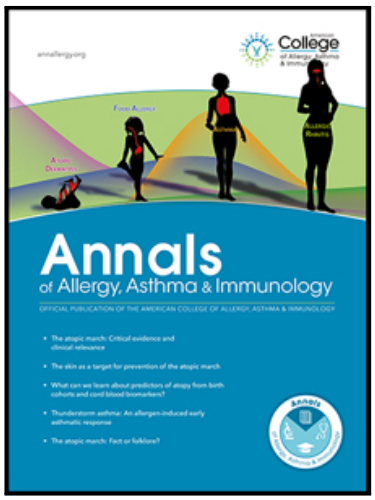

Patient-burden and quality of life in atopic dermatitis in US adults: A population-based cross-sectional study

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Running Header: Burden of adult AD.

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Abstract

Background: The patient-burden and quality of life (QOL) impact of atopic dermatitis (AD) in the United States population is not wellestablished.
Objective: To elucidate the patient-burden of AD in the US population.
Methods: A cross-sectional, population-based study of 602 adults was performed. AD was determined using modified UK Diagnostic Criteria for AD. AD severity was assessed using self-reported global AD severity, Patient-Oriented Eczema Measure (POEM), Patient-Oriented Scoring AD (POSCORAD), PO-SCORAD-itch and sleep. QOL was assessed using short-form (SF-)12 mental and physical health scores and Dermatology Life Quality Index (DLQI).
Results: Adults with AD reported higher proportions of having only fair/poor overall health (25.8% vs. 15.8%), being somewhat/very dissatisfied with life (16.7% vs. 11.4%), lower weighted mean [SD] SF-12 mental (45.9 [9.9] vs. 50.9 [9.2]) and physical health subscores (53.0 [2.5] vs. 53.5 [2.3]) and higher DLQI (4.9 [6.5] vs. 1.1 [2.8]). In multivariable regression models adjusting for socio-demographics and multiple comorbid health disorders, there were significant stepwise decreases by AD severity (self-reported, POEM, PO-SCORAD) of overall health, life satisfaction, SF-12 mental health and increases of DLQI scores. SF-12 physical health scores were only associated with moderate AD. Concurrently severe PO-SCORAD, POEM and/or PO-SCORAD-itch was associated with very low mean SF-12 mental health (34.7) and high DLQI scores (24.7). AD commonly limited lifestyle (51.3%), led to avoidance of social interaction (39.1%) and impacted activities (43.3%).The most burdensome AD symptoms were itch (54.4%), excessive dryness/scaling (19.6%) and red/inflamed skin (7.2%).
Conclusion:These data support the heavy burden that AD places on patients, particularly moderate and severe AD.

Keywords: Atopic dermatitis; eczema; epidemiology; quality of life; patient-burden; activities of daily living; relationship; social

Abbreviations used: AD=atopic dermatitis; BMI=body mass index; CI=confidence interval; OR=odds ratio; aOR=adjusted odds ratio; DLQI = Dermatology Life Quality Index; POEM = Patient-Oriented Eczema Measure; PO-SCORAD = Patient-Oriented Scoring Atopic Dermatitis; SF-12 = Short-Form 12 items

Introduction

Atopic Dermatitis (AD) is a chronic inflammatory disorder characterized by eczematous skin lesions, itch, skin pain, sleep disturbances, and multiple atopic and non-atopic comorbidities, all of which can lead to significant morbidity[1-4]. While many studies showed quality of life (QOL) impairment in clinical cohorts of AD, the patient-burden and QOL impact

of AD in the United States population is not well-established. Moreover, little is known about how the burden of AD compares with other chronic health disorders. We hypothesized that AD is associated with impaired QOL overall in the US population, and even greater QOL impairment than other common chronic diseases.

AD is a heterogeneous disorder with variable intensity and extent of lesions, frequency and intensity of symptoms. All of these may variably impact the burden of disease. Yet, the complex relationship between these different aspects of AD severity and QOL impact has not been examined in depth. We hypothesized that patients with severe skin lesions, high frequency of symptoms and severe pruritus have a greater QOL decrement compared to those with only one or none of these disease aspects being severe.

Moderate and severe AD patients have a greater likelihood of having comorbid asthma[5], hay fever[5], food allergies[5], mental health disturbances[6] and possibly cardio-metabolic comorbidities[3]. Each of these comorbidities may negatively impact QOL. We hypothesized that AD, in particular moderate and severe AD, is associated with poor QOL independent of these comorbidities. In the present study, data were analyzed from a US-population based survey to explore the complex relationship between different constructs of AD severity, comorbidities and overall QOL.

Methods

Data Source

Data were obtained from the Atopic Dermatitis in America survey whose population was sampled from the long-standing GfK Knowledge Panel. The GfK Knowledge panel is the largest and oldest probability-based web panel in the US and contains between 40,000 to 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 US 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[7-9]. The survey questionnaire and protocol were approved by the ICF Institutional Review Board.

Study design

This was a cross-sectional study involving a two-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 2,137 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 to members of the web panel to avoid biasing participation based on respondent interest or disinterest in the subject. A total of 1,278 adults completed the survey (response rate=59.80%). 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 AD patients to investigate differences between different levels of disease severity. In stage 2, an additional sample of 8,217 adults from the GfK knowledge panel completed screening to identify and interview an additional group of adults with AD. The final cohort consisted of 602 adults who met an adapted UK working party (UKWP) definition of AD (Figure 1). 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. Sample weights were included in all analyses to allow for representative estimates of the US population.

Assessment of AD and comorbidities

An adaptation of the UKWP criteria was selected by the *AD in America* advisory committee as the screening tool for patient eligibility[10]. This 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] visible flexural eczema and/or [5] onset under the age of two), except assessment of visible flexural eczema by a clinician was not performed. The following comorbidities were self-reported: ever history of either asthma or hay fever, 1-year history of food allergy, anxiety or depression, high blood pressure, diabetes, heart disease, autoimmune disease, other chronic diseases, and current obesity (body mass index ≥30).

