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Higher self-reported severity of atopic dermatitis in adults is associated with poorer self-reported health-related quality of life in France, Germany, the U.K. and the U.S.A.

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Summary

Background Better understanding of the relationship between atopic dermatitis (AD) severity and health-related quality of life (HRQoL) could help improve knowledge of a more effective treatment for people with AD.
Objectives To assess the relationship between AD severity and HRQoL and perception of AD symptoms in adults with moderate-to-severe AD in Europe and the U.S.A.
Methods Participants for this cross-sectional, internet-based survey were recruited from the larger population-based National Health and Wellness Survey. AD severity was measured by Patient-Oriented SCORing of AD. HRQoL was measured by the five-level EuroQol-5D, Dermatology Life Quality Index (DLQI) and Patient-Oriented Eczema Measure (POEM).
Results Altogether, 1232 respondents were included: 1098 (89·1%) with moderate-to-severe AD [221 (20·1%) from France, 209 (19·0%) from Germany, 118 (10·7%) from the U.K. and 550 (50·1%) from the U.S.A.]. An additional 134 (10·9%) respondents with mild AD were included. Sociodemographic and clinical AD characteristics were similar between countries. In adults with moderate-to-severe AD, higher AD severity correlated with poorer HRQoL (Spearman's $r = -0{\cdot}38$ and 0·61 for EQ-5D and DLQI, respectively; both $P < 0{\cdot}001$). AD severity was positively correlated with POEM (Spearman's $r = 0{\cdot}51$; $P < 0{\cdot}001$). People with moderate-to-severe vs. those with mild AD had poorer health outcomes (EQ-5D, DLQI and POEM, $P < 0{\cdot}001$ for all). These results were similar and consistent for the European and the U.S. populations separately.
Conclusions Higher AD severity is associated with poorer HRQoL across Europe and the U.S.A. This is a burden for patients and may provide encouragement for more effective management of AD.

What's already known about this topic?

- Atopic dermatitis (AD) is associated with a detrimental effect on health-related quality of life (HRQoL), including sleep disturbance, anxiety and depression.
- Limited data describing the relationship between different levels of AD severity and self-reported HRQoL have been published.

What does this study add?

- There is a positive association between increasing AD severity (Patient-Oriented SCORing of AD) and decreasing HRQoL (EQ-5D and Dermatology Life Quality Index) and the perception of AD symptoms (Patient-Oriented Eczema Measure) from the patient's perspective.

- AD severity according to geographic locations was explored (France, Germany, the U.K., and the U.S.A.), showing that the decreasing HRQoL associated with increasing AD severity was quite consistent between the geographic locations.

What are the clinical implications of this work?

- The results of this study showed that higher AD severity is associated with poorer HRQoL from the subject's perspective in both Europe and the US. This fact confirms that there is a burden for these patients and may provide encouragement for a more effective management of AD, especially among those with greater AD severity.

Atopic dermatitis (AD) is a complex, immune-mediated, chronic relapsing inflammatory skin condition characterized by red, itchy, swollen, cracked and weeping lesions with crusting and/or scaling.[1,2]

Prevalence data on AD in adults are limited and variable. The results of an international, cross-sectional, web-based survey in adults with AD reported a prevalence rate of 4·4% in Europe (with individual country ranges of 2·2% for Germany to 8·1% for Italy).[3] Moreover, the results of two different web-based surveys in adults in the U.S.A. showed a prevalence rate between 4·9% and 7·3%.[3,4] In previous studies, prevalence rates between 3·2% and 10·7% in the U.S.A. have been reported, depending on the definition of AD used and the population studied.[5–8] The European Community Respiratory Health Survey II reported AD prevalence rates based on self-report and measured atopy of 0·3–6·2% in different European countries.[8]

AD is associated with a high burden of disease that includes impacts on health-related quality of life (HRQoL) and social, academic and occupational impacts.[9–11] A real-world survey based on self-reported outcomes in adults with AD reported significantly higher rates of anxiety, depression and sleep disorders, as well as a high impact on HRQoL, work productivity and daily activities compared with non-AD controls. Moreover, people with AD showed a similar impairment in HRQoL and productivity to those with psoriasis.[9] Unlike psoriasis, few studies in adults have assessed the relationship between self-reported AD severity and HRQoL.[4,12]

