0-10. 5D-sleep asks to rate the impact of itching on sleep over the last 2 weeks (1=Never affects sleep/2=Occasionally delays falling asleep/3=Frequently delays falling asleep/4=Delays falling asleep and occasionally wakes me up at night/5=Delays falling asleep and frequently wakes me up at night). ItchyQOL-sleep asks how often their itchy skin condition affects their sleep in the past week (1=Never/2=Rarely/3=Sometimes/4=Often/5=All the time).

Statistical Analyses

Summary statistics were determined. The distribution of and concordance (kappa, weighted kappa) between POEM-sleep, SCORAD-sleep, 5D-sleep, ItchyQOL-sleep were determined. Concurrent and convergent construct validity of POEM-sleep, SCORAD-sleep, 5D-sleep, ItchyQOL-sleep was established using Spearman correlations. Correlation coefficients were interpreted as: ≥ 0.70 or ≤ -0.70 =very strong, 0.50–0.69 or -0.69–-0.50=strong, 0.30–0.49 or -0.49–-0.30=moderate, and 0.10-0.29 or -0.29–-0.10=weak²⁷. Discriminant construct validity was established using Wilcoxon rank-sum tests that compared differences between severity groups for patient-reported and physician-reported global AD severity. Monotonic and statistically significant between-group differences support discriminant validity. Analyses were

done as per the COnsensus-based Standards for the selection of health status Measurement
INstruments criteria (COSMIN)²⁸.

Floor or ceiling effects of total scores and individual items were considered present if
15% of responses fell in the lowest or highest scores^{29, 30}. Responsiveness was evaluated by
Spearman correlations between the change of sleep scores with the change of AD severity scores
at the subsequent visit. The above statistical analyses were performed in SAS version 9.4.3 and
sample weights were incorporated into all analyses (SAS Institute, Cary, IN). Complete case
analysis was performed. A two-sided P-value of 0.05 was considered statistically significant.

Results

Baseline Characteristics

Overall, 115 patients with 405 encounters were included in the study. Patients included 62 (53.9%) females, 58 (50.4%) Caucasians/whites, and had mean $\pm$ SD age of 44.5 ± 18.6 years. Baseline characteristics of AD severity are included in Table 1.

Overlap of sleep scores

Overall, 104 (90.4%) of patients had at least one response indicating sleep disturbance for POEM-sleep, SCORAD-sleep, 5D-sleep and ItchyQOL-sleep. SCORAD-sleep had the highest proportion of responses indicating sleep disturbances (75.7%), followed by ItchyQOL-sleep (71.3%), 5D-sleep (64.4%) and POEM-sleep (53.9%). There was partial overlap of the four scores, with 18 (15.7%) reporting sleep disturbances on 2 items, 21 (18.3%) on 3 items, and 47 (40.9%) on all 4 items. Furthermore, there was only weak to moderate concordance of responses indicating any vs. no sleep disturbance as judged by kappa coefficients between any two scores and for weighted kappa coefficients between responses for POEM-sleep, 5D-sleep and ItchyQOL-sleep that all use 5-point Likert responses (Table 2). That is, each sleep-related question performed differently from each other, and there was only modest overlap between question responses.

Concurrent and Convergent Validity

Regarding concurrent validity, POEM-sleep, SCORAD-sleep, 5D-sleep and ItchyQOL-sleep showed significant moderate correlations with each other. Regarding convergent validity, all items showed moderate correlation with total POEM and SCORAD-itch scores, but weak

correlations with ClinROs for AD (EASI, objective and total SCORAD), moderate to strong correlations with QOL (mean ItchyQOL and DLQI), but poor or no significant correlation with NRS worst or average itch (Table 3). That is, sleep disturbances as measured by each of these sleep-related question were only partially related to each other and other measures AD severity.

Discriminant Validity

POEM-sleep, SCORAD-sleep, 5D-sleep and ItchyQOL-sleep all showed significant and stepwise increases for each level of self-reported and physician-reported global AD severity (Kruskal Wallis, $P < 0.01$ for all) (Figure 1). That is, each sleep-related question was able to discriminate between different levels of AD severity overall.

Floor or Ceiling Effects

Floor effects were observed for POEM-sleep ($n=53$, 46.1%), SCORAD-sleep ($n=28$, 24.4%), 5D-sleep ($n=41$, 35.7%) and ItchyQOL-sleep ($n=33$, 28.7%). However, no ceiling effects were observed for any of the items. That is, none of these sleep-related questions may be able to capture the variance in low levels of sleep disturbance, but all appear to perform well with more severe sleep disturbances.

Responsiveness

POEM-sleep, SCORAD-sleep, 5D-sleep and ItchyQOL-sleep changed significantly between first and subsequent visits (Wilcoxon signed-rank, $P < 0.001$ for all). Change in POEM-sleep, SCORAD-sleep, 5D-sleep and ItchyQOL-sleep showed weak to strong correlations with each other, moderate to strong correlations with change in other PROs (SCORAD-itch, POEM,

126 5D-itch, mean ItchyQOL and DLQI), and ClinROs (objective and total SCORAD, EASI), but no
127 significant correlations with change of NRS worst itch (Table 3). Changes in NRS average itch
128 were only correlated with changes in SCORAD-sleep and ItchyQOL-sleep, but not POEM-sleep
129 and 5D-sleep. That is, scores for each sleep-related question generally improved as other aspects
130 of AD severity improved.

Discussion

This study shows that sleep-items from POEM, SCORAD, 5D-itch and ItchyQOL had overall similar performance and demonstrated good validity. All four questions had reasonably good convergent validity with multiple PROs and ClinROs in AD, discriminative validity between levels of AD severity and QOL impact, and good responsiveness. These are all important measurement properties, which indicate that the sleep-related questions assess an aspect of AD severity that is related to other aspects of AD severity, but only partially measured by other AD severity assessments. All the items suffered from floor effects, suggesting that may not be reliable when assessing mild sleep disturbances. No items were particularly good at discriminating between milder and moderate AD. Whereas, POEM-sleep and SCORAD-sleep may have a slight advantage as they appeared to be better at discriminating severe from mild or moderate AD. Despite their similarities, each item had distinct measurement properties, and there was only modest overlap and concordance between them.

The preferred approach for assessing patient-reported sleep disturbance has yet to be established. Each of the sleep-items that we studied measures different facets of sleep. POEM-sleep measures the number of nights of sleep disturbance due to eczema over the past week. SCORAD-sleep measures intensity of sleep loss over the past 3 days. 5D-sleep measures frequency of delay falling asleep and/or awakening from sleep at night due to itch over the past two weeks. ItchyQOL-sleep measures how often itch impacted sleep over the past week. Only 5D-sleep distinguishes between problems initiating vs. maintaining sleep, but combines both to define more severe sleep problems. None of these sufficiently distinguishes between causes of sleep disturbance, e.g. problems initiating or maintaining sleep, poor sleep quality, the severity of sleep disturbance, and degree of functional impairment due to sleep disturbance.

Nevertheless, they are all single-items that take less than 1 minute to complete, feasible to implement in clinical practice, and easy to interpret. In comparison, the Pittsburgh Sleep Quality Index (PSQI) is one of the most commonly used sleep PROs and takes 5-10 minutes to complete and requires manual scoring of 7 sub-components before calculating a global score³¹. Thus, the greatest utility of these items may be their potential integration into routine clinical practice to efficiently identify AD patients with prominent sleep disturbances. They can be used to screen and monitor patients with more severe sleep disturbances. However, the floor-effects and lack of discriminative ability in milder AD patients we observed suggest that they are not sensitive enough to identify patients with mild sleep disturbances.

The four sleep-items had similar measurement properties. Ultimately, the clinician may decide which items to use based on other considerations. For example, if a clinician is already using POEM, SCORAD, ItchyQOL or 5D routinely in practice, they could also rely on the individual sleep-related items to particularly assess sleep disturbances. For example, SCORAD is commonly used in Europe and incorporated into treatment guidelines³², though was not the preferred measure of AD signs by the Harmonizing Outcome Measures in Eczema (HOME) group^{33,34}. Clinicians already using SCORAD can also rely on SCORAD-sleep to assess sleep disturbance. For clinicians who are not already using one of these assessments, POEM may be the most pragmatic option. POEM is the preferred PRO for assessing AD symptoms in clinical trials by international consensus of the HOME group^{35,36}. Thus, clinicians could get a dual benefit in using POEM in practice by being able to measure both AD severity overall and sleep disturbance in particular.

Interestingly, the four sleep-item responses correlated consistently with AD signs, symptoms and QOL-impact, but inconsistently with severity of itch. Furthermore, change of

sleep scores was not consistently correlated with change of itch severity. Together, these results suggest that sleep disturbances are not solely attributable to itch. As such, sleep disturbances should be assessed separately from itch severity and not assumed to be absent or present based only on itch severity. Moreover, sleep disturbance and related impact may be driven more by other disease aspects, such as skin pain, chronic disease, systemic inflammation, and treatment burden^{1, 3, 37}. Future studies are needed to sort out the precise mechanisms of sleep disturbance in AD.

This study has a number of strengths, including being prospective, with good representation across gender, age, ethnicity, and AD severity. However, it is a single-center study, which limits generalizability. This study also did not investigate test-retest reliability. While not formally assessed in this study, content validity of the individual items was partially assessed in the context of the instruments they are a part of.^{38, 39} Finally, we did not compare the sleep items with objective measures of sleep, e.g. actigraphy or polysomnography. These points should be addressed in future studies.

In conclusion, this study shows that POEM-sleep, SCORAD-sleep, 5D-sleep and ItchyQOL-sleep have good construct validity, modest discriminative validity, good responsiveness and are feasible for use in clinical practice in adults with AD. One or more of these instruments may be incorporated into routine practice to screen for prominent sleep disturbance in AD patients.

References

1. Silverberg JI, Gelfand JM, Margolis DJ, et al. Patient burden and quality of life in atopic dermatitis in US adults: A population-based cross-sectional study. *Ann Allergy Asthma Immunol.* 2018;121:340-347.
2. Silverberg JI, Gelfand JM, Margolis DJ, et al. Pain Is a Common and Burdensome Symptom of Atopic Dermatitis in United States Adults. *The Journal of Allergy and Clinical Immunology: In Practice.*
3. Vakharia PP, Chopra R, Sacotte R, et al. Burden of skin pain in atopic dermatitis. *Annals of allergy, asthma & immunology : official publication of the American College of Allergy, Asthma, & Immunology.* 2017;119:548-552 e543.
4. Cheng BT, Silverberg JI. Depression and psychological distress in US adults with atopic dermatitis. *Annals of allergy, asthma & immunology : official publication of the American College of Allergy, Asthma, & Immunology.* 2019;123:179-185.
5. Yu SH, Silverberg JI. Association between Atopic Dermatitis and Depression in US Adults. *Journal of Investigative Dermatology.* 2015;135:3183-3186.
6. Chang Y-S, Chiang B-L. Sleep disorders and atopic dermatitis: A 2-way street? *Journal of Allergy and Clinical Immunology.* 2018;142:1033-1040.
7. Yu SH, Attarian H, Zee P, Silverberg JI. Burden of Sleep and Fatigue in US Adults With Atopic Dermatitis. *Dermatitis : contact, atopic, occupational, drug : official journal of the American Contact Dermatitis Society, North American Contact Dermatitis Group.* 2016;27:50-58.
8. Silverberg JI, Garg NK, Paller AS, Fishbein AB, Zee PC. Sleep Disturbances in Adults with Eczema Are Associated with Impaired Overall Health: A US Population-Based Study. *Journal of Investigative Dermatology.* 2015;135:56-66.
9. Li JC, Fishbein A, Singam V, et al. Sleep Disturbance and Sleep-Related Impairment in Adults With Atopic Dermatitis: A Cross-sectional Study. *Dermatitis : contact, atopic, occupational, drug.* 2018;29:270-277.
10. Fishbein AB, Vitaterna O, Haugh IM, et al. Nocturnal eczema: Review of sleep and circadian rhythms in children with atopic dermatitis and future research directions. *The Journal of allergy and clinical immunology.* 2015;136:1170-1177.
11. Patel KR, Immaneni S, Singam V, Rastogi S, Silverberg JI. Association between atopic dermatitis, depression, and suicidal ideation: A systematic review and meta-analysis. *Journal of the American Academy of Dermatology.* 2019;80:402-410.
12. Silverberg JI, Gelfand JM, Margolis DJ, et al. Symptoms and diagnosis of anxiety and depression in atopic dermatitis in U.S. adults. *The British journal of dermatology.* 2019;181:554-565.
13. Silverberg JI, Greenland P. Eczema and cardiovascular risk factors in 2 US adult population studies. *The Journal of allergy and clinical immunology.* 2015;135:721-728 e726.
14. Garg N, Silverberg JI. Association between eczema and increased fracture and bone or joint injury in adults: a US population-based study. *JAMA dermatology.* 2015;151:33-41.
15. Garg NK, Silverberg JI. Eczema is associated with osteoporosis and fractures in adults: a US population-based study. *The Journal of allergy and clinical immunology.* 2015;135:1085-1087 e1082.
16. Ancoli-Israel S, Cole R, Alessi C, Chambers M, Moorcroft W, Pollak CP. The role of actigraphy in the study of sleep and circadian rhythms. *Sleep.* 2003;26:342-392.
17. Vakharia PP, Cella D, Silverberg JI. Patient-reported outcomes and quality of life measures in atopic dermatitis. *Clin Dermatol.* 2018;36:616-630.
18. Chopra R, Silverberg JI. Assessing the severity of atopic dermatitis in clinical trials and practice. *Clin Dermatol.* 2018;36:606-615.

19. Hanifin J, Rajka G. Diagnostic features of atopic eczema. *Acta dermato-venereologica*. 1980;92.
20. Spuls PI, Gerbens LAA, Simpson E, et al. Patient-Oriented Eczema Measure (POEM), a core instrument to measure symptoms in clinical trials: a Harmonising Outcome Measures for Eczema (HOME) statement. *The British journal of dermatology*. 2017;176:979-984.
21. Elman S, Hynan LS, Gabriel V, Mayo MJ. The 5-D itch scale: a new measure of pruritus. *The British journal of dermatology*. 2010;162:587-593.
22. Finlay AY, Khan GK. Dermatology Life Quality Index (DLQI)--a simple practical measure for routine clinical use. *Clinical and experimental dermatology*. 1994;19:210-216.
23. Vakharia PP, Chopra R, Sacotte R, et al. Validation of patient-reported global severity of atopic dermatitis in adults. *Allergy*. 2018;73:451-458.
24. Silverberg JI, Chiesa Fuxench ZC, Gelfand JM, et al. Content and construct validity, predictors, and distribution of self-reported atopic dermatitis severity in US adults. *Annals of allergy, asthma & immunology : official publication of the American College of Allergy, Asthma, & Immunology*. 2018;121:729-734 e724.
25. 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. *Experimental dermatology*. 2001;10:11-18.
26. Severity scoring of atopic dermatitis: the SCORAD index. Consensus Report of the European Task Force on Atopic Dermatitis. *Dermatology*. 1993;186:23-31.
27. Overholser BR, Sowinski KM. Biostatistics Primer: Part 2. *Nutrition in Clinical Practice*. 2008;23:76-84.
28. Mokkink LB, Terwee CB, Patrick DL, et al. The COSMIN study reached international consensus on taxonomy, terminology, and definitions of measurement properties for health-related patient-reported outcomes. *Journal of clinical epidemiology*. 2010;63:737-745.
29. Terwee CB, Bot SD, de Boer MR, et al. Quality criteria were proposed for measurement properties of health status questionnaires. *Journal of clinical epidemiology*. 2007;60:34-42.
30. Lim CR, Harris K, Dawson J, Beard DJ, Fitzpatrick R, Price AJ. Floor and ceiling effects in the OHS: an analysis of the NHS PROMs data set. *BMJ open*. 2015;5:e007765.
31. Buysse DJ, Reynolds CF, 3rd, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatry Res*. 1989;28:193-213.
32. Wollenberg A, Barbarot S, Bieber T, et al. Consensus-based European guidelines for treatment of atopic eczema (atopic dermatitis) in adults and children: part I. *Journal of the European Academy of Dermatology and Venereology : JEADV*. 2018;32:657-682.
33. Schmitt J, Langan S, Deckert S, et al. Assessment of clinical signs of atopic dermatitis: a systematic review and recommendation. *The Journal of allergy and clinical immunology*. 2013;132:1337-1347.
34. Chalmers JR, Schmitt J, Apfelbacher C, et al. Report from the third international consensus meeting to harmonise core outcome measures for atopic eczema/dermatitis clinical trials (HOME). *The British journal of dermatology*. 2014;171:1318-1325.
35. 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). *The British journal of dermatology*. 2016;175:69-79.
36. Spuls PI, Gerbens LA, Simpson E, et al. POEM a core instrument to measure symptoms in clinical trials: a HOME statement. *The British journal of dermatology*. 2016.
37. Silverberg JI, Gelfand JM, Margolis DJ, et al. Pain Is a Common and Burdensome Symptom of Atopic Dermatitis in United States Adults. *The journal of allergy and clinical immunology. In practice*. 2019.

- 95 **38.** Patel KR, Singam V, Vakharia PP, et al. Measurement properties of three assessments of burden
96 used in atopic dermatitis in adults. *The British journal of dermatology*. 2019;180:1083-1089.
- 97 **39.** Charman CR, Venn AJ, Williams HC. The patient-oriented eczema measure: development and
98 initial validation of a new tool for measuring atopic eczema severity from the patients'
99 perspective. *Archives of dermatology*. 2004;140:1513-1519.

Figure 1. Discriminant validity of POEM-sleep, SCORAD-sleep, 5D-sleep and ItchyQOL-sleep. Box-whisker plots and overlaid jitter plots of POEM-sleep (A, B), SCORAD-sleep (C, D), 5D-sleep (E, F) and ItchyQOL-sleep (G, H) are presented for severity levels of patient-reported (A, C, E, G), and physician-reported (B, D, F, H) global AD severity.

Table 1. Subject characteristics.		1
Variable	Value	2
Demographics (n=115)		
Age (yr)		3
mean $\pm$ std. dev.	44.5 $\pm$ 18.6	4
Min – max	18.9 – 97.4	
Female sex – freq (%)	62 (53.9%)	5
Race/ethnicity – freq (%)		6
Caucasian/white	58 (50.4%)	
African-American/black	17 (14.8%)	7
Hispanic	14 (12.2%)	8
Asian	26 (22.6%)	
Patient-reported outcomes		9
POEM-sleep – median (min,max) (n=115)	1 (0, 4)	
SCORAD-sleep – median (min, max) (n=115)	2 (0, 10)	10
SCORAD-itch – median (min, max) (n=115)	3 (0, 10)	11
5D-sleep (n=115)	2 (1, 5)	
ItchyQOL-sleep (n=115)	3 (1, 5)	12
NRS worst-itch – median (min, max) (n=60)	5 (0, 10)	13
NRS average-itch – median (min, max) (n=60)	5 (0, 10)	
POEM – median (min, max) (n=115)	9 (0, 28)	14
Patient-reported global AD severity – freq (%) (n=108)		15
Clear	2 (1.9%)	
Almost clear	5 (4.6%)	16
Mild	56 (51.9%)	
Moderate	34 (31.5%)	17
Severe	11 (10.2%)	18
Clinical-reported outcomes		
EASI – median (min, max) (n=115)	3.35 (0, 66.6)	19
Objective-SCORAD – median (min, max) (n=115)	18.3 (0, 65.0)	20
SCORAD – median (min, max) (n=115)	27.5 (0, 85.0)	

Table 2. Concordance of responses to POEM-sleep, SCORAD-sleep, 5D-sleep and ItchyQOL-sleep.

Sleep assessment	Kappa coefficient		
	Positive vs. negative responses		
	SCORAD-sleep	5D-sleep	ItchyQOL-sleep
POEM-sleep	0.26	0.61	0.42
SCORAD-sleep	1.00	0.20	0.27
5D-sleep		1.00	0.56
ItchyQOL-sleep			1.00
	Weighted kappa coefficient		
	5-point Likert responses		
	SCORAD-sleep	5D-sleep	ItchyQOL-sleep
POEM-sleep		0.64	0.44
5D-sleep		1.00	0.51
ItchyQOL-sleep			1.00

Table 3. Spearman correlation of baseline and change of sleep scores with baseline and change of severity of atopic dermatitis, itch, and quality of life.

Baseline sleep assessment	Spearman rho													
	POEM sleep	SCORAD-sleep	5D-sleep	ItchyQOL-sleep	POEM	NRS Worst Itch	NRS Average Itch	Objective-SCORAD	SCORAD-itch	SCORAD	EASI	5D-Itch	Mean ItchyQOL	DLQI
POEM-sleep	1.00	0.55[#]	0.71[#]	0.65[#]	0.64[#]	0.27[*]	0.40^{&}	0.34[#]	0.53[#]	0.49[#]	0.32[#]	0.66[#]	0.48[#]	0.58[#]
SCORAD-sleep		1.00	0.49[#]	0.50[#]	0.50[#]	0.30[*]	0.36^{&}	0.20[*]	0.50[#]	0.46[#]	0.21^{&}	0.55[#]	0.43[#]	0.55[#]
5D-sleep			1.00	0.68[#]	0.58[#]	0.02	0.10	0.34[#]	0.47[#]	0.47[#]	0.34[#]	0.72[#]	0.50[#]	0.57[#]
ItchyQOL-sleep				1.00	0.60[#]	-0.05	0.10	0.29[*]	0.49[#]	0.42[#]	0.20[*]	0.59[#]	0.75[#]	0.49[#]
Δ assessment	Δ POEM sleep	Δ SCORAD-sleep	Δ 5D-sleep	Δ ItchyQOL-sleep	Δ POEM	Δ NRS Worst Itch	Δ NRS Average Itch	Δ Objective-SCORAD	Δ SCORAD-itch	Δ SCORAD	Δ EASI	Δ 5D-Itch	Δ Mean ItchyQOL	Δ DLQI
POEM-sleep	1.00	0.33[#]	0.75[#]	0.69[#]	0.79[#]	0.39	0.44	0.64[#]	0.68[#]	0.66[#]	0.63[#]	0.74[#]	0.71[#]	0.71[#]
SCORAD-sleep		1.00	0.37[#]	0.48[#]	0.42[#]	0.57	0.78^{&}	0.46[#]	0.53[#]	0.60[#]	0.41[#]	0.52[#]	0.53[#]	0.38[#]
5D-sleep			1.00	0.67[#]	0.67[#]	0.01	-0.12	0.56[#]	0.69[#]	0.60[#]	0.55[#]	0.80[#]	0.69[#]	0.73[#]
ItchyQOL-sleep				1.00	0.68[#]	0.25	0.70[*]	0.58[#]	0.64[#]	0.64[#]	0.59[#]	0.65[#]	0.79[#]	0.59[#]

Bold-face indicated statistical significance.

* P<0.05; & P<0.01; # P<0.0001

Δ=change of score