Self-assessments of AD severity and burden included the self-reported global AD severity question "Would you describe your atopic dermatitis or eczema as mild, moderate, or severe?" [11], as well as patient-reported outcomes (PRO) related to AD, including Patient-Oriented Scoring AD (PO-SCORAD) index [range: 0-103] and numeric rating scale (NRS)-itch

and sleep subscores of PO-SCORAD [range: 0-10] [12], Patient-Oriented Eczema Measure (POEM) [7 questions; range: 0-28] [13] and Dermatology Life Quality Index (DLQI) [10 questions; range: 0-30] [14], and Short-Form 12 (SF-12) [2 subscales, 12 items; range: 0-100] [15, 16] For all analyses of AD severity, scores were divided into four categories (none, clear/almost-clear/mild, moderate, severe/very severe) using the respective previously reported severity strata [13, 17].

Statistical analyses

All data analyses and statistical processes were performed using SAS version 9.4 (SAS Institute) and included representative sample weights. Baseline respondent characteristics were determined. Chi-square was used to test the association between AD severity and the impact of AD on limiting lifestyle, social interaction and activity. Kruskal-Wallis was used to test the association between combined severe vs. mild-moderate POEM, PO-SCORAD and/or PO-SCORAD-itch. The most and second-most burdensome self-reported symptoms and signs of AD were examined. These are referred to as symptoms throughout the manuscript owing to their self-report.

To determine the relationship of AD with overall health rating and life satisfaction, logistic regression models were constructed with health rating and life satisfaction (excellent/very good/good/fair/poor) as the independent variables and AD (yes/no) as the dependent variable. To determine the relationship of AD severity, ordinal logistic regression models were constructed with self-reported global AD severity as the dependent variable, and health rating and life satisfaction as the independent variables. Linear regression models were also constructed with POEM or PO-SCORAD (continuous) as the dependent variable, and health rating and life satisfaction as the independent variables. To determine the relationship of AD and

AD severity with SF-12 mental and physical subscores and DLQI scores, linear regression models were constructed with SF-12 mental and physical subscores and DLQI scores as the dependent variable (continuous) and AD (yes/no) or AD severity (mild/moderate/severe). Crude odds ratio (OR) and beta coefficients and 95% confidence intervals (CI) were estimated.

Multivariable model-1 included age (continuous), sex (male/female), race/ethnicity (white/black/Hispanic/multiracial or other), level of education (less than high school/high school or equivalent/more than high school), household size (continuous), and poverty income ratio (PIR; ≤1/1-1.9/2-3.9/≥4). Model-2 included age (continuous), sex (male/female), race/ethnicity (white/black/Hispanic/multiracial or other), level of education (less than high school/high school or equivalent/more than high school), household size (continuous), and poverty income ratio (≤1/1-1.9/2-3.9/≥4), as well as history of asthma, hay fever, food allergy, high blood pressure, diabetes, heart disease, depression/anxiety and other chronic conditions (yes/no) and body mass index (continuous). Adjusted OR and 95% CI were estimated.

The multiple dependent tests performed in this study increase the risk of falsely rejecting the null hypothesis. Therefore, P-values were corrected for the false discovery rate [18]; corrected P-values are presented. A 2-sided corrected P-value <0.05 was taken to indicate statistical significance for all estimates.

Results

Respondent characteristics

Overall, the prevalence (95% CI) of AD was 7.3% (5.9-8.8%). Six hundred and two subjects met AD criteria and were included in the final cohort. Subjects were 53.6% female and 71.9% Caucasian/white, with a mean ± std. dev. age of 52.0 ± 16.3 years. Of those reporting global AD severity, 289 (wtd prev: 53.1%) reported having mild, 172 (38.8%) moderate and 34 (8.1%) severe AD. The mean ± std. dev. PO-SCORAD was 27.5 ± 18.0, POEM was 7.5 ± 6.8, and DLQI was 4.9 ± 6.6.

Health rating and satisfaction with life

A higher proportion of adults with AD reported having only fair or poor overall health (25.8% vs. 15.8%) and being somewhat or very dissatisfied with life (16.7% vs. 11.4%) compared to those without AD (Table 1). In bivariable and multivariable logistic regression models, AD was associated with significantly poorer health rating and satisfaction with life.

More severe AD was associated with even stronger effects on health rating and life satisfaction. In particular, 35.0% and 31.6% of patients with self-reported severe AD reported only fair or poor health, and being somewhat or very dissatisfied with life (eTable 2). In multivariable ordinal logistic regression models adjusting for socio-demographics, self-reported global AD severity (adjusted OR [95% CI]: 3.89 [1.51–10.03]), POEM (multivariable linear regression; adjusted beta [95% CI]: 7.22 [4.06–10.37]) and PO-SCORAD (14.86 [6.79–22.93]) were all significantly associated with poor health in multivariable models controlling for socio-demographics. In addition, global AD severity, POEM and PO-SCORAD were all associated

with being neither satisfied or dissatisfied, somewhat or very dissatisfied with life in multivariable models.

SF-12 mental and physical health and DLQI

The weighted mean (SD) SF-12 mental and physical health subscores for adults with AD were 45.9 (9.9) and 53.0 (2.5), respectively. These scores were compared with 9 different disorders, and healthy persons without any of these disorders (Table 2). AD ranked 7th and 8th, respectively. SF-12 mental health subscores for moderate AD were lower than virtually all other disorders, and for severe AD, dramatically lower than all disorders (Tables 2 and 3). Interestingly, there was little difference between physical health subscores across disorders (Table 2).

In bivariable linear regression and multivariable models controlling for socio-demographics, AD was associated with significantly lower SF-12 mental and physical health subscores and significantly higher DLQI (all indicating worse quality of life) (Table 3). However, these associations only remained significant for DLQI in multivariable models that also controlled for comorbid health conditions. In particular, asthma and other chronic disorders were the confounding variables in the multivariable models of SF-12 mental and physical health subscores.

In contrast, there were significant and stepwise decreases of SF-12 mental health subscores, and increases of DLQI scores, in all models for moderate and severe AD as judged by global AD severity, POEM, PO-SCORAD, PO-SCORAD itch and sleep. Whereas, moderate global AD severity, POEM, PO-SCORAD, PO-SCORAD itch and severe PO-SCORAD sleep were associated with lower SF-12 physical health scores in fully adjusted multivariable models.

Since AD severity can be defined by different constructs, weighted mean SF-12 mental and physical health subscores and DLQI scores were stratified by the lesional severity and extent (PO-SCORAD), frequency of symptoms (POEM) and intensity of itch (PO-SCORAD itch) (Figure 2). Severe compared to mild-moderate POEM and PO-SCORAD itch alone as judged by existing interpretability bands were associated with significantly lower SF-12 mental health and higher DLQI scores ($P<0.0001$). Concurrent severe PO-SCORAD, POEM and/or PO-SCORAD-itch were associated with even lower SF-12 mental health and higher DLQI scores compared with severe scores for only one of these assessments ($P<0.0001$). However, there were no significant differences of mean SF-12 physical health subscores even among persons with severe PO-SCORAD, POEM and PO-SCORAD-itch ($P=0.39$).

Impact of AD on lifestyle, social interaction and activity

Overall, substantial proportions of adults with AD reported that AD limits their lifestyle (51.3%), causes them to avoid social interaction because of their appearance (39.1%) and impacts their activities (43.3%) (Figure 3A-C). Even patients with mild AD reported that AD limited their lifestyle (34.5%), impacted activities (23.2%), or led to avoidance of social interactions (17.7%). These harmful effects of AD were even more burdensome in persons with self-reported global moderate and severe AD ($P<0.0001$ for all). In particular, almost 1 in 2 adults with severe AD reported quite a bit or a great deal of burden in these areas.

Most burdensome symptoms of AD

The most burdensome symptoms reported by adults with AD were itch (54.4%), followed by excessive dryness or scaling (19.6%) and red or inflamed skin (7.2%) (Figure 3D). These were also the second most burdensome symptoms. Notably, skin pain and sleep disturbance were

more commonly reported as second most burdensome symptoms (8.2 and 11.4%, respectively). However, adults with moderate and severe AD were less likely to report itch or excessive dryness and scaling as their most burdensome symptoms (Figure 3E). A higher proportion reported blisters or bumps, red or inflamed skin, sleep disturbance, pain, and open sores or oozing as their most burdensome symptoms.

Discussion

Using a US population-based sample, we found that adults with AD had lower overall health rating and life satisfaction, significantly lower SF-12 mental health subscores, and higher DLQI scores; all of these indicate significant QOL impairment. Virtually all of these outcomes were associated with AD severity, such that those with moderate and severe AD had significantly worse burden than those with mild AD. Adults with severe vs. mild-moderate POEM, PO-SCORAD and PO-SCORAD-itch scores had dramatically lower SF-12 mental health and higher DLQI scores. These associations remained significant even after extensively controlling for socio-demographics and multiple comorbid health conditions. It appears that AD *per se* can lead to mental health disturbance and impaired QOL. AD also limited lifestyle, led to avoidance of social interaction and impacted activity in a large subset of persons with AD, particularly those with severe AD. A previous study of 380 adults with moderate-to-severe AD enrolled in a clinical trial demonstrated substantially impaired DLQI and 5-dimension EuroQol scores[2]. However, that study had limited generalizability given the potential selection biases of enrolling in a clinical trial for a systemic treatment from predominantly academic centers. The present study demonstrated major QOL impairments in AD among a cohort that is representative of the US population. Further, we found that even persons with mild AD had impaired QOL. Together, these results indicate that AD, especially moderate-to-severe disease, is associated with a profound patient-burden among US adults.

The SF-12 is a generic, multi-dimensional QOL assessment that is not specific to skin disease, and has been studied extensively in many medical disorders. The mean SF-12 mental health scores for AD, particularly moderate and severe AD, were lower than other chronic health conditions such as heart disease, diabetes and high blood pressure. These results suggest that AD

is as burdensome or even more burdensome than many other medical disorders. The high burden of AD should be an important consideration in disease awareness and prioritizing appropriate resource allocation.

Itch has been reported to be the most common symptom in AD [2, 19, 20]. A previous study of 284 AD patients found that itch, difficulty sleeping and pain to be the most frequent symptoms in adults with AD [19]. A web survey of 304 persons with AD found that daily itch occurred in 91% of respondents [20]. A study of 380 adults with moderate-to-severe AD found that 70.5% reported severe or unbearable itch in the past 2 weeks, 85.8% reported daily itch, and 62.8% reported itch lasting at least 12 hours per day [2]. The present study found that itch was also the most burdensome symptoms in adult AD. Though, other symptoms such as sleep disturbance were also commonly reported. Similarly, a study of 265 adult AD patients found that numerical rating scale of itch, a measure of itch intensity, correlated better with overall AD severity than all other PRO examined[11]. However, adults with moderate and severe AD, in particular, were more likely to report that other symptoms were most burdensome. Taken together, itch is both the most common and burdensome symptom across all severities of adult AD, though additional signs, symptoms and sequela of scratching become more prominent in severe AD.

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, use of multiple and well-validated assessments of AD severity, and controlling for multiple confounding variables in multivariable models. We used an adaptation of the extensively validated UKWP criteria[10] to establish the diagnosis of AD. Thus, we believe that the case-definition of AD is valid. POEM, PO-SCORAD, self-reported global AD severity and DLQI have all been studied in AD patients and found to have overall 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[11, 21-36]. However, this study has limitations. All exposures and outcomes in the study were assessed by self-report, not verified by physical exam and may be subject to misclassification. It is possible that AD treatments such as frequent use of systemic steroids, may play an important role in mediating the observed relationship between AD and SF-12 scores. However, the effects of past and present treatment were not examined. Future studies are warranted to examine the mediating effects of medication on QOL.

In conclusion, AD is associated with lower overall health rating and life satisfaction, impaired QOL related to mental health and skin-related QOL in the US population. AD was associated with worse QOL than a number of other common chronic illnesses, including heart disease, diabetes and high blood pressure. Moderate and severe AD were particularly associated with dramatically lower QOL than all other chronic disorders examined. These data support the heavy burden that moderate and severe AD place on patients. We recommend that clinicians incorporate QOL assessments in clinical practice to determine disease-burden, identify patients requiring step-up treatment of their skin disease and potentially screen for patients with mental health disturbances.

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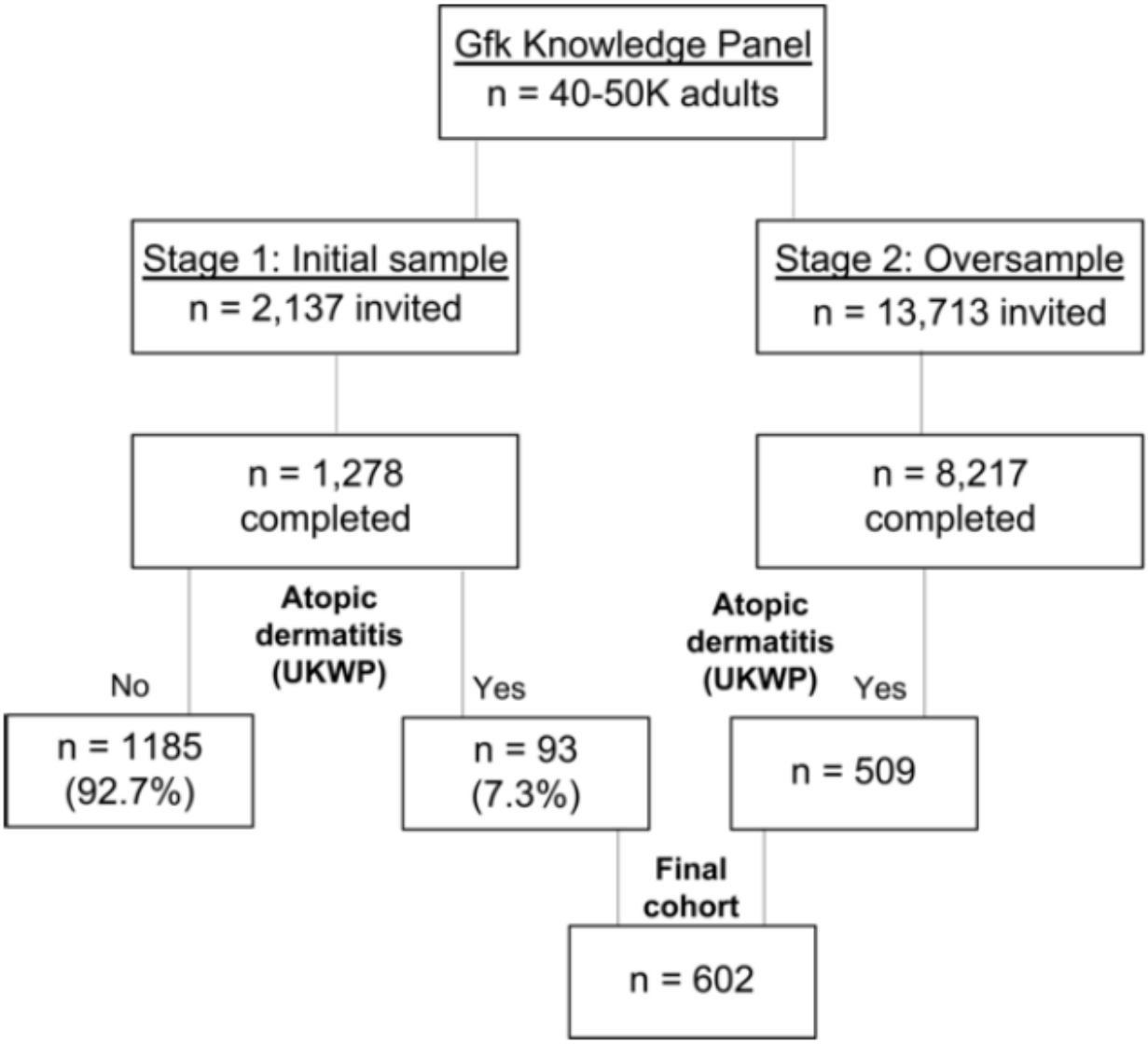
Figure 1. Flowchart of study design.



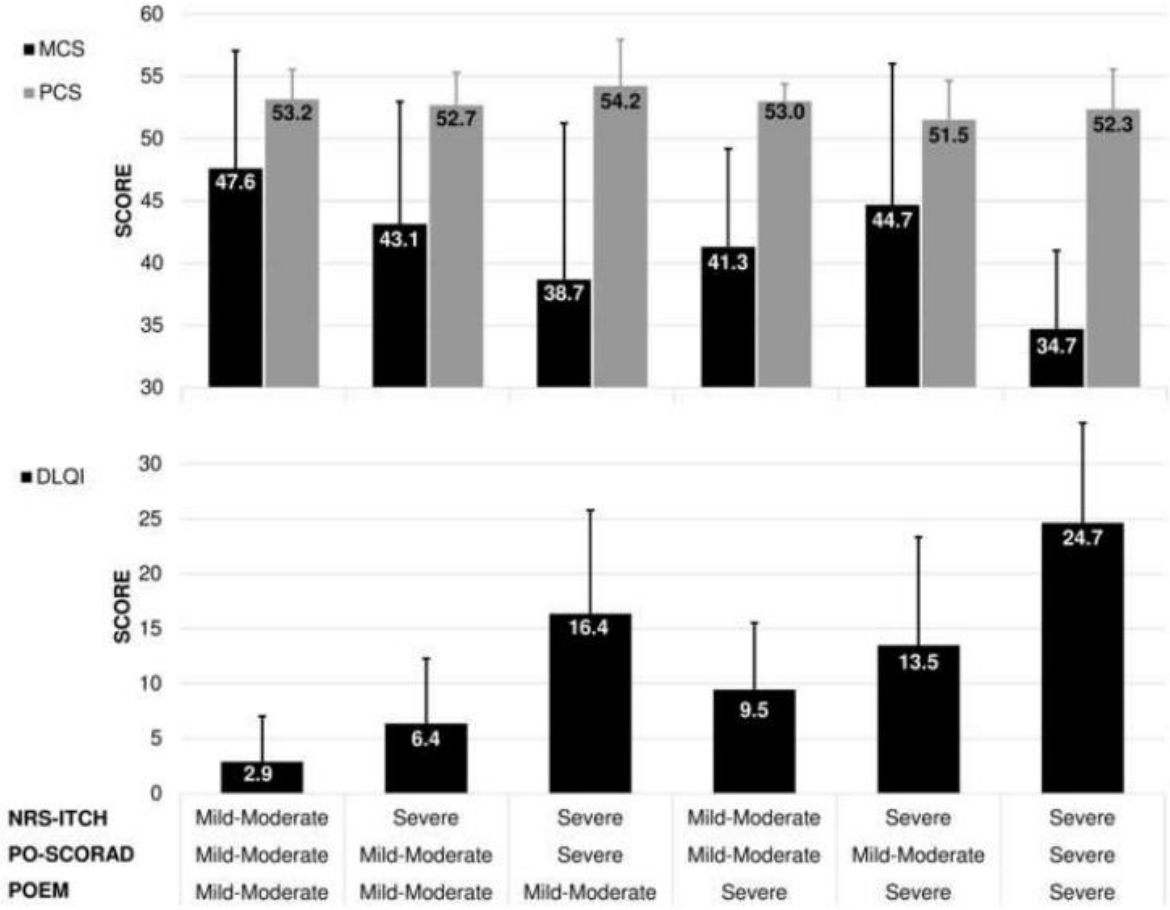


Figure 2. Combined effects of mild-to-moderate and severe AD (PO-SCORAD), frequency of symptoms (POEM) and severity of pruritus (PO-SCORAD itch) on weighted mean (std. dev.) (A) short-form 12 mental (MCS) and physical (PCS) component subscores and (B) dermatology life quality index (DLQI). All subsets of combined AD severity had significantly lower MCS and higher DLQI scores compared to patients with mild-moderate scores for all three assessments ($P<0.0001$). Patients with severe PO-SCORAD and severe PO-SCORAD itch had significantly lower MCS and higher DLQI than those with only severe PO-SCORAD itch ($P<0.0001$). Patients with severe scores for all three assessments had significantly lower MCS and higher

DLQI compared with all other subsets (P<0.0001). Finally, patients severe PO-SCORAD itch and POEM had significantly lower MCS and higher DLQI compared to those with severe PO-SCORAD itch alone (P<0.0001), but did not have significant differences of MCS or DLQI compared with severe POEM alone (P≥0.15).

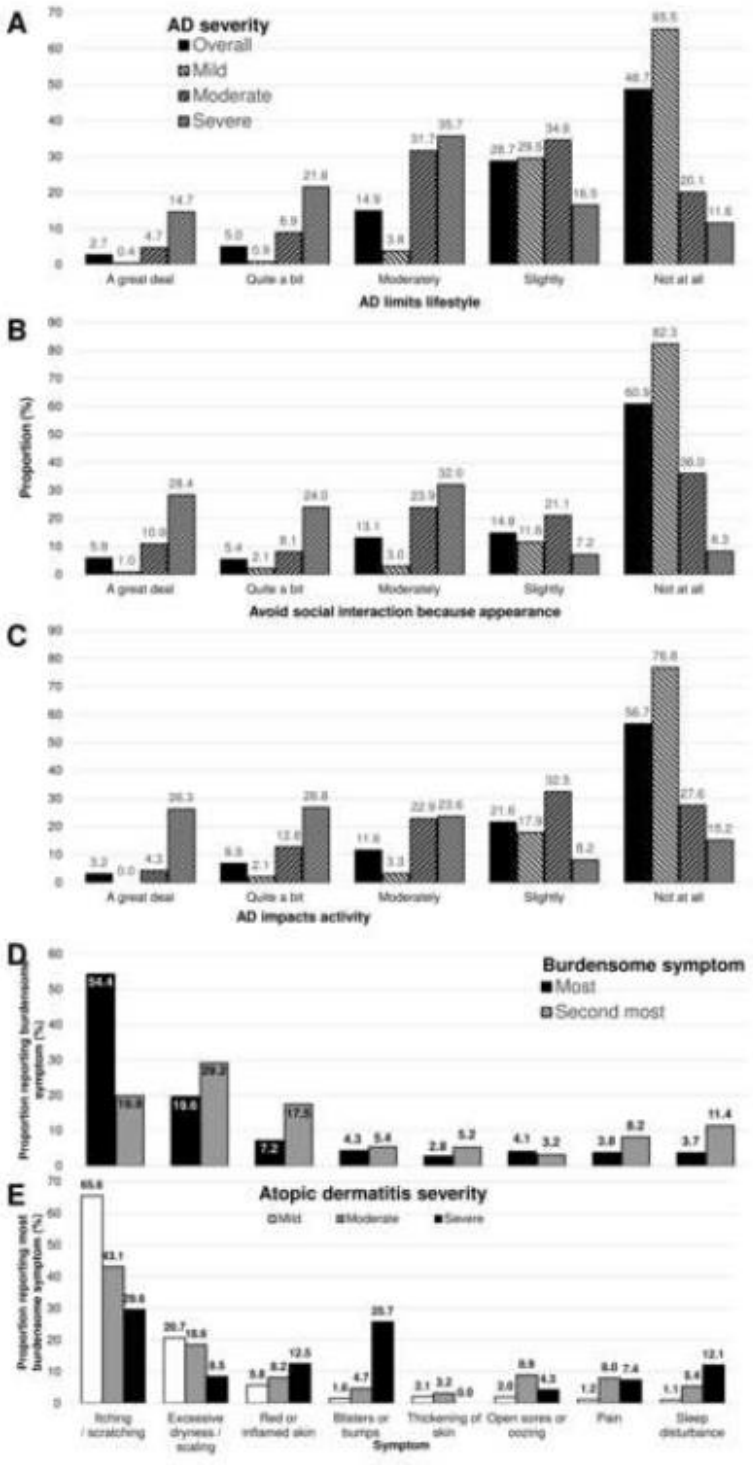

A
AD severity
Overall
Mild
Moderate
Severe
A great deal
Quite a bit
Moderately
Slightly
Not at all
AD limits lifestyle
B
Proportion (%)
Avoid social interaction because appearance
C
AD impacts activity
D
Burdensome symptom
Most
Second most
Proportion reporting burdensome symptom (%)
E
Atopic dermatitis severity
Mild
Moderate
Severe
Proportion reporting most burdensome symptom (%)
Itching / scratching
Excessive dryness / scaling
Red or inflamed skin
Blisters or bumps
Thickening of skin
Open sores or oozing
Pain
Sleep disturbance
Symptom

Figure 3. Impact and most burdensome symptoms of AD. The weighted proportion of adults who reported that (A) AD limited lifestyle, (B) AD led to avoidance of social interaction because of appearance and (C) AD impacted activity are presented for adults with AD overall and stratified by AD severity. The most burdensome and second most burdensome AD symptoms are presented for adults with (D) AD overall and (E) stratified by self-reported global AD severity.

Table 1. Association between atopic dermatitis and negative quality of life impact.

Variable	Atopic dermatitis							
	No	Yes			Model-1		Model-2	
	Freq. (Wtd Prev)[#]	Freq. (Wtd Prev)[#]	Crude OR (95% CI)	P-value	Adjusted OR (95% CI)	P-value*	Adjusted OR (95% CI)	P-value*
Overall health rating								
Excellent	194 (9.4%)	30 (6.5%)	1.00 [ref]	–	1.00 [ref]	–	1.00 [ref]	–
Very good	861 (38.3%)	171 (28.0%)	1.05 (0.72–1.52)	0.8498	1.04 (0.72–1.51)	0.8498	0.90 (0.60–1.35)	0.6730
Good	866 (36.8%)	245 (39.7%)	1.55 (1.08–2.22)	**0.0267**	1.51 (1.05–2.18)	**0.0376**	1.15 (0.77–1.72)	0.5513
Fair	308 (13.1%)	126 (20.7%)	2.28 (1.54–3.27)	**<0.0001**	2.24 (1.50–3.34)	**<0.0001**	1.42 (0.92–2.21)	0.1555
Poor	62 (2.5%)	30 (5.1%)	2.95 (1.71–5.08)	**<0.0001**	2.86 (1.64–4.99)	**0.0005**	2.19 (1.18–4.08)	**0.0206**
Satisfaction with life								
Very satisfied	833 (35.6%)	190 (30.7%)	1.00 [ref]	–	1.00 [ref]	–	1.00 [ref]	–
Somewhat satisfied	926 (39.0%)	211 (35.8%)	1.07 (0.86–1.32)	0.6259	1.06 (0.85–1.31)	0.673	1.04 (0.82–1.31)	0.7966
Neither satisfied nor dissatisfied	273 (14.1%)	98 (16.8%)	1.51 (1.10–2.07)	**0.0257**	1.31 (0.99–1.72)	0.0788	1.24 (0.92–1.68)	0.1983
Somewhat dissatisfied	192 (8.4%)	73 (10.9%)	1.51 (1.10–2.07)	**0.0173**	1.46 (1.06–2.01)	**0.0325**	1.31 (0.93–1.87)	0.1671
Very dissatisfied	64 (3.0%)	29 (5.8%)	2.22 (1.45–3.40)	**0.0006**	2.14 (1.38–3.31)	**0.0012**	1.97 (1.22–3.18)	**0.0095**

* Corrected P-values are corrected for the false discovery rate. Bold-face P-values indicate statistical significance.
# Proportion of respondents for overall health rating and satisfaction with life are presented for subjects with AD and without AD. Weighted prevalences are presented as column percentages including sample weights.

Binary logistic regression models were created with each comorbid health condition as the binary dependent variable. The independent variable was having atopic dermatitis as defined by the UK Working Party criteria. Crude adjusted odds ratios (OR) and 95% confidence intervals (CI) were estimated. Multivariable model-1 included age (continuous), sex (male/female), race/ethnicity (white/other), level of education (less than high school/high school or greater), household size and poverty income ratio (continuous). Multivariable model-2 included all covariates from model-1 and history of asthma, hay fever, food allergy, high blood pressure, diabetes, heart disease, depression/anxiety and other chronic conditions (yes/no) and body mass index (continuous).

Table 2. Mean short-form 12 mental and physical health subscores and ranks for different health disorder.

Disorder	MCS				PCS		
	N Obs	Wtd Mean	(SD)	Rank	Wtd Mean	(SD)	Rank
Anxiety or depression	634	41.4	(9.4)	1	52.8	(2.6)	6
Other serious chronic	425	41.9	(9.9)	2	51.7	(2.7)	1
Autoimmune condition	238	43.0	(9.7)	3	52.4	(2.7)	3
Food allergy	226	45.2	(10.0)	4	53.4	(2.5)	10
Asthma	725	45.7	(9.8)	5	52.9	(2.5)	7
Heart disease	201	45.5	(8.6)	6	52.5	(2.5)	4
Atopic dermatitis	602	45.9	(9.9)	7	53.0	(2.5)	8
Diabetes	337	46.1	(9.7)	8	52.3	(2.5)	2
High blood pressure	865	47.6	(9.2)	9	52.7	(2.3)	5
Hay fever	1502	48.4	(9.1)	10	53.2	(2.2)	9
None of the above disorders	1255	52.7	(8.1)	11	53.9	(2.0)	11

Table 3. Association between atopic dermatitis severity and Short form-12 physical and mental health subscores and skin-related quality of life.

Variable	Wtd Mean (std. dev.)[#]	Crude beta (95% CI)	P-value*	Model-1 Adjusted beta (95% CI)	Model-1 P-value*	Model-2 Adjusted beta (95% CI)	Model-2 P-value*
Short-form 12 Mental health subscore							
Atopic dermatitis							
No	50.9 (9.2)	0.00 [ref]	–	0.00 [ref]	–	0.00 [ref]	–
Yes	45.9 (9.9)	-4.94 (-5.76, -4.11)	**<0.0001**	-4.58 (-5.37, -3.79)	**<0.0001**	-0.81 (-1.64, 0.01)	0.0736
Self-reported global atopic dermatitis severity							
Mild	49.0 (8.8)	0.00 [ref]	–	0.00 [ref]	–	0.00 [ref]	–
Moderate	43.0 (10.6)	-6.21 (-7.93, -4.49)	**<0.0001**	-4.88 (-6.58, -3.18)	**<0.0001**	-3.07 (-4.65, -1.48)	**0.0005**
Severe	38.8 (9.4)	-10.21 (-13.25, -7.16)	**<0.0001**	-8.52 (-11.49, -5.55)	**<0.0001**	-4.90 (-7.73, -2.06)	**<0.0001**
Patient-Oriented Eczema Measure (POEM)							
Mild	48.3 (9.0)	0.00 [ref]	–	0.00 [ref]	–	0.00 [ref]	–
Moderate	42.9 (10.5)	-5.43 (-7.01, -3.86)	**<0.0001**	-4.41 (-5.91, -2.91)	**<0.0001**	-2.35 (-3.78, -0.92)	**0.0024**
Severe	40.1 (10.0)	-8.21 (-11.57, -4.85)	**<0.0001**	-7.60 (-10.78, -4.41)	**<0.0001**	-4.37 (-7.48, -1.26)	**0.0099**
Patient-Oriented Scoring Atopic Dermatitis (PO-SCORAD)							
Mild	49.2 (8.6)	0.00 [ref]	–	0.00 [ref]	–	0.00 [ref]	–
Moderate	42.3 (9.9)	-6.96 (-8.47, -5.46)	**<0.0001**	-5.68 (-7.17, -4.20)	**<0.0001**	-2.66 (-4.15, -1.16)	**0.0010**
Severe	36.9 (10.7)	-12.35 (-15.45, -9.26)	**<0.0001**	-10.30 (-13.35, -7.26)	**<0.0001**	-3.61 (-6.78, -0.43)	**0.0369**
PO-SCORAD itch							
Mild	49.3 (9.2)	0.00 [ref]	–	0.00 [ref]	–	0.00 [ref]	–
Moderate	44.9 (9.3)	-4.47 (-6.26, -2.69)	**<0.0001**	-4.03 (-5.72, -2.34)	**<0.0001**	-2.54 (-4.09, -0.99)	**0.0025**
Severe	42.1 (10.3)	-7.25 (-9.06, -5.44)	**<0.0001**	-6.03 (-7.77, -4.28)	**<0.0001**	-2.99 (-4.65, -1.32)	**0.0010**
PO-SCORAD sleep							
Mild	50.4 (8.6)	0.00 [ref]	–	0.00 [ref]	–	0.00 [ref]	–
Moderate	44.0 (8.1)	-6.43 (-8.24, -4.61)	**<0.0001**	-5.76 (-7.50, -4.02)	**<0.0001**	-3.51 (-5.17, -1.84)	**<0.0001**
Severe	40.6 (10.2)	-9.79 (-11.42, -8.17)	**<0.0001**	-8.66 (-10.23, -7.10)	**<0.0001**	-5.58 (-7.14, -4.02)	**<0.0001**
Short-form 12 Physical health subscore							
Atopic dermatitis							
No	53.5 (2.3)	0.00 [ref]	–	0.00 [ref]	–	0.00 [ref]	–
Yes	53.0 (2.5)	-0.46 (-0.67, -0.26)	**<0.0001**	-0.39 (-0.59, -0.20)	**<0.0001**	-0.008 (-0.23, 0.21)	0.9455
Self-reported global atopic dermatitis severity							
Mild	53.4 (2.3)	0.00 [ref]	–	0.00 [ref]	–	0.00 [ref]	–
Moderate	52.6 (2.9)	-0.74 (-1.21, -0.27)	**0.0035**	-0.65 (-1.11, -0.19)	**0.0089**	-0.66 (-1.14, -0.18)	**0.0118**
Severe	53.4 (3.4)	0.09 (-0.75, 0.92)	0.8601	0.30 (-0.50, 1.10)	0.5244	-0.09 (-0.96, 0.77)	0.855
Patient-Oriented Eczema Measure (POEM)							
Mild	53.3 (2.1)	0.00 [ref]	–	0.00 [ref]	–	0.00 [ref]	–
Moderate	52.7 (3.0)	-1.18 (-2.06, -0.31)	**0.0131**	-0.46 (-0.86, -0.07)	**0.0322**	-0.50 (-0.92, -0.08)	**0.0287**
Severe	52.1 (2.8)	-0.57 (-0.98, -0.16)	**0.0103**	-1.03 (-1.87, -0.19)	**0.025**	-0.68 (-1.59, 0.24)	0.19
Patient-Oriented Scoring Atopic Dermatitis (PO-SCORAD)							
Mild	53.3 (2.2)	0.00 [ref]	–	0.00 [ref]	–	0.00 [ref]	–
Moderate	52.5 (2.8)	-0.81 (-1.22, -0.40)	**0.0002**	-0.69 (-1.10, -0.29)	**0.0013**	-0.61 (-1.05, -0.17)	**0.0103**
Severe	53.4 (3.6)	-0.10 (-0.74, 0.94)	0.8498	0.06 (-0.76, 0.88)	0.8904	-0.58 (-1.51, 0.36)	0.2649
PO-SCORAD itch							
Mild	53.6 (2.4)	0.00 [ref]	–	0.00 [ref]	–	0.00 [ref]	–
Moderate	52.6 (2.2)	-0.98 (-1.45, -0.52)	**<0.0001**	-0.80 (-1.24, -0.36)	**0.0008**	-0.81 (-1.27, -0.36)	**0.0010**
Severe	52.8 (2.9)	-0.80 (-1.27, -0.33)	**0.0017**	-0.55 (-1.01, -0.09)	**0.0295**	-0.35 (-0.84, 0.13)	0.19
PO-SCORAD sleep							
Mild	53.5 (2.2)	0.00 [ref]	–	0.00 [ref]	–	0.00 [ref]	–
Moderate	53.0 (2.3)	-0.48 (-0.98, 0.02)	0.0779	-0.34 (-0.81, 0.14)	0.1983	-0.35 (-0.85, 0.14)	0.1983

Severe	52.4 (2.9)	-1.11 (-1.56, -0.67)	<**0.0001**	-1.01 (-1.44, -0.58)	<**0.0001**	-1.16 (-1.62, -0.70)	<**0.0001**
	Dermatology life quality index (DLQI)						
Variable	**Wtd Mean (std. dev.)#**	**Crude beta (95% CI)**	**P-value***	**Model-1**		**Model-2**	
				Adjusted beta (95% CI)	**P-value***	**Adjusted beta (95% CI)**	**P-value***
Atopic dermatitis							
No	1.1 (2.8)	0.00 [ref]	–	0.00 [ref]	–	0.00 [ref]	–
Yes	4.9 (6.5)	3.74 (3.40, 4.08)	<**0.0001**	3.65 (3.31, 3.99)	<**0.0001**	1.62 (1.20, 2.05)	<**0.0001**
Self-reported global atopic dermatitis severity							
Mild	2.3 (3.3)	0.00 [ref]	–	0.00 [ref]	–	0.00 [ref]	–
Moderate	7.8 (6.9)	5.50 (4.46, 6.53)	<**0.0001**	5.02 (3.95, 6.09)	<**0.0001**	3.57 (2.53, 4.62)	<**0.0001**
Severe	14.8 (12.3)	12.57 (10.72, 14.42)	<**0.0001**	11.90 (10.03, 13.77)	<**0.0001**	8.91 (7.04, 10.77)	<**0.0001**
Patient-Oriented Eczema Measure (POEM)							
Mild	2.2 (3.0)	0.00 [ref]	–	0.00 [ref]	–	0.00 [ref]	–
Moderate	7.3 (7.2)	5.09 (4.21, 5.97)	<**0.0001**	4.79 (3.92, 5.66)	<**0.0001**	3.21 (2.35, 4.08)	<**0.0001**
Severe	17.0 (10.9)	14.78 (12.89, 16.67)	<**0.0001**	14.55 (12.69, 16.41)	<**0.0001**	11.43 (9.55, 13.31)	<**0.0001**
Patient-Oriented Scoring Atopic Dermatitis (PO-SCORAD)							
Mild	2.3 (3.4)	0.00 [ref]	–	0.00 [ref]	–	0.00 [ref]	–
Moderate	6.6 (6.4)	4.33 (3.49, 5.16)	<**0.0001**	4.01 (3.15, 4.86)	<**0.0001**	2.48 (1.60, 3.36)	<**0.0001**
Severe	19.2 (10.2)	16.95 (15.22, 18.67)	<**0.0001**	16.69 (14.83, 18.35)	<**0.0001**	13.42 (11.56, 15.29)	<**0.0001**
PO-SCORAD itch							
Mild	2.2 (4.0)	0.00 [ref]	–	0.00 [ref]	–	0.00 [ref]	–
Moderate	4.1 (4.5)	1.87 (0.78, 2.97)	**0.0015**	1.79 (0.71, 2.87)	<**0.0001**	1.43 (0.46, 2.41)	**0.0070**
Severe	9.5 (9.1)	7.32 (6.20, 8.43)	<**0.0001**	6.91 (5.79, 8.02)	<**0.0001**	5.70 (4.65, 6.75)	<**0.0001**
PO-SCORAD sleep							
Mild	2.7 (3.9)	0.00 [ref]	–	0.00 [ref]	–	0.00 [ref]	–
Moderate	4.9 (6.0)	2.22 (0.98, 3.46)	**0.0010**	1.90 (0.66, 3.13)	**0.0045**	1.08 (-0.07, 2.23)	0.0876
Severe	8.1 (8.8)	5.46 (4.34, 6.58)	<**0.0001**	4.92 (3.80, 6.04)	<**0.0001**	3.43 (2.35, 4.51)	<**0.0001**

* Corrected P-values are corrected for the false discovery rate. Bold-face P-values indicate statistical significance.
# Weighted mean (SD) are presented including sample weights.

Bold-face P-values indicate statistical significance.
Linear regression models were created with short form-12 mental or physical health subscores or Dermatology Life Quality Index (DLQI) as the dependent variables. The independent variable was having atopic dermatitis as defined by modified UK Working Party criteria or atopic dermatitis severity using self-reported global atopic dermatitis severity, POEM, PO-SCORAD, PO-SCORAD itch and PO-SCORAD sleep subscores. Crude beta and 95% confidence intervals (CI) were estimated. Multivariable model-1 included age (continuous), sex (male/female), race/ethnicity (white/other), level of education (less than high school/high school or greater), household size and poverty income ratio (continuous). Multivariable model-2 included all covariates from model-1 and history of asthma, hay fever, food allergy, high blood pressure, diabetes, heart disease, depression/anxiety and other chronic conditions (yes/no) and body mass index (continuous).