The main objective of this study was to assess the relationship between the severity of AD [Patient-Oriented SCORing of AD (PO-SCORAD)] and HRQoL [five-level EuroQol-5D (EQ-5D-5L) and Dermatology Life Quality Index (DLQI)] as a specific self-reported measure in adults with moderate-to-severe AD in Europe (France, Germany and the U.K.) and the U.S.A. Secondary objectives included (i) assessment of the relationship between AD severity and the perception of the AD symptoms by the patient [Patient-Oriented Eczema Measure (POEM)]; (ii) assessment of the relationship between AD severity and sociodemographic characteristics; and (iii) the exploratory comparison of AD sociodemographic and clinical characteristics and health outcomes between people with moderate-to-severe and mild AD.

Patients and methods

This was a cross-sectional, internet-based survey investigating the burden of disease in adults with AD in France, Germany, the U.K. and the U.S.A., using the National Health and Wellness Survey (NHWS) as a sampling frame. Selected participants with AD were re-contacted to participate in the 35-min online survey used in this study.

The European respondents had participated in the 2016 European NHWS, and the U.S. respondents were from the 2015 and 2016 U.S. NHWS.

The moderate-to-severe AD sample was stratified by region (Europe and the U.S.A.) and country. France, Germany and the U.K. were grouped as the Europe region in order to have a European sample to compare with the U.S. sample. This moderate-to-severe sample was the focus of this study and constituted the major part of the study sample. Additionally, a subgroup of patients with mild AD was also included to serve as a comparison with ('baseline' context for) patients with moderate-to-severe AD, but this group was smaller as it was not the main focus, owing to resource constraints. Inclusion and exclusion criteria were designed to achieve a thorough and specific definition of AD based on multiple survey questions to identify respondents with a current physician diagnosis of clearly stated AD and who had recently been seen by a dermatologist or allergist/immunologist; they are described in detail in the Supplementary Information.

Current severity status categories were determined by the PO-SCORAD scores obtained in the survey (< 25 mild, 25–50 moderate, > 50 severe).[13–15]

The five-dimension, five-level version of the EQ-5D (EQ-5D-5L) is a generic self-completion instrument for describing the patient health state (referring to the day that the measurement is done) in terms of five dimensions: Mobility; Self-Care; Usual Activities; Pain/Discomfort; Anxiety/Depression. Each dimension has five levels: no problems; slight problems; moderate problems; severe problems; extreme problems. Each state is referred to in terms of a five-digit code. The EQ-5D-5L defined 3125 health states, which were converted into a single index [ranging from states worse than dead (< 0) to 1 (full health)]. In addition, the measure includes a visual analogue scale (EQ-VAS) where health is rated on a scale from 0 (worst imaginable health) to 100 (best imaginable health).[16]

The DLQI is a dermatology-specific HRQoL instrument.[17,18] This questionnaire asks patients to consider the impact of the skin problem on their life over the previous week. It consists

of 10 questions about the most commonly identified aspects of life affected by skin disease: symptoms and feelings; daily activities; leisure, school and work; personal relationships; treatments. Each question has four alternative responses: 'not at all'; 'a little'; 'a lot'; or 'very much', with corresponding scores of 0, 1, 2 and 3, respectively. The answer 'not relevant' is scored as 0. The DLQI is calculated by summing the score of each question, resulting in a maximum of 30 and minimum of 0. The higher the score, the greater the impairment of HRQoL.

The perception of AD symptoms by the patient were assessed using the POEM.[19–21] The POEM is a validated, reliable and simple tool for assessing AD severity in adults and children, and for monitoring aspects of the disease that are important to patients. It records how frequently they experienced a symptom during a 1-week period (using a 5-point scale). POEM scores can range from 0 to 28 (a higher score indicates more severe symptoms).

In the survey, there were some questions asking how often respondents experienced flares and how long the flares typically last. Flare was defined as a 'sudden appearance or worsening of symptoms'.

Assessment of exercise was done by asking respondents about the days of vigorous exercise in the past month, defined as 'exercising vigorously for at least 20 minutes for the purpose of improving or maintaining your health, with the purpose of losing weight, or for enjoyment'.

Statistical analysis

For the descriptive analyses, continuous variables were presented as the number of observations (mean ± SD) and categorical variables as frequencies and percentages. χ^2-tests, Cochran–Armitage trend tests or t-tests were used to assess any statistically significant differences between groups based on their baseline characteristics. Spearman correlations (r) were used to estimate the raw association between PO-SCORAD scores and outcome measures.

For the adjusted statistical analysis, multivariable linear regression models were used to examine associations between the level of PO-SCORAD scores and outcomes, controlling for covariates. PO-SCORAD was the main independent variable treated as a categorized variable (mild: < 25; moderate: 25–50; severe 1: 51–60; severe 2: 61–70; severe 3+: ≥ 71). Country, age, sex, alcohol use, smoking, body mass index (BMI) categories, household income, Charlson Comorbidity Index (CCI; used here as a summary measure of comorbidity and general health) and years since AD diagnosis were included as covariates to adjust for confounding. This list of covariates was the result of a priori inclusion of age, sex, CCI, alcohol use, smoking and BMI categories, and evaluation of additional significant predictors, resulting in this total model.

All EQ-5D index scores were calculated using their respective 5L value sets.

Analyses were done by country and region (Europe and U.S.A.), and were also conducted for the total sample (all respondents). A statistical significance level of 0·05 was adopted. Statistical analyses and data management were conducted using SAS software (version 9·4; SAS Institute, Cary, NC, U.S.A.).

Results

Sociodemographic and clinical characteristics of patients with moderate-to-severe atopic dermatitis

A total of 21 852 individuals in the NHWS surveys were invited. Total response rate was 39·7%. Of those responding to the study survey by the time it was closed, after excluding a majority who did not meet the inclusion criteria, and for patients with mild AD accepting only our predefined lower quota, 1232 respondents were finally included in the analysed study sample, based on predefined target numbers across countries and severities: 1098 with moderate-to-severe AD and 134 with mild AD.

Of the 1098 patients with moderate-to-severe AD, 548 (49·9%) were from Europe [221 (20·1%) from France, 209 (19·0%) from Germany, 118 (10·7%) from the U.K.] and 550 (50·1%) from the U.S.A.

Sociodemographic and clinical characteristics by AD severity category are shown for the total population in Table 1. Comparison among the moderate and three severe AD groups showed similar results, except for a higher frequency of flares and a younger age at AD diagnosis in those with more severe AD. This difference in flare frequency was strongest in the European population (months between flares: 3·6 ± 7·4 for moderate; 1·2 ± 3·6 for severe 1; 1·7 ± 2·8 for severe 2; 0·5 ± 2·3 for severe 3+). A similar trend was observed in the U.S. population, but it was not statistically significant. The overall trend for age at diagnosis was seen only in the U.S. population, where a younger age at AD diagnosis was related to a more severe AD level (34·4 ± 21·1 years for moderate; 32·0 ± 18·3 years for severe 1; 31·4 ± 18·3 years for severe 2; 17·7 ± 13·7 years for severe 3+), while this trend was not seen in the European population (27·3 ± 17·8 years for moderate; 28·0 ± 17·8 years for severe 1; 25·6 ± 14·2 years for severe 2; 29·3 ± 19·2 years for severe 3+).

A higher percentage of patients on immunosuppressant treatment was observed in the European populations than in the U.S. population, especially in those with severe AD [immunosuppressants (ever): 10·7% vs. 6·8% for moderate; 25·8% vs. 20·3% for severe 1; 41·3% vs. 21·6% for severe 2; 40·7% vs. 18·2% for severe 3+] (more information on the sociodemographic and clinical characteristics by AD severity in the total population is provided in Table S1; see Supporting Information).

Sociodemographic and clinical characteristics by region (Europe and U.S.A.) (without categorization by AD severity) showed a significantly younger age at AD diagnosis in the European population. Moreover, significant differences were also reported in terms of BMI (with a higher percentage of obese participants in the U.S.A.), smoking habits (higher percentage of current smokers in Europe) and AD treatments (Table S2; see Supporting Information).

Table 1 Sociodemographic and clinical characteristics of adults with mild and moderate-to-severe atopic dermatitis (AD), by level of severity (total population)

AD severity (PO-SCORAD)	Mild (< 25)	Moderate (25–50)	Severe 1 (51–60)	Severe 2 (61–70)	Severe 3+ (71+)
n	134	825	141	83	49
Mean ± SD age (years)	47·7 ± 17·2	48·5 ± 15·3	49·3 ± 13·1	46·7 ± 12·7	45·5 ± 12·4
Country					
U.S.A.	50 (37·3)	412 (49·9)	79 (56·0)	37 (45)	22 (45)
Europe	84 (62·7)	413 (50·0)	62 (44·0)	46 (55)	27 (55)
France	31 (23·1)	169 (20·5)	19 (13·5)	24 (29)	9 (18)
Germany	30 (22·4)	167 (20·2)	24 (17·0)	10 (12)	8 (16)
U.K.	23 (17·2)	77 (9·3)	19 (13·5)	12 (14)	10 (20)
Female	75 (56·0)	573 (69·5)	90 (63·8)	55 (66)	37 (76)
Mean ± SD age at AD diagnosis (years)	31·0 ± 19·0	31·0 ± 19·9	30·3 ± 18·1	28·2 ± 16·3	23·9 ± 17·7
Mean ± SD months between flares	8·8 ± 10·8	3·4 ± 7·2	1·8 ± 5·1	1·7 ± 4·5	0·8 ± 2·2
Treatment (ever)[a]					
Nonprescription only	14 (10·4)	54 (6·5)	8 (5·7)	0 (0)	3 (6)
TCS[b]	81 (60·4)	411 (49·8)	46 (32·6)	22 (27)	14 (29)
TCI	8 (6·0)	44 (5·3)	7 (5·0)	3 (4)	2 (4)
Oral or injectable CS	19 (14·2)	196 (23·8)	34 (24·1)	25 (30)	10 (20)
Phototherapy	3 (2·2)	41 (5·0)	14 (9·9)	6 (7)	5 (10)
Immunosuppressants	4 (3·0)	72 (8·7)	32 (22·7)	27 (33)	15 (31)
None	5 (3·7)	7 (0·8)	0 (0·0)	0 (0)	0 (0)
Smoking behaviour					
Current smoker	22 (16·4)	182 (22·1)	46 (32·6)	27 (33)	16 (33)
Former smoker	39 (29·1)	258 (31·3)	35 (24·8)	23 (28)	13 (27)
Never smoker	73 (54·5)	385 (46·7)	60 (42·6)	33 (40)	20 (41)

Data are n (%) unless otherwise indicated. PO-SCORAD, Patient-Oriented SCORing of AD; TCS, topical corticosteroids; TCI, topical calcineurin inhibitors; CS, corticosteroids. [a]Multiple answers were possible. Highest level of treatment is given. [b]TCS as needed and/or proactively.

Relationship between severity of atopic dermatitis and health-related quality of life in patients with moderate-to-severe atopic dermatitis

AD severity and EQ-5D scores in patients with moderate-to-severe AD showed a negative correlation (Spearman's r = −0·38; P < 0·001, total population), indicating that a higher AD severity was associated with lower EQ-5D, i.e. a poorer generic HRQoL. Mean EQ-5D score by PO-SCORAD severity category, adjusted for covariates, is illustrated in Figure 1, with consistent results for the U.S. and European populations. The unadjusted mean ± SD EQ-5D scores per country for the study sample across all severity categories were 0·71 ± 0·27 in France, 0·79 ± 0·19 in Germany, 0·62 ± 0·30 in the U.K. and 0·66 ± 0·27 in the U.S. populations.

EQ-VAS scores were lower in patients with a higher severity of AD, suggesting poorer health (as expected). Comparable results among the European and U.S. populations were seen (Table 2). Additionally, for comparison purposes of AD severity, the EQ-VAS scores of patients with mild AD are included (Table 2).

AD severity showed a higher positive correlation (Spearman's r = 0·61; P < 0·001, total population) with DLQI scores than with EQ-5D scores, indicating that a higher AD severity was strongly associated with poorer dermatology-specific HRQoL. DLQI score by PO-SCORAD severity category, adjusted for covariates, is illustrated in Figure 2; the results for EQ-5D and DLQI were very similar in the European and the U.S. populations.

The results of the multivariable regression analysis (controlled for potential confounding variables) showed an association between higher AD severity and a poorer EQ-5D score, with a 0·03-point decrease for each 5-point increase in PO-SCORAD severity category (P < 0·001). The association with a higher DLQI was a 1·4-point increase for each 5-point increase in PO-SCORAD severity category (P < 0·001).

When multivariable regression analysis using the scores as continuous outcomes was controlled for potential confounding variables, the association between a higher AD severity and a poorer EQ-5D score was a 0·03-point decrease for each 5-point increase in PO-SCORAD (P < 0·001), and the association with a higher DLQI was a 1·4-point increase for each 5-point increase in PO-SCORAD (P < 0·001).

Relationship between severity of atopic dermatitis and perception of atopic dermatitis symptoms in patients with moderate-to-severe atopic dermatitis

AD severity and the perception of the AD symptoms by the patient (POEM) showed a positive correlation (Spearman's r = 0·51; P < 0·001, total population). After adjustment, this association between AD severity and perception of AD symptoms by the patient remained in adjusted regression analysis, where each 5-point increase in PO-SCORAD severity category was

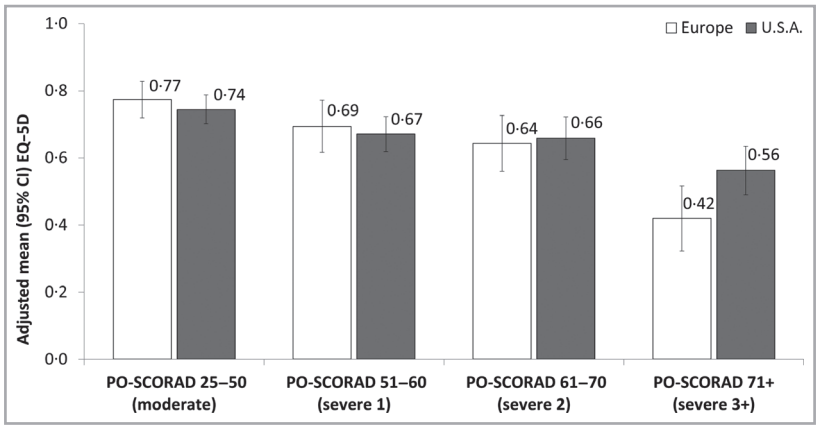

Fig 1. Mean EuroQol-5D (EQ-5D) score by Patient-Oriented SCORing of Atopic Dermatitis (PO-SCORAD) severity, adjusted for covariates. The mean was adjusted for country, age, sex, alcohol use, smoking, body mass index category, household income, Charlson Comorbidity Index and years since atopic dermatitis diagnosis. The EQ-5D score can range from < 0 to 1. A higher score indicates better health-related quality of life. There were a total of 26 patients with negative EQ-5D values (range –0·003 to –0·53). CI, confidence interval.

Table 2 EuroQol visual analogue scale (EQ-VAS) by level of severity in Europe, the U.S.A. and total population

	Mean ± SD EQ-VAS score		
	Europe (n = 632)	U.S.A. (n = 600)	Total (n = 1232)
AD severity (PO-SCORAD)			
Mild (< 25)	75·6 ± 20·3	75·0 ± 20·3	75·4 ± 20·2
Moderate (25–50)	65·0 ± 22·2	67·8 ± 22·5	66·4 ± 22·4
Severe 1 (51–60)	57·7 ± 22·3	63·5 ± 23·4	61·0 ± 23·0
Severe 2 (61–70)	56·1 ± 23·4	60·8 ± 24·7	58·2 ± 23·9
Severe 3 (71+)	45·0 ± 25·6	55·4 ± 29·5	49·7 ± 27·6

AD, atopic dermatitis; PO-SCORAD, Patient-Oriented SCORing of AD.

associated with a 1·3-point increment in POEM ($P < 0·001$). POEM score by PO-SCORAD severity category, adjusted for covariates, is illustrated in Figure 3. Comparable results were observed in the European and the U.S. populations.

Scatter plots with regression lines illustrating the correlation between PO-SCORAD and EQ-5D, DLQI and POEM scores, respectively, are displayed in Figures S1–S3 (see Supporting Information).

Comparison of patients with moderate-to-severe vs. mild atopic dermatitis

Sociodemographic characteristics were similar in patients with mild and moderate-to-severe AD in the total population (Table 1), and in the European and U.S. populations, respectively (data not shown). As expected, the frequency of flares was higher in those with moderate-to-severe AD than in those with mild AD (Table 1). Similarly, immunosuppressant AD treatments were administered to more patients with moderate-to-severe than mild AD (13·3% vs. 3·0%).

All studied health outcomes were clearly better in those with mild AD than in those with moderate-to-severe AD [unadjusