

Pain Is a Common and Burdensome Symptom of Atopic Dermatitis in United States Adults



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What is already known about this topic? Little is known about the prevalence and impact of pain in adult atopic dermatitis (AD).

What does this article add to our knowledge? Pain was reported by 61% of adults with AD, has heterogeneous severity and characteristics, and negatively impacts on quality of life.

How does this study impact current management guidelines? Pain is a distinct symptom in AD and may have important ramifications in clinical decision making and assessing therapeutic efficacy.

BACKGROUND: Atopic dermatitis (AD) is associated with skin pain. However, little is known about the prevalence and associations of pain in AD.

OBJECTIVE: To characterize the frequency, intensity, characteristics, and associations of pain from AD.

METHODS: A cross-sectional, US population internet survey-based study of 602 adults with AD from the AD in

America Study was performed (modified UK Working Party Criteria).

RESULTS: Overall, 365 (61%) reported pain from AD, with 199 (33%) experiencing pain at least once per week and 30 (5%) with pain daily. Among those with AD pain, 22% reported worst pain intensity ≥ 7 . The frequency and intensity of AD pain were associated with Patient-Oriented Scoring Atopic Dermatitis

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Abbreviations used

AD- Atopic dermatitis
 CI- Confidence interval
 DLQI- Dermatology Life Quality Index
 PO-SCORAD- Patient-Oriented Scoring Atopic Dermatitis
 POEM- Patient-Oriented Eczema Measure
 QOL- Quality of life
 UKWP- United Kingdom Working Party

(PO-SCORAD), PO-SCORAD itch and sleep, and Patient-Oriented Eczema Measure ($P \leq .004$ for all). Among those experiencing AD pain, 179 (48%) reported pain occurring only after frequent scratching, 156 (42%) reported intermittent pain, and 27 (11%) reported constant pain throughout the day. AD pain was most commonly associated with open areas caused by scratching (27%) and fissures in the skin (27%), followed by inflamed red skin (25%), with only a minority reporting pain mostly caused by burning from creams or ointments (10%). Mild AD was associated with more pain from scratching, whereas severe AD was associated with more constant pain and pain from inflamed skin.

CONCLUSIONS: Pain is a distinct symptom in AD, with heterogeneous frequency, characteristics, intensity, and quality of life impact. Pain was related to scratching, fissures, and/or inflamed red skin, and least from burning from topical medications. Skin pain should be assessed in patients with AD and monitoring treatment response. © 2019 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2019;7:2699-706)

Key words: Atopic dermatitis; Eczema; Epidemiology; Pain; Itch; Severity; Burden; Symptom; Sign

Atopic dermatitis (AD) is a chronic, inflammatory skin disease, associated with substantial patient^{1,2} and public health burden.³ The most burdensome symptom of adult AD is itch, with additional burden from skin lesions and sleep disturbances.² AD is also associated with multiple medical and mental health comorbidities.³⁻⁶

Recent studies found that skin pain is an important symptom in AD.^{7,8} A study of the patient burden of 380 adults with moderate-severe AD enrolled in a clinical trial found that 76.8% reported moderate or extreme pain/discomfort at baseline.⁸ A study of 305 adult patients with AD found higher rates of skin pain in the past week, which was associated with poorer quality of life (QOL).⁷

However, many questions remain about pain in AD. First, previous studies of skin pain were performed in clinical cohorts or clinical trial populations of moderate-severe AD, which may not be representative of the general population. Second, previous studies examined the prevalence and/or intensity of skin pain, but not the frequency of pain or its impact on QOL. Third, pain is a complex symptom and might occur in AD for a variety of reasons, for example, secondary to scratching, adverse reaction to topical medications, and/or secondary to inflammation. We hypothesized that (1) skin pain is common throughout the entire population of adults with AD, and occurs even among adults with mild AD; (2) both frequency and intensity of pain are

important predictors of QOL impact; and (3) pain in AD is heterogeneous, with different characteristics and predictors occurring across distinct patient subsets.

In the present study, we sought to determine the prevalence and associations of pain in US adults with AD. Moreover, we sought to determine the characteristics of pain in AD and understand its impact on QOL.

METHODS

Study design

Data were obtained from the AD in America Survey (see the [Methods](#) section in this article's Online Repository at www.jaci-inpractice.org). Briefly, this was a cross-sectional, internet survey-based study that used 2-stage sampling of respondents from a long-standing nationally representative web panel. Respondents provided informed consent electronically. The survey questionnaire and protocol were approved by the ICF Institutional Review Board.

An adaptation of the United Kingdom Working Party (UKWP) criteria was selected by the AD in America advisory committee as the screening tool for patient eligibility⁹ (see the [Methods](#) section in this article's Online Repository at www.jaci-inpractice.org).

Self-assessments of AD severity included the previously validated Patient-Oriented Scoring AD (PO-SCORAD) index (range: 0-103) and PO-SCORAD itch and sleep subscores (range: 0-10);¹⁰ Patient-Oriented Eczema Measure (POEM) (7 questions; range: 0-28)¹¹ QOL was assessed using Dermatology Life Quality Index (DLQI) (10 questions; range: 0-30).¹² These patient-reported outcomes were selected *a priori* based on their feasibility, preference for use in research by international consensus of the Harmonizing Outcome Measures in Eczema group,^{13,14} and/or having been previously validated.¹³⁻¹⁶ Scores were divided into 3 categories (clear/almost-clear/mild, moderate, severe/very severe) using previously reported severity strata.¹⁷

Assessment of pain

Frequency of pain was assessed by the question "How often would you say that you experience pain from your eczema or atopic dermatitis? (Less than once a week; 1-2 days a week; 3-4 days a week; 5-6 days a week; Every day; Never)." Those who responded "Never" were considered as not having pain from AD, whereas all other responses were considered as having pain. Pain characteristics were assessed by "When you experience pain from your eczema or atopic dermatitis, would you say you feel it? Constantly and throughout the day; Comes and goes throughout the day; Only after I scratch a lot" and "What causes the most pain from your eczema or atopic dermatitis? The inflamed red skin; Small cracks in the skin (fissures); Open areas caused by scratching; Burning from creams or ointments." Pain intensity was assessed by the following question: "On a scale of 0 to 10, with 0 being no pain and 10 being the worst unbearable pain, how would you rate your pain at the worst moment during the past week? (Select one number)."

Statistical analyses

Statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC) and included representative sample weights. Baseline characteristics were determined. Descriptive statistics were determined for pain frequency, characteristics, and intensity. Associations of demographics (age [18-39/40-59/60+ years], sex [male/female], race/ethnicity [white/black/Hispanic/Asian/other]), AD severity (PO-SCORAD [0-27/28-56/57-104], PO-SCORAD itch and sleep [0-3/4-6/7-10], POEM [0-7/8-19/20-28]), and/or site of

AD lesions (trunk, face, flexural, hands, genitals/buttocks) with pain frequency ($\leq 2/3$ - $6/7$ days a week), characteristics, and/or intensity (0- $3/4$ - $6/7$ -10) were tested by Rao-Scott χ^2 tests. Pearson correlations compared AD pain intensity with PO-SCORAD, PO-SCORAD itch and sleep, and POEM. Rao-Scott χ^2 and Fisher exact tests tested the associations of experiencing any AD pain, pain frequency, and intensity with QOL impact (individual items of DLQI).

Multivariable logistic regression models were constructed with AD pain frequency (≥ 1 vs < 1 day per week) as the binary dependent variable. Multivariable linear regression models were constructed with AD pain intensity as the continuous dependent variable. The independent variables included measures of AD severity (PO-SCORAD, PO-SCORAD itch and sleep, POEM) and sociodemographics (sex, age, race/ethnicity, poverty income ratio, level of education), and the presence of AD lesions on the face or hands. Adjusted odds ratios, β , and 95% confidence intervals (CIs) were estimated. Of note, ordinal logistic regression models were tested for AD frequency, but did not meet the proportional odds assumption (Score test, $P < .0001$).

Multivariable linear regression models were constructed that examined the relationship of pain intensity and frequency (independent variables) with DLQI scores (dependent variable). We hypothesized that adults with both frequent and intense pain may have more QOL impact than those with either alone. Models tested interactions of pain frequency with intensity and intensity of itch with pain. Two- and three-way interaction terms between other covariables were tested. Interactions were included in final models if the P value $< .05$ and modification of estimates by $> 20\%$. *Post hoc* analyses were conducted of differences among the levels of pain intensity at fixed levels of pain frequency. Least squared means and adjusted β (95% CI) were estimated for each combination of intensity and frequency. Sex, age, PO-SCORAD, PO-SCORAD itch and sleep, and POEM were included as covariables. Complete data analysis was performed, that is, subjects with missing data were excluded. Correction for multiple dependent tests¹⁸ yielded a critical P value of .023. A 2-sided P value $\leq .023$ was taken to indicate statistical significance for all estimates.

RESULTS

Patient characteristics

Six hundred and two adults met AD criteria, resulting in a prevalence (95% CI) of AD of 7.4% (5.8% to 9.0%). Subjects with AD were 54% female and 72% Caucasian/white, with a mean $\pm$ SD age of 52.0 ± 16.3 years (Table E1, available in this article's Online Repository at www.jaci-inpractice.org). The weighted mean (95% CI) PO-SCORAD was 27.5 (25.7-29.3) and POEM was 7.5 (6.8-8.1).

Pain frequency

Overall, 365 (61%) adults with AD reported pain from their AD or eczema, with 199 (33%) experiencing pain at least once per week and 30 (5%) with pain every day of the week (Figure 1, A). The prevalence of any pain from AD or eczema significantly decreased with age (18-39 years: 74%; 40-59 years: 63%; ≥ 60 years: 52%; $P = .0008$), but did not significantly differ with sex ($P = .9$) or race/ethnicity ($P = .6$).

Increased frequency of pain was also significantly associated with more severe PO-SCORAD ($P < .0001$), PO-SCORAD itch ($P < .0001$) and sleep ($P = .004$), and POEM ($P < .0001$) (Figure 1, B-E).

In multivariable regression models, AD pain frequency ≥ 1 day per week was associated with PO-SCORAD, PO-SCORAD itch, and POEM, but not PO-SCORAD sleep, lesions on face or hands, sex, age, race/ethnicity, level of income, or education (Table 1).

Pain characteristics

Among those 365 adults experiencing any pain, 179 (48%) reportedly occurred *only after scratching a lot*, 156 (42%) reported pain that *comes and goes throughout the day*, and 27 (11%) reported pain *constantly throughout the day* (Figure 1, F). Most patients with mild AD reported pain occurring *only after scratching a lot*. However, as the severity of PO-SCORAD ($P = .0004$), POEM ($P < .0001$), and PO-SCORAD itch ($P = .02$) increased, so did the proportion of patients reporting that pain *comes and goes throughout the day* and is *constant throughout the day* (Figure 1, F-J).

Overall, pain was most commonly thought to be caused by *open areas caused by scratching* (27%) and *small cracks in the skin* (fissure; 27%), followed by *inflamed red skin* (25%), with only a minority reporting pain mostly caused by *burning from creams or ointments* (10%) (Figure 1, K). Among persons with mild PO-SCORAD, PO-SCORAD itch, and POEM, *open areas caused by scratching* was the most common cause of pain (31%, 33%, and 31%). In contrast, among persons with severe PO-SCORAD and PO-SCORAD itch, *inflamed red skin* was the most common cause of pain (33% and 35%), whereas among persons with severe POEM scores, *open areas caused by scratching* remained the most common cause of pain (39%) (Figure 1, L-O).

In particular, patients with lesions on the face versus those without had higher proportions of pain that *comes and goes throughout the day* (face: 58% vs 37%) and lower proportions of pain *only after scratching a lot* (face: 33% vs 52%, $P = .02$) (Table E2, available in this article's Online Repository at www.jaci-inpractice.org). Furthermore, patients with lesions on the face had higher proportions of pain thought to be caused mostly by *inflamed red skin* (35% vs 22%), less from *open areas caused by scratching* (19% vs 30%), and similar rates of *burning from creams or ointments* (11% vs 9%). Moreover, patients with lesions on the back versus those without reported less *pain from open areas by scratching* (24% vs 30%, $P = .01$). Otherwise, no other site of lesions was specifically associated with pain characteristics.

Pain intensity

Among those 365 adults with pain, the weighted mean (95% CI) intensity of worst pain in the past week was 4.3 (4.0-4.7), with 22% reporting worst pain intensity ≥ 7 . Persons with more frequent pain also reported significantly increased pain intensity ($P < .0001$) (Table E3, available in this article's Online Repository at www.jaci-inpractice.org).

There were no significant differences of pain intensity in females versus males (4.7 vs 4.1, $P = .6$), age (18-39 years: 4.2; 40-59 years: 4.5; ≥ 60 years: 4.2; $P = .6$), or race/ethnicity (white: 4.3; black: 4.6; Hispanic: 4.5; Asians: 3.2; multiracial/other: 4.9; $P = 0.6$).

Pain intensity was significantly correlated with PO-SCORAD (Pearson correlation; $r = 0.72$, $P < .0001$), PO-SCORAD itch ($r = 0.65$, $P < .0001$) and sleep ($r = 0.55$, $P < .0001$), and POEM ($r = 0.66$, $P < .0001$). There was a stepwise increase in the proportion of patients with moderate (4-6) or severe (7-10) pain intensity among those with severe versus moderate versus mild PO-SCORAD, PO-SCORAD itch and sleep, and POEM;

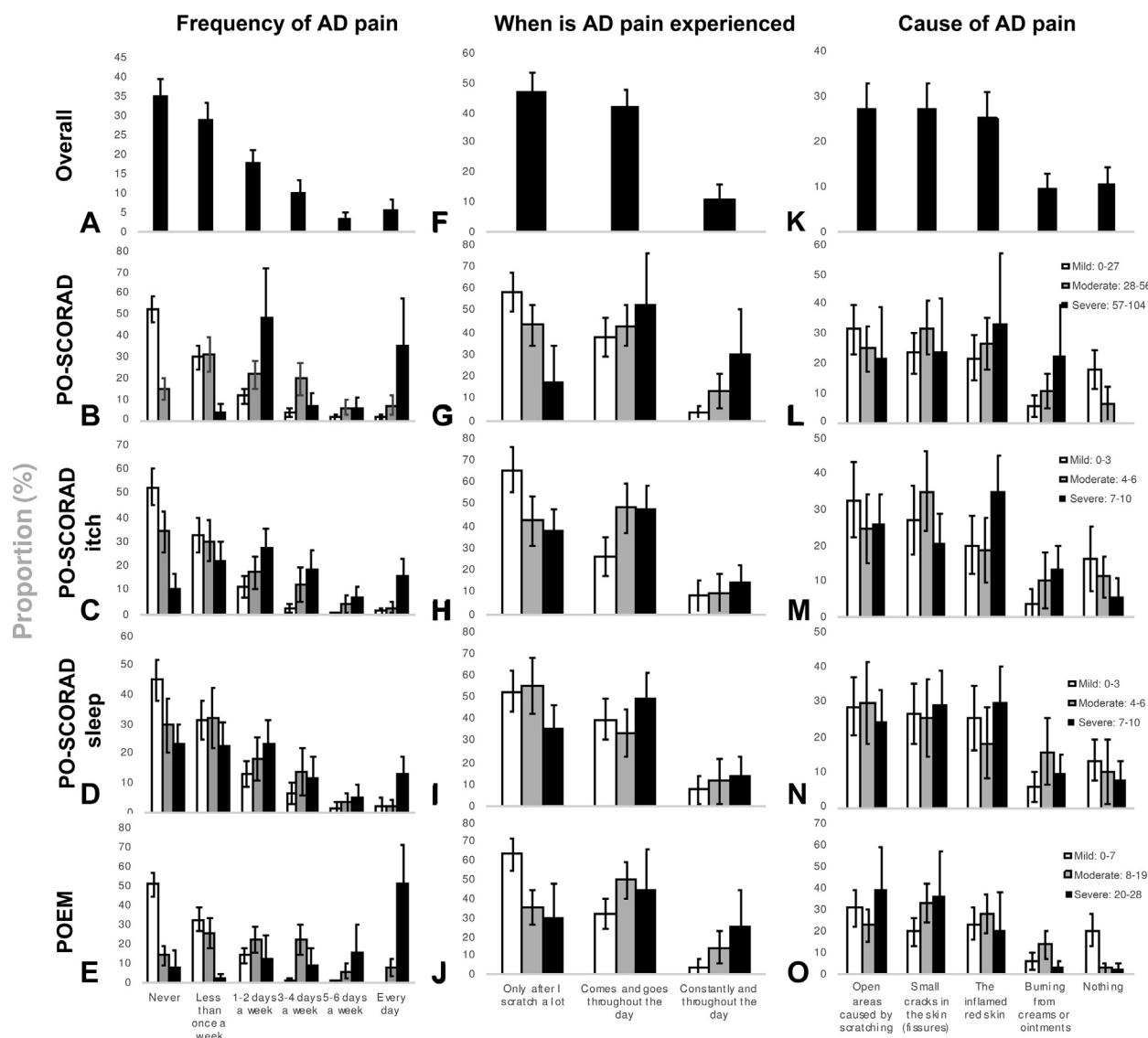


FIGURE 1. Frequency and characteristics of pain in atopic dermatitis (AD). The distribution of frequency (A) and characteristics (F, K) of pain from AD among US adults are presented. The relationships of AD pain frequency and characteristics with PO-SCORAD (B, G, L), PO-SCORAD itch (C, H, M), PO-SCORAD sleep (D, I, N), and POEM (E, J, O) were also examined. *PO-SCORAD*, Patient-Oriented Scoring Atopic Dermatitis; *POEM*, Patient Oriented Eczema Measure.

though, PO-SCORAD was the strongest predictor of pain ($P < .0001$ for all; Figure 2). Of note, 9% of adults with clear or mild itch (0-3) had moderate or severe pain (3.7% of all adult AD), whereas 28% of those with severe itch (7-10) had only mild pain (8.1% of all adult AD).

In multivariable regression models, AD pain intensity was associated with PO-SCORAD, PO-SCORAD itch, POEM, facial lesions, and less than high school education level, but not PO-SCORAD sleep, hand lesions, sex, race/ethnicity, age, or household income (Table II).

Quality of life impact

Pain was associated with increased self-consciousness and had a negative impact on the ability to shop and perform other

activities of daily living, make clothing decisions, socialize or pursue leisure activities, play sports, work or study, have relationships with others, and have normal sexual function, as well as a negative impact on treatment burden (Table E4, available in this article's Online Repository at www.jaci-inpractice.org). Moreover, there was a significant dose-response effect with an even more harmful impact on the above aspects of QOL with increasing frequency or severity of skin pain (Tables E5 and E6, available in this article's Online Repository at www.jaci-inpractice.org).

In multivariable linear regression models, PO-SCORAD, PO-SCORAD itch and sleep, and POEM, there were significant 2-way statistical interactions between frequency and intensity of pain as predictors of QOL ($P = .04$). That is, persons

TABLE I. Associations of atopic dermatitis pain frequency and intensity (n = 596)

Covariables	AD pain frequency (≥1 d per week)		AD pain intensity	
	Adjusted odds ratio (95% confidence interval)*	P value	Adjusted β (95% confidence interval)†	P value
PO-SCORAD	1.04 (1.01, 1.07)	<.0001	0.06 (0.03, 0.08)	<.0001
PO-SCORAD itch	1.15 (1.02, 1.30)	<.0001	0.20 (0.08, 0.32)	.0008
PO-SCORAD sleep	1.02 (0.92, 1.13)	.73	0.07 (−0.01, 0.14)	.09
POEM	1.15 (1.02, 1.30)	<.0001	0.12 (0.07, 0.17)	<.0001
Female sex	0.65 (0.38, 1.10)	.11	−0.008 (−0.43, 0.41)	.97
Age (y)	0.99 (0.97, 1.01)	.07	−0.001 (−0.01, 0.01)	.82
Race/ethnicity				
White	1.00 (ref)	—	0.00 (ref)	—
Black	0.87 (0.43, 1.74)	.69	0.09 (−0.48, 0.66)	.76
Hispanic	0.72 (0.32, 1.63)	.43	−0.04 (−0.68, 0.60)	.90
Multiracial/other	1.39 (0.52, 3.74)	.51	0.14 (−0.49, 0.76)	.67
Poverty income ratio	0.92 (0.84, 1.01)	.09	−0.03 (−0.09, 0.03)	.39
Level of education				
Less than high school	1.00 (ref)	—	0.00 (ref)	—
High school or equivalent	2.04 (0.85, 4.89)	.11	−0.79 (−1.50, −0.08)	.03
More than high school	1.47 (0.66, 3.30)	.35	−0.78 (−1.51, −0.07)	.03
AD lesions on face	0.97 (0.50, 1.89)	.93	0.72 (0.12, 1.32)	.02
AD lesions on hands	1.23 (0.65, 2.31)	.53	0.05 (−0.52, 0.63)	.85

AD, Atopic dermatitis; DLQI, Dermatology Life Quality Index; PO-SCORAD, Patient-Oriented Scoring Atopic Dermatitis; POEM, Patient Oriented Eczema Measure. Bold values indicate statistically significant P-values.

Missing values occurred in 4 (0.7%) for pain frequency, 3 (0.5%) for pain intensity, 4 (0.7%) for PO-SCORAD itch, 6 (1.0%) for PO-SCORAD sleep, 0 (0.0%) for other elements of PO-SCORAD, 0 (0.0%) for POEM, DLQI, age, sex, level of education, race/ethnicity, poverty income ratio.

*Weighted logistic regression models were constructed with AD pain frequency (≥1 vs <1 d per week) as the binary dependent variable. The independent variables include PO-SCORAD (continuous), PO-SCORAD itch (continuous), PO-SCORAD sleep (continuous), POEM (continuous), sex (female vs male), age (y), race/ethnicity (black, Hispanic, multiracial/other vs white), poverty income ratio (continuous), level of education (high school, greater than high school vs less than high school), AD lesions on the face or hands (yes vs no). Adjusted odds ratios and 95% confidence intervals were estimated. Note: ordinal logistic regression models were tested, but did not meet the proportional odds assumption (Score test, $P < .0001$).

†Weighted linear regression models were constructed with AD pain intensity as the continuous dependent variable. The independent variables include PO-SCORAD (continuous), PO-SCORAD itch (continuous), PO-SCORAD sleep (continuous), POEM (continuous), sex (female vs male), age (y), race/ethnicity (black, Hispanic, multiracial/other vs white), poverty income ratio (continuous), level of education (high school, greater than high school vs less than high school), AD lesions on the face or hands (yes vs no). Adjusted β and 95% confidence intervals were estimated.

with more frequent and intense pain had higher DLQI scores (ie, worse impact on QOL) compared with those with less frequent or less intense pain (Table II).

Similarly, there were significant 2-way statistical interactions between intensity of AD pain and itch as predictors of QOL ($P < .0001$). Among persons with mild itch, severe pain was associated with worse QOL, whereas among persons with severe itch, moderate and severe pain were associated with a stepwise worse impact on QOL (Table E7, available in this article's Online Repository at www.jaci-inpractice.org).

DISCUSSION

The present study found that the majority of US adults with AD report pain from AD. Patients most commonly reported pain originating from scratching, fissures, and from the inflammation itself. AD pain was both frequent and intense in a subset of adults. In general, AD pain intensity was significantly higher among those who reported more frequent pain. Frequency and intensity of AD pain were both associated with more severe AD and itch. AD pain intensity, but not frequency, was associated with AD lesions on the face and lower level of education. AD pain, particularly more frequent and/or severe pain, was associated with significantly worse QOL overall and for all individual aspects of QOL examined. The results of the present study are consistent with a previous clinical study of 305 adult patients

with AD that found slightly higher rates of skin pain in the past week (42%) than the present study (33.3%), increased prevalence and intensity of pain among patients with more severe AD, and poorer QOL associated with the presence and severity of skin pain.⁷ In that study, substantial proportions reported that their pain was not exclusively attributable to scratching and described their pain with distinct terms resembling neuropathic pain. In a case-control study of 25 patients with AD and 25 controls, patients with AD had an average pain visual analog score of 39.7, increased sensitivity to mechanically induced pain both on lesional and extralesional skin, and hyperknesis.¹⁹ Taken together, pain is a commonly reported and burdensome symptom in adults with AD.

Importantly, pain appears to be a distinct symptom from itch in AD. First, a subset of patients with AD reported having only mild itch but moderate or severe pain, or mild pain and moderate or severe itch. Second, approximately one-half of adults who experienced AD pain reported that it was not merely related to scratching. Third, AD pain appears to be multifactorial, with subsets of AD pain attributed to scratching, fissures, inflamed red skin *per se*, and only a minority from poor tolerability of topical medications. In particular, pain attributed with inflamed red skin was most commonly reported in those with severe AD and AD lesions on the face. Finally, AD pain was associated with worse QOL even after controlling for severity of AD and itch. Taken together, AD pain appears to be multifactorial and a distinct symptom from itch.

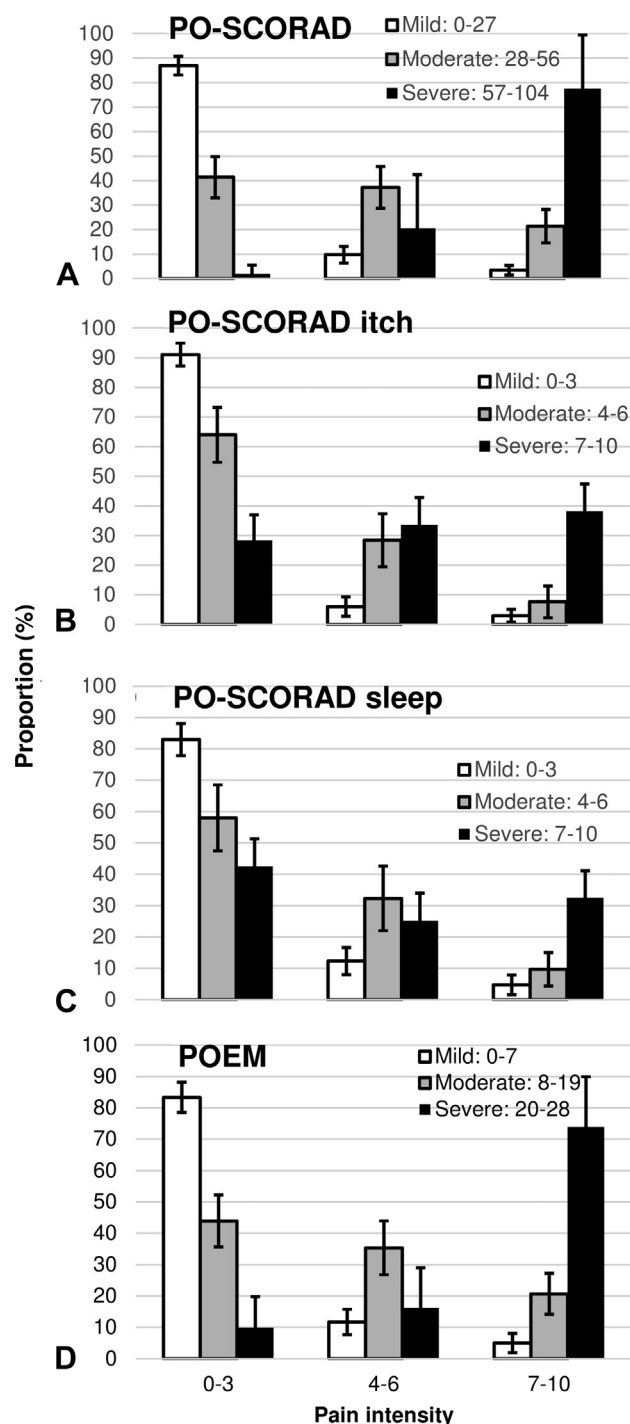


FIGURE 2. Intensity of pain in atopic dermatitis. The relationships of atopic dermatitis pain intensity and mild, moderate versus severe atopic dermatitis severity as judged by PO-SCORAD (mild: 0-27; moderate: 28-56; severe: 57-104) (A), PO-SCORAD itch (mild: 0-3; moderate: 4-6; severe: 7-10) (B), PO-SCORAD sleep (mild: 0-3; moderate: 4-6; severe: 7-10) (C), and POEM (mild: 0-7; moderate: 8-19; severe: 20-28) (D) in US adults were examined. AD, Atopic dermatitis; POEM, Patient Oriented Eczema Measure; PO-SCORAD, Patient-Oriented Scoring Atopic Dermatitis.

TABLE II. Association of pain frequency and intensity with quality of life in atopic dermatitis (n = 596)

AD pain		Dermatology Life Quality Index (DLQI)	
Frequency per week (d)	Intensity	Adjusted β (95% CI)	P value
≤ 2	0-3	0.00 (ref)	—
	4-6	1.65 (0.47, 2.84)	.006
	7-10	3.34 (1.72, 4.97)	<.0001
3-6	0-3	0.00 (ref)	—
	4-6	3.76 (1.41, 6.12)	.002
	7-10	6.38 (3.70, 9.06)	<.0001
7	0-3	0.00 (ref)	—
	4-6	5.69 (−3.77, 15.15)	.24
	7-10	11.37 (2.47, 20.28)	.01
Covariables			
PO-SCORAD		0.21 (0.17, 0.25)	<.0001
PO-SCORAD itch		0.36 (0.18, 0.54)	<.0001
PO-SCORAD sleep		−0.03 (−0.16, 0.10)	.65
POEM		0.11 (0.03, 0.20)	.008
Female sex		−0.31 (−1.00, 0.37)	.37
Age (y)		−0.02 (−0.04, 0.002)	.08
Race/ethnicity			
White		0.00 (ref)	—
Black		1.17 (0.23, 2.11)	.01
Hispanic		0.89 (−0.05, 1.83)	.06
Multiracial/other		2.14 (0.91, 3.38)	.0007
Level of education			
Less than high school		0.00 (ref)	—
High school or greater		−0.23 (−1.14, 0.68)	.62
Poverty income ratio		−0.002 (−0.10, 0.09)	.97
AD lesions on face		−0.48 (−0.41, 1.36)	.29
AD lesions on hands		1.32 (0.42, 2.22)	.004

AD, Atopic dermatitis; CI, confidence interval; DLQI, Dermatology Life Quality Index; PO-SCORAD, Patient-Oriented Scoring Atopic Dermatitis; POEM, Patient Oriented Eczema Measure.

Bold values indicate statistically significant P values.

This study found that AD severity was the major predictor of AD pain and the strongest predictor of AD pain intensity. AD pain intensity was also associated with less than high school level of education. AD pain frequency was not associated with any sociodemographics. AD pain frequency was inversely associated with age in bivariable analyses. This was due to the confounding effects of decreasing AD severity with age. Age did not remain a significant association of AD pain in multivariable models that adjusted for AD severity. Previous studies did not examine the sociodemographic associations of AD pain. However, prior studies showed higher frequency and/or intensity of pain in African Americans/blacks compared with whites with a variety of etiologies, including osteoarthritis, migraine headaches, post-operative pain, myofascial pain, angina pectoris, bone and joint pain, compared with whites.²⁰⁻²² The increased pain observed in these disorders may be related to more severe disease, similar to the increased AD severity we observed in African Americans/blacks. However, there are no apparent racial/ethnic differences of pain frequency or intensity when controlling for AD severity.

Yet, African American/black and/or multiracial/other race/ethnicity was associated with worse QOL, which may be related to other factors, for example, postinflammatory hyperpigmentation.

The mechanisms of increased pain in AD remain unknown, but are likely multifactorial and differ by the pain characteristics. A subset of AD pain appears to be secondary to mechanical trauma of the skin from open sores secondary to excoriations. However, pain attributed to inflamed red skin might be mediated by cutaneous inflammation or aberrant nerve signaling. It is important to note that only a small minority of adults with AD reported that their pain was primarily caused by burning from topical medications. Of course, some patients may experience multiple types of pain. Future studies are needed to better understand the mechanisms of pain in AD. However, it is imperative that such studies thoroughly assess the frequency, intensity, characteristics, and attribution of pain.

The strengths of this study include being large scaled and population based with a diverse sample and sample weights that allow for generalization of results to the US population, assessment of multiple aspects of pain in AD, and use of multiple and well-validated assessments of AD severity. We used an adaptation of the extensively validated UKWP criteria⁹ to establish the diagnosis of AD. PO-SCORAD and POEM have been studied in patients with AD and found to have good face validity, construct validity, internal consistency, reliability, and/or responsiveness; POEM is the preferred assessment of AD symptoms for clinical trials by the Harmonizing Outcome Measures in Eczema group.^{12,15,23-37} However, this study has limitations. Diagnosis and severity classification were not verified by physical examination and may be subject to misclassification. AD pain frequency and intensity paralleled the question about itch frequency in POEM and numeric rating scale-itch, respectively. However, assessments of AD pain were developed for this study and not previously validated. Future studies are warranted to address these points.

CONCLUSIONS

AD is associated with higher prevalence, frequency, and intensity of pain. Pain in AD appears to be multifactorial and related to scratching, inflamed red skin, and to a lesser extent poor tolerance of topical medications. AD pain was associated with increased severity of AD overall and itch in particular, and impacted all aspects of QOL. We recommend that frequency and intensity of pain be assessed along with itch in clinical practice and/or trials of AD. Future studies are needed to determine the precise mechanisms and optimal treatment approaches for pain in AD.

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REFERENCES

- Chiesa Fuxench ZC, Block JK, Boguniewicz M, Boyle J, Fonacier L, Gelfand JM, et al. Atopic Dermatitis in America Study: a cross-sectional study examining the prevalence and disease burden of atopic dermatitis in the US adult population. *J Invest Dermatol* 2019;139:583-90.
- Silverberg JI, Gelfand JM, Margolis DJ, Boguniewicz M, Fonacier L, Grayson MH, 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;121:340-7.
- Silverberg JI, Gelfand JM, Margolis DJ, Boguniewicz M, Fonacier L, Grayson MH, et al. Health utility scores of atopic dermatitis in US adults. *J Allergy Clin Immunol Pract* 2019;7:1246-1252.e1.
- Silverberg JI, Gelfand JM, Margolis DJ, Boguniewicz M, Fonacier L, Grayson MH, et al. Association of atopic dermatitis with allergic, autoimmune, and cardiovascular comorbidities in US adults. *Ann Allergy Asthma Immunol* 2018;121:604-612.e3.
- Yu SH, Silverberg JI. Association between atopic dermatitis and depression in US adults. *J Invest Dermatol* 2015;135:3183-6.
- Silverberg JI. Selected comorbidities of atopic dermatitis: atopy, neuropsychiatric, and musculoskeletal disorders. *Clin Dermatol* 2017;35:360-6.
- Vakharia PP, Chopra R, Sacotte R, Patel KR, Singam V, Patel N, et al. Burden of skin pain in atopic dermatitis. *Ann Allergy Asthma Immunol* 2017;119:548-552.e3.
- Simpson EL, Bieber T, Eckert L, Wu R, Ardeleanu M, Graham NMH, et al. Patient burden of moderate to severe atopic dermatitis (AD): insights from a phase 2b clinical trial of dupilumab in adults. *J Am Acad Dermatol* 2016;74:491-8.
- Williams HC, Burney PG, Pembroke AC, Hay RJ. The U.K. Working Party's Diagnostic Criteria for Atopic Dermatitis: III. Independent hospital validation. *Br J Dermatol* 1994;131:406-16.
- Stalder JF, Barbarot S, Wollenberg A, Holm EA, De Raeve L, Seidenari S, et al. Patient-Oriented SCORAD (PO-SCORAD): a new self-assessment scale in atopic dermatitis validated in Europe. *Allergy* 2011;66:1114-21.
- Charman CR, Venn AJ, Ravenscroft JC, Williams HC. Translating Patient-Oriented Eczema Measure (POEM) scores into clinical practice by suggesting severity strata derived using anchor-based methods. *Br J Dermatol* 2013;169:1326-32.
- Finlay AY, Khan GK. Dermatology Life Quality Index (DLQI)—a simple practical measure for routine clinical use. *Clin Exp Dermatol* 1994;19:210-6.
- Spuls PI, Gerbens LAA, Simpson E, Apfelbacher CJ, Chalmers JR, Thomas KS, et al. Patient-Oriented Eczema Measure (POEM), a core instrument to measure symptoms in clinical trials: a Harmonising Outcome Measures for Eczema (HOME) statement. *Br J Dermatol* 2017;176:979-84.
- Chalmers JR, Thomas KS, Apfelbacher CJ, Williams HC, Prinsen CA, Spuls PI, et al. Report from the fifth international consensus meeting to harmonize core outcome measures for atopic eczema/dermatitis clinical trials (HOME initiative). *Br J Dermatol* 2018;178:e332-41.
- Vakharia PP, Chopra R, Sacotte R, Patel N, Immaneni S, White T, et al. Validation of patient-reported global severity of atopic dermatitis in adults. *Allergy* 2018;73:451-8.
- Silverberg JI, Chiesa Fuxench ZC, Gelfand JM, Margolis DJ, Boguniewicz M, Fonacier L, et al. Content and construct validity, predictors, and distribution of self-reported atopic dermatitis severity in US adults. *Ann Allergy Asthma Immunol* 2018;121:729-734.e4.
- Silverberg JI, Gelfand JM, Margolis DJ, Fonacier L, Boguniewicz M, Schwartz LB, et al. Severity strata for POEM, PO-SCORAD, and DLQI in US adults with atopic dermatitis. *Ann Allergy Asthma Immunol* 2018;121:464-71.
- Benjamini Y, Hochberg Y. Controlling the false discovery rate—a practical and powerful approach to multiple testing. *J R Stat Soc Series B Stat Methodol* 1995;57:289-300.
- Andersen HH, Elberling J, Solvsten H, Yosipovitch G, Arendt-Nielsen L. Nonhistaminergic and mechanical itch sensitization in atopic dermatitis. *Pain* 2017;158:1780-91.
- Vaughn IA, Terry EL, Bartley EJ, Schaefer N, Fillingim RB. Racial-ethnic differences in osteoarthritis pain and disability: a meta-analysis. *J Pain* 2019;20:629-44.
- Klonoff EA. Disparities in the provision of medical care: an outcome in search of an explanation. *J Behav Med* 2009;32:48-63.
- Green CR, Anderson KO, Baker TA, Campbell LC, Decker S, Fillingim RB, et al. The unequal burden of pain: confronting racial and ethnic disparities in pain. *Pain Med* 2003;4:277-94.
- Badia X, Mascaro JM, Lozano R. Measuring health-related quality of life in patients with mild to moderate eczema and psoriasis: clinical validity, reliability and sensitivity to change of the DLQI. The Cavide Research Group. *Br J Dermatol* 1999;141:698-702.

24. Coutanceau C, Stalder JF. Analysis of correlations between patient-oriented SCORAD (PO-SCORAD) and other assessment scores of atopic dermatitis severity and quality of life. *Dermatology* 2014;229:248-55.
25. Holm EA, Wulf HC, Stegmann H, Jemec GB. Life quality assessment among patients with atopic eczema. *Br J Dermatol* 2006;154:719-25.
26. Herd RM, Tidman MJ, Ruta DA, Hunter JA. Measurement of quality of life in atopic dermatitis: correlation and validation of two different methods. *Br J Dermatol* 1997;136:502-7.
27. Jobanputra R, Bachmann M. The effect of skin diseases on quality of life in patients from different social and ethnic groups in Cape Town, South Africa. *Int J Dermatol* 2000;39:826-31.
28. Holm EA, Esmann S, Jemec GB. Does visible atopic dermatitis affect quality of life more in women than in men? *Gend Med* 2004;1:125-30.
29. Twiss J, Meads DM, Preston EP, Crawford SR, McKenna SP. Can we rely on the Dermatology Life Quality Index as a measure of the impact of psoriasis or atopic dermatitis? *J Invest Dermatol* 2012;132:76-84.
30. Chalmers JR, Schmitt J, Apfelbacher C, Dohil M, Eichenfield LF, Simpson EL, et al. Report from the third international consensus meeting to harmonise core outcome measures for atopic eczema/dermatitis clinical trials (HOME). *Br J Dermatol* 2014;171:1318-25.
31. Chalmers JR, Simpson E, Apfelbacher CJ, Thomas KS, von Kobyletzki L, Schmitt J, 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;175:69-79.
32. Gerbens LA, Chalmers JR, Rogers NK, Nankervis H, Spuls PI. Reporting of symptoms in randomized controlled trials of atopic eczema treatments: a systematic review. *Br J Dermatol* 2016;175:678-86.
33. Gerbens LA, Prinsen CA, Chalmers JR, Drucker AM, von Kobyletzki LB, Limpens J, et al. Evaluation of the measurement properties of symptom measurement instruments for atopic eczema: a systematic review. *Allergy* 2017;72:146-63.
34. Heint D, Chalmers J, Nankervis H, Apfelbacher CJ. Eczema trials: quality of life instruments used and their relation to patient-reported outcomes. A systematic review. *Acta Derm Venereol* 2016;96:596-601.
35. Heint D, Prinsen CA, Deckert S, Chalmers JR, Drucker AM, Ofenloch R, et al. Measurement properties of adult quality-of-life measurement instruments for eczema: a systematic review. *Allergy* 2016;71:358-70.
36. Heint D, Prinsen CAC, Sach T, Drucker AM, Ofenloch R, Flohr C, et al. Measurement properties of quality-of-life measurement instruments for infants, children and adolescents with eczema: a systematic review. *Br J Dermatol* 2017;176:878-89.
37. Schmitt J, Williams H. Harmonising Outcome Measures for Eczema (HOME). Report from the First International Consensus Meeting (HOME 1), 24 July 2010, Munich, Germany. *Br J Dermatol* 2010;163:1166-8.

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METHODS

Data source

Data were obtained from the Atopic Dermatitis (AD) in America Survey whose population was sampled from the long-standing GfK Knowledge Panel. The AD in America Study was designed to examine multiple facets of the patient burden, comorbidities, and resource utilization of US adults with AD. The GfK Knowledge panel is the largest and oldest probability-based web panel in the United States and contains between 40,000 and 50,000 adult panel members at any given time. The GfK web panel was initially constructed from a national address-based sample of households in the United States who are recruited to join in and receive small incentives for participating in web surveys on a regular basis. This approach uses a single sampling frame via the Delivery Sequence File of the US Postal Service to provide a statistically valid representation of the US population as well as many difficult-to-survey populations. The GfK web panel also provides internet access to households without existing internet access. This web-based panel has been previously used in other large, epidemiological studies and has been shown to be representative of the US population.^{E1-E3}

Study design

This was a cross-sectional study involving a 2-stage sampling process. Stage 1 was designed to determine the prevalence of AD in US adults. In this stage, an initial cross-sectional sample of 2137 adults from the existing GfK Knowledge web panel was

invited to participate in the survey. The focus of the survey was not disclosed in the invitation (for stage 1 or 2) to members of the web panel to avoid biasing participation based on respondent interest or disinterest in the subject. A total of 1278 adults completed the survey (completion rate = 60.2%). Although this sample provided a precise estimate of the prevalence of AD among the adult population, it did not yield a large enough sample of patients with AD to investigate differences between different levels of disease severity. In stage 2, an additional sample of 8217 adults from the GfK knowledge panel completed screening to identify and interview an additional group of adults with AD; 19.7% met United Kingdom Working Party (UKWP) criteria and were eligible for inclusion (completion rate = 59.9%). Using data from the US Census Bureau, sample weights were created that adjusted for age, gender, race, ethnicity, education level, census region, household income, home ownership status, and metropolitan area using an iterative proportional fitting procedure.^{E4,E5} Sample weights were included in all analyses to allow for representative estimates of the US population.

UKWP criteria for AD

The modified UKWP definition of AD included all aspects of the UKWP criteria (having an itchy skin condition during the past 12 months and 3 or more of the following: (1) history of skin crease involvement; (2) a personal history of asthma or hay fever; (3) a history of general dry skin during the past year; (4) onset under the age of 2), except assessment of visible flexural eczema by a clinician, which could not be performed.

TABLE E1. Subject characteristics

Variable	Atopic dermatitis	
	No (n = 2291)	Yes (n = 602)
Age (y)—wtd mean (95% CI)	46.7 (45.8-47.6)	46.6 (45.1-48.1)
Female sex—freq (wtd %)	1202 (53%)	349 (58%)
Race/ethnicity—freq (wtd %)		
Caucasian/white	1684 (64%)	396 (58%)
African American/black	195 (10%)	74 (17%)
Hispanic	264 (6%)	77 (17%)
Multiracial/other	148 (8%)	55 (9%)
Level of education—freq (wtd %)		
Less than high school	140 (15%)	48 (19%)
High school or equivalent	668 (28%)	164 (23%)
Some college	703 (29%)	186 (29%)
Bachelor's degree or higher	780 (28%)	204 (29%)
Self-reported AD severity—freq (wtd %)		
Mild	—	289 (53%)
Moderate	—	172 (39%)
Severe	—	34 (8%)

AD, Atopic dermatitis; CI, confidence interval; wtd, weighted.

TABLE E2. Association of body site affected with atopic dermatitis lesions and characteristics of pain

	Freq (wtd %)			Freq (wtd %)			Freq (wtd %)			Freq (wtd %)			Freq (wtd %)		
	No	Yes	P	No	Yes	P	No	Yes	P	No	Yes	P	No	Yes	P
	Trunk			Flexural			Face			Hands			Genitals and buttocks		
When is atopic dermatitis pain experienced															
Constantly and throughout the day	12 (11%)	15 (11%)	.45	14 (14%)	13 (8%)	.21	21 (11%)	6 (9%)	.021	23 (10%)	4 (11%)	.05	23 (11%)	4 (11%)	.87
Comes and goes throughout the day	68 (38%)	88 (45%)		86 (43%)	70 (40%)		113 (37%)	43 (58%)		105 (37%)	51 (57%)		137 (37%)	19 (57%)	
Only after I scratch a lot	95 (52%)	84 (43%)		88 (43%)	91 (52%)		152 (52%)	27 (33%)		148 (52%)	31 (33%)		159 (52%)	20 (33%)	
What causes the most pain from atopic dermatitis															
The inflamed red skin	44 (28%)	47 (23%)	.13	42 (22%)	49 (29%)	.77	67 (22%)	24 (35%)	.04	72 (26%)	19 (24%)	.13	81 (26%)	10 (21%)	.55
Small cracks in the skin (fissures)	50 (29%)	48 (26%)		51 (29%)	47 (25%)		71 (26%)	27 (32%)		63 (24%)	35 (39%)		87 (27%)	11 (29%)	
Open areas caused by scratching	57 (31%)	47 (25%)		55 (28%)	49 (27%)		90 (30%)	14 (19%)		84 (29%)	20 (24%)		93 (28%)	11 (21%)	
Burning from creams or ointments	11 (6%)	23 (13%)		18 (11%)	16 (9%)		26 (9%)	8 (11%)		26 (10%)	8 (10%)		27 (8%)	7 (18%)	
Nothing	15 (7%)	23 (13%)		23 (11%)	15 (10%)		35 (13%)	3 (4%)		34 (12%)	4 (4%)		34 (10%)	4 (11%)	

wtd, Weighted.

Bold values indicate statistically significant *P* values.

TABLE E3. Association between frequency and intensity of pain from atopic dermatitis

Pain from atopic dermatitis	Intensity—Freq (wtd %)			P
	0-3	4-6	7-10	
Never	233 (100%)	0 (0%)	0 (0%)	<.0001
<1 or 1-2 d a week	163 (58%)	68 (28%)	34 (14%)	
3-6 d a week	14 (22%)	31 (53%)	22 (26%)	
Daily	1 (2%)	6 (15%)	23 (83%)	

wtd, Weighted.

TABLE E4. Impact of atopic dermatitis pain on individual aspects of the DLQI (n = 598)

	DLQI questions—n (%)				
Pain from atopic dermatitis	Not at all/not relevant	A little	A lot	Very much	P value
Q1. Itching and/or burning of skin					
No	85 (39%)	130 (53%)	13 (7%)	5 (1%)	<.0001
Yes	43 (11%)	211 (57%)	78 (20%)	33 (13%)	
Q2. Self-conscious					
No	196 (83%)	29 (14%)	6 (3%)	1 (0.4%)	<.0001
Yes	179 (45%)	124 (32%)	39 (14%)	23 (8%)	
Q3. Ability to shop, take care of home and garden					
No	224 (94%)	8 (5%)	0 (0%)	1 (0.4%)	<.0001
Yes	267 (69%)	61 (17%)	23 (9%)	14 (5%)	
Q4. Clothing decisions					
No	203 (85%)	20 (11%)	6 (3%)	3 (2%)	<.0001
Yes	197 (52%)	95 (25%)	43 (12%)	30 (11%)	
Q5. Socializing or leisure activities					
No	224 (95%)	5 (4%)	1 (0.2%)	2 (0.8%)	<.0001
Yes	246 (63%)	79 (23%)	26 (9%)	14 (5%)	
Q6. Sports					
No	228 (99%)	4 (2%)	0 (0%)	0 (0%)	<.0001
Yes	259 (68%)	58 (16%)	32 (11%)	15 (5%)	
Q7-1. Work or study in past week (yes/no)					
No	232 (100%)	0 (0%)	N/A	N/A	<.0001
Yes	338 (93%)	26 (8%)	N/A	N/A	
Q7-2. Work or study overall					
No	142 (89%)	16 (10%)	1 (1%)	0 (0%)	<.0001
Yes	160 (58%)	89 (40%)	5 (2%)	0 (0%)	
Q8. Relationship with partner, friend, or relative					
No	221 (94%)	11 (6%)	0 (0%)	0 (0%)	<.0001
Yes	263 (67%)	64 (21 %)	21 (6%)	16 (6%)	
Q9. Sexual function					
No	28 (98%)	4 (2%)	0 (0%)	0 (0%)	<.0001
Yes	277 (71%)	52 (17%)	17 (6%)	18 (5%)	
Q10. Effect of treatment on quality of life					
No	217 (94%)	15 (6%)	0 (0%)	0 (0%)	<.0001
Yes	228 (59%)	95 (28%)	26 (8%)	16 (5%)	

DLQI, Dermatology Life Quality Index.

Bold values indicate statistically significant P values.

TABLE E5. Impact of atopic dermatitis pain frequency on individual aspects of the DLQI (n = 598)

	DLQI questions—n (%)				
Pain from atopic dermatitis or eczema	Not at all/not relevant	A little	A lot	Very much	P value
Q1. Itching and/or burning of skin					
Never	85 (39%)	130 (53%)	13 (7%)	5 (1%)	<.0001
Less than once a week	35 (19%)	110 (67%)	19 (12%)	2 (2%)	
1-2 d a week	6 (7%)	65 (60%)	19 (17%)	12 (17%)	
3-4 d a week	1 (1%)	23 (53%)	21 (31%)	4 (15%)	
5-6 d a week	1 (3%)	7 (34%)	8 (48%)	2 (16%)	
Every day	0 (0%)	6 (15%)	11 (34%)	13 (52%)	
Q2. Self-conscious about lesions					
Never	196 (83%)	29 (14%)	6 (3%)	1 (0.4%)	<.0001
Less than once a week	109 (63%)	50 (32%)	7 (6%)	0 (0%)	
1-2 d a week	44 (38%)	42 (41%)	9 (14%)	7 (8%)	
3-4 d a week	15 (28%)	18 (33%)	13 (34%)	3 (6%)	
5-6 d a week	3 (16%)	7 (24%)	5 (30%)	3 (29%)	
Every day	8 (28%)	7 (14%)	5 (13%)	10 (45%)	
Q3. Ability to shop, take care of home and garden					
Never	224 (94%)	8 (5%)	0 (0%)	1 (0.4%)	<.0001
Less than once a week	151 (90%)	12 (7%)	2 (3%)	1 (0.2%)	
1-2 d a week	70 (62%)	22 (22%)	7 (11%)	3 (5%)	
3-4 d a week	28 (56%)	14 (30%)	6 (12%)	1 (2%)	
5-6 d a week	7 (33%)	5 (18%)	3 (20%)	3 (29%)	
Every day	11 (30%)	8 (26%)	5 (22%)	6 (22%)	
Q4. Clothing decisions					
Never	203 (85%)	20 (11%)	6 (3%)	3 (2%)	<.0001
Less than once a week	121 (75%)	33 (16%)	10 (8%)	2 (0.6%)	
1-2 d a week	39 (36%)	35 (33%)	15 (13%)	13 (19%)	
3-4 d a week	22 (39%)	18 (44%)	8 (15%)	1 (3%)	
5-6 d a week	7 (27%)	5 (24%)	2 (10%)	4 (39%)	
Every day	8 (23%)	4 (14%)	8 (26%)	10 (38%)	
Q5. Socializing or leisure activities					
Never	224 (95%)	5 (4%)	1 (0.2%)	2 (0.8%)	<.0001
Less than once a week	141 (83%)	22 (13%)	3 (4%)	0 (0%)	
1-2 d a week	62 (56%)	31 (33%)	5 (5%)	4 (5%)	
3-4 d a week	25 (48%)	15 (35%)	9 (17%)	0 (0%)	
5-6 d a week	8 (33%)	4 (18%)	3 (20%)	3 (29%)	
Every day	10 (28%)	7 (23%)	6 (24%)	7 (26%)	
Q6. Sports					
Never	228 (99%)	4 (2%)	0 (0%)	0 (0%)	<.0001
Less than once a week	146 (87%)	15 (9%)	4 (3%)	1 (0.3%)	
1-2 d a week	64 (57%)	24 (24%)	10 (14%)	4 (5%)	
3-4 d a week	30 (59%)	9 (24%)	8 (16%)	1 (1%)	
5-6 d a week	8 (42%)	5 (23%)	3 (20%)	2 (16%)	
Every day	11 (31%)	5 (10%)	7 (29%)	7 (31%)	
Q7-1. Work or study in past week (yes/no)					
Never	232 (100.0%)	0 (0%)			<.0001
Less than once a week	164 (99%)	2 (1%)			
1-2 d a week	95 (92%)	7 (8%)			
3-4 d a week	45 (96%)	3 (4%)			
5-6 d a week	15 (84%)	3 (16%)			
Every day	19 (57%)	11 (44%)			
Q7-2. Work or study overall					
Never	142 (89%)	16 (11%)	1 (1%)	0 (0%)	.0001
Less than once a week	102 (72%)	31 (28%)	0 (0%)	0 (0%)	
1-2 d a week	39 (47%)	30 (51%)	1 (2%)	0 (0%)	

(continued)

TABLE E5. (Continued)

Pain from atopic dermatitis or eczema	DLQI questions—n (%)				P value
	Not at all/not relevant	A little	A lot	Very much	
3-4 d a week	10 (33%)	20 (61%)	2 (7%)	0 (0%)	
5-6 d a week	3 (65%)	3 (35%)	0 (0%)	0 (0%)	
Every day	6 (46%)	5 (39%)	2 (16%)	0 (0%)	
Q8. Relationship with partner, friend, or relative					
Never	221 (94%)	11 (6%)	0 (0%)	0 (0%)	<.0001
Less than once a week	152 (86%)	13 (13%)	1 (0.4%)	0 (0%)	
1-2 d a week	65 (58%)	25 (26%)	6 (7%)	6 (10%)	
3-4 d a week	29 (60%)	12 (25%)	7 (15%)	0 (0%)	
5-6 d a week	7 (34%)	6 (42%)	4 (17%)	1 (7%)	
Every day	10 (31%)	8 (26%)	3 (12%)	9 (31%)	
Q9. Sexual function					
Never	228 (98%)	4 (2%)	0 (0%)	0 (0%)	<.0001
Less than once a week	150 (87%)	13 (10%)	3 (3%)	0 (0%)	
1-2 d a week	69 (60%)	22 (25%)	4 (7%)	7 (8%)	
3-4 d a week	31 (59%)	11 (27%)	5 (13%)	1 (1%)	
5-6 d a week	9 (45%)	5 (34%)	3 (15%)	1 (7%)	
Every day	18 (64%)	1 (2%)	2 (4%)	9 (30%)	
Q10. Effect of treatment on quality of life					
Never	217 (94%)	15 (6%)	0 (0%)	0 (0%)	<.0001
Less than once a week	133 (81%)	31 (19%)	2 (0.4%)	0 (0%)	
1-2 d a week	58 (51%)	33 (39%)	5 (4%)	6 (7%)	
3-4 d a week	21 (39%)	18 (41%)	9 (19%)	1 (1%)	
5-6 d a week	6 (33%)	6 (24%)	5 (33%)	1 (10%)	
Every day	10 (32%)	7 (18%)	5 (22%)	8 (29%)	

DLQI, Dermatology Life Quality Index.

Bold values indicate statistically significant *P* values.

TABLE E6. Impact of atopic dermatitis pain intensity on individual aspects of the DLQI (n = 599)

	DLQI questions—n (%)				
Pain intensity from atopic dermatitis or eczema	Not at all/not relevant	A little	A lot	Very much	P value
Q1. Itching and/or burning of skin					
0-3	121 (30%)	254 (60%)	30 (8%)	6 (1%)	<.0001
4-6	7 (6%)	55 (52%)	34 (286%)	9 (14%)	
7-10	0 (0%)	29 (34%)	27 (3%)	23 (35%)	
Q2. Self-conscious about lesions					
0-3	313 (74%)	82 (21%)	13 (4%)	2 (0.7%)	<.0001
4-6	41 (33%)	43 (40%)	16 (24%)	5 (3%)	
7-10	19 (25%)	27 (26%)	16 (19%)	17 (31%)	
Q3. Ability to shop, take care of home and garden					
0-3	389 (93%)	19 (6%)	1 (1%)	2 (0.7%)	<.0001
4-6	65 (59%)	31 (28%)	9 (13%)	0 (0%)	
7-10	34 (39%)	19 (23%)	13 (18%)	13 (20%)	
Q4. Clothing decisions					
0-3	327 (78%)	61 (15%)	14 (4%)	8 (2%)	<.0001
4-6	47 (41%)	37 (36%)	16 (15%)	5 (7%)	
7-10	25 (29%)	16 (19%)	18 (18%)	20 (34%)	
Q5. Socializing or leisure activities					
0-3	377 (91%)	27 (7%)	3 (2%)	3 (0.9%)	<.0001
4-6	60 (51%)	34 (37%)	10 (11%)	1 (0.6%)	
7-10	31 (35%)	22 (27%)	14 (18%)	12 (21%)	
Q6. Sports					
0-3	385 (93%)	19 (4%)	5 (2%)	1 (0.5%)	<.0001
4-6	64 (56%)	27 (29%)	12 (14%)	2 (1%)	
7-10	36 (43%)	15 (16%)	15 (21%)	12 (20%)	
Q7-1. Work or study in past week (yes/no)					
0-3	408 (99.6%)	2 (0.4%)			<.0001
4-6	99 (96%)	6 (4%)			
7-10	60 (73%)	18 (27%)			
Q7-2. Work or study overall					
0-3	259 (83%)	49 (17%)	1 (0.5%)		<.0001
4-6	29 (35%)	32 (62%)	2 (3%)		
7-10	12 (28%)	23 (62%)	3 (10%)		
Q8. Relationship with partner, friend, or relative					
0-3	383 (92%)	25 (8%)	2 (0.4%)	0 (0%)	<.0001
4-6	64 (53%)	32 (35%)	7 (8%)	2 (4%)	
7-10	34 (40%)	18 (25%)	12 (15%)	14 (20%)	
Q9. Sexual function					
0-3	393 (95%)	15 (4%)	2 (0.5%)	0 (0%)	<.0001
4-6	66 (54%)	29 (31%)	8 (13%)	2 (2%)	
7-10	43 (53%)	12 (17%)	7 (8%)	16 (22%)	
Q10. Effect of treatment on quality of life					
0-3	393 (95%)	15 (4%)	2 (0.5%)	0 (0%)	<.0001
4-6	66 (54%)	29 (31%)	8 (13%)	2 (2%)	
7-10	43 (53%)	12 (17%)	7 (8%)	16 (22%)	

DLQI, Dermatology Life Quality Index.

Bold values indicate statistically significant P values.

TABLE E7. Association of itch and pain intensity with quality of life in atopic dermatitis (n = 596)

Intensity		Dermatology Life Quality Index	
Itch	Pain	Adjusted β (95% CI)	P value
0-3	0-3	0.00 (ref)	—
	4-6	−1.01 (−3.15, 1.14)	.36
	7-10	9.38 (6.25, 12.50)	<.0001
4-6	0-3	0.00 (ref)	—
	4-6	1.95 (0.51, 3.39)	.008
	7-10	−1.73 (−4.03, 0.58)	.14
7-10	0-3	0.00 (ref)	—
	4-6	3.55 (1.98, 5.11)	<.0001
	7-10	6.10 (4.37, 7.82)	<.0001
Covariables			
Pain frequency (nights per week)		−0.17 (−1.00, 0.65)	.68
≤2		1.02 (−0.33, 2.38)	.14
3-6		3.43 (1.45, 5.40)	.0007
7		0.19 (0.16, 0.23)	<.0001
PO-SCORAD		0.02 (−0.11, 0.14)	.80
PO-SCORAD sleep		0.11 (0.03, 0.19)	.009
POEM		−0.30 (−0.95, 0.36)	.37
Female sex		−0.02 (−0.04, −0.002)	.03
Age (y)			
Race/ethnicity		0.00 (ref)	—
White		0.92 (0.02, 1.82)	.046
Black		0.62 (−0.29, 1.53)	.18
Hispanic		1.96 (0.77, 3.16)	.001
Multiracial/other			
Level of education		0.00 (ref)	—
Less than high school		−0.72 (−1.61, 0.17)	.11
High school or greater		0.02 (−0.08, 0.11)	.72
Poverty income ratio		0.46 (−0.39, 1.32)	.28
AD lesions on face		1.45 (0.59, 2.31)	.001
AD lesions on hands			

AD, Atopic dermatitis; CI, confidence interval; PO-SCORAD, Patient-Oriented Scoring Atopic Dermatitis; POEM, Patient-Oriented Eczema Measure. Bold values indicate statistically significant P values.

REFERENCES

- E1. Rowen TS, Gaither TW, Awad MA, Osterberg EC, Shindel AW, Breyer BN. Pubic hair grooming prevalence and motivation among women in the United States. *JAMA Dermatol* 2016;152:1106-13.
- E2. Hays RD, Liu H, Kapteyn A. Use of internet panels to conduct surveys. *Behav Res Methods* 2015;47:685-90.
- E3. Heckman CJ, Darlow S, Manne SL, Kashy DA, Munshi T. Correspondence and correlates of couples' skin cancer screening. *JAMA Dermatol* 2013;149:825-30.
- E4. Cleave N, Brown PJ, Payne CD. Evaluation of methods for ecological inference. *J R Stat Soc Ser A Stat Soc* 1995;158:55-72.
- E5. de Mesnard L. Biproportional techniques in input-output analysis: table updating and structural analysis AU—Lahr, Michael. *Econ Syst Res* 2004;16:115-34.