Content Validity and Assessment of Psychometric Properties and Score Interpretation of a Sleep-loss Scale Score in Atopic Dermatitis

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BACKGROUND

- Sleep interference associated with pruritus is a key impact of atopic dermatitis (AD) and can negatively affect quality of life[1]; mitigating itch and its impact on sleep is thus an important outcome of AD treatment.
- However, no gold-standard patient-reported outcome (PRO) measure of sleep interference due to itch exists.
- A novel PRO measure, the Sleep-Loss Scale, is a single item developed to assess itch interference with sleep during the previous night using a 5-point response scale ranging from 0 ("not at all") to 4 ("unable to sleep at all") (Figure 1).

OBJECTIVE

- This mixed-methods study gathered evidence regarding the content validity and psychometric properties of the Sleep-Loss Scale to determine whether it is fit-for-purpose[2] for use in AD clinical trials.

KEY RESULTS

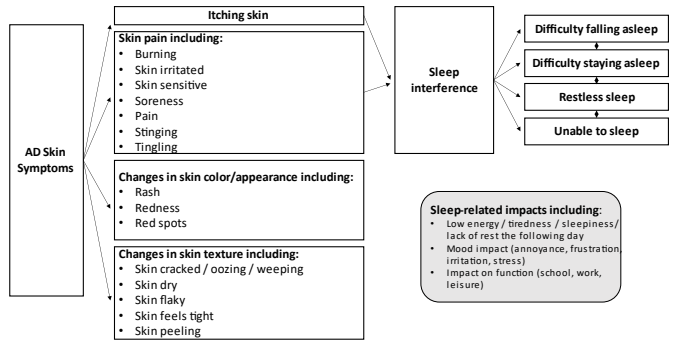
Qualitative Results

- Cognitive interview results indicated that the Sleep-Loss Scale is relevant, appropriate, and interpreted as intended by adults and adolescents.
- 11/19 patients queried stated that a 1-point decrease in score indicated meaningful improvement.

Quantitative Results

- The highest correlation was with the POEM 'Nights of disturb sleep question' (r=0.90), showing the construct validity of the Sleep Loss scale.(Table 2).
- Medium to large ES (> 0.50) were observed for improvement according to the change in IGA (Figure 3) and the GAC-AD at Week 16. (Figure 4).
- Meaningful within-patient change (MWPC) was defined as a 1-point improvement using the clinical trial data.

Figure 2. Conceptual model of sleep interference related to itch in AD



Abbreviations: AD = Atopic Dermatitis

Table 2. Correlations between the Sleep-Loss Scale and IGA, EASI, BSA, DLQI, POEM and HADS at baseline and Week 16

	Polychoric Correlation coefficients	
	Sleep-Loss Scale score at baseline N=262	Sleep-Loss Scale score at Week 16 N=180
IGA Score	0.09	0.52
EASI Score	0.24	0.48
BSA	0.17	0.48
DLQI Total Score	0.57	0.66
POEM Total Score	0.55	0.66
POEM-Nights of Disturbed Sleep	0.69	0.90
HADS-Total Score Anxiety	0.26	0.18
HADS-Total Score Depression	0.32	0.16

Abbreviations: IGA: Investigator Global Assessment; EASI: Eczema Area and Severity Index; BSA: Body Surface Area; DLQI: Dermatology Life Quality Index; POEM: Patient Oriented Eczema Measure; HADS: Hospital Anxiety and Depression Scale

CONCLUSIONS

- The Sleep-Loss Scale has content validity, test-retest reliability, validity, and responsiveness, and meets interpretation standards
- A 1-point improvement on the scale reflects an MWPC according to qualitative and quantitative data.
- These findings provide evidence supporting the scale is fit-for-purpose for inclusion as an endpoint in moderate-to-severe AD.

LIMITATIONS

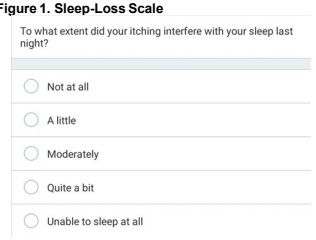
- The phase 2b study used for the quantitative analyses was only conducted in an adult population.
- There is not an even distribution of races and ethnicity for the adolescent population in the qualitative analysis.

METHODS

Qualitative Methods

- Concept elicitation and cognitive interviews were conducted with moderate-to-severe AD patients to examine the impact of AD-related itch on sleep and debrief the Sleep-Loss Scale (Figure 1) with both adults and adolescents **(≥12 years)** .
- Interview transcripts were analyzed thematically[3], and saturation was assessed[4].
- Concepts extracted from interviews were categorized into a conceptual model of patient experience of itch interference on sleep in AD.
- Debriefing analysis assessed patients' understanding of the item and response choices. Patients' interpretations of meaningful change for the scale were compiled.

Figure 1. Sleep-Loss Scale



Quantitative Methods

- Data collected daily from adults with moderate-to-severe AD enrolled in a phase 2b, randomized, double-blind, placebo-controlled study (NCT03443024) were used to assess the psychometric performance of the Sleep-Loss scale.
- The Sleep-Loss scale was summarized by a prorated weekly average for each visit. Test-retest reliability, construct validity, and ability to detect change (responsiveness) were assessed.
  - Reliability was assessed by computing intraclass correlation coefficients (ICCs) between Week 12 and Week 16 in patients with no change in the Investigator Global Assessment (IGA) between the two timepoints of interest.
  - Construct validity was assessed by computing polychoric correlation coefficients with clinician-reported outcomes (ClinROs) and PROs.
  - Responsiveness was assessed by calculating effect-sizes (ES) in subgroups of patients defined by the Global Assessment of Change – AD (GAC-AD) and change from baseline in IGA at Week 16.
- Anchor-based methods (using IGA and GAC-AD as anchors) were used to determine MWPC in the Sleep-Loss scale score.

RESULTS

Qualitative Results

- Fifteen adult and six adolescent patients aged 12-64 years were interviewed (Table 1). 19/21 patients rated their previous night's sleep interference from 1 - "a little" to 3-"quite a bit" on the 5-point Sleep Loss Scale.
- Patients confirmed that sleep loss due to itch is an important impact of AD; all patients reported experiencing this impact over the course of disease. (Figure 2)
- The scale's recall period and response scale are acceptable and well-understood, and patients were able to distinguish among the five severity levels of the scale.
- Patients stated that the daily life impact of an improved score would be reflected in improved rest/energy, functioning at work or school, and mood.

Quantitative Results

- Mean age of the clinical trial population was 39 years (range: 18-87) with 59% of females. Mean time with atopic dermatitis was 23 years (range: 1-73).
- In stable patients defined by IGA, ICC was 0.81 between Week 12 and Week 16.
- Lower correlations were observed with ClinROs than with PROs (except for HADS), as expected, correlations were higher at Week 16 than at baseline.

Table 1. Qualitative study demographic and health data (N=21)

	Adult (n=15)	Adolescent (n=6)
Age (in years)		
Mean (SD)	30.4 (12.9)	13.0 (1.0)
Gender, n (%)		
Female	11 (73%)	3 (50%)
Race, n (%)		
Asian	8 (53%)	5 (83%)
Black	0 (0%)	1 (17%)
Native Hawaiian/Pacific Islander	1 (7%)	0 (0%)
White	4 (27%)	0 (0%)
Biracial	1 (7%)	0 (0%)
Missing	1 (7%)	0 (0%)
Ethnicity, n (%)		
Non-Hispanic/Non-Latino	13 (87%)	6 (100%)
Education level, n (%)		
Elementary/primary school	0 (0%)	3 (50%)
Some high school	0 (0%)	3 (50%)
Some college	5 (33%)	0 (0%)
Associate degree	1 (7%)	0 (0%)
Bachelor's degree	7 (47%)	0 (0%)
Post-graduate	1 (7%)	0 (0%)
Trade	1 (7%)	0 (0%)
BSA (in %)		
Mean (SD)	17.1 (1.0)	16.8 (7.1)
Min-Max (%)	10-40	10-30

Abbreviations: Max = maximum, Min = minimum, n = number of patients in the specified category, SD = standard deviation, BSA=body surface area

Figure 3. Effect-sizes of the change in Sleep-Loss scale score according to change in IGA at Week 16

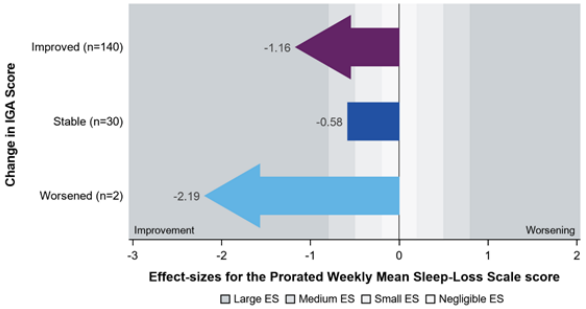
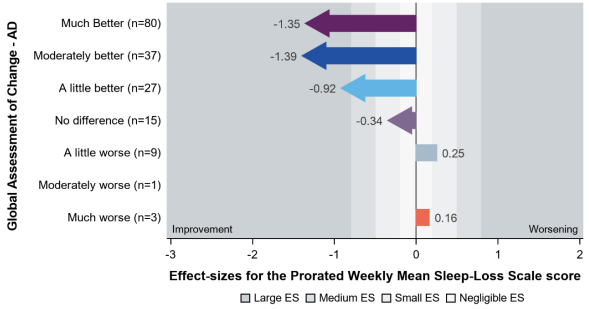


Figure 4. Effect-sizes of the change in Sleep-Loss scale score according to GAC-AD at Week 16



DISCLOSURES

- Gil Yosipovitch conducted clinical trials or received honoraria for serving as a member of the Scientific Advisory Board of Eli Lilly, TREVI, Novartis, Regeneron, Sanofi, Galderma, Pfizer, Bellus, Kiniksa, and LEO and received research funds from Pfizer, LEO, Novartis, and Eli Lilly. Alissa Rams, Jessica Baldasaro, Laurine Bunod, Sara Strzok, and Juliette Meunier are employees of Modus Outcomes, which was hired to conduct this research. Laure Delbecque, Hany Elmaraghy, Luna Sun, and Evangeline Pierce are employees of Eli Lilly & Company.
- This study was funded by Eli Lilly and Company. Almirall has licensed the rights to develop and commercialize lebrikizumab for the treatment of dermatology indications including atopic dermatitis in Europe. Lilly has exclusive rights for development and commercialization of lebrikizumab in the United States and the rest of the world outside of Europe.

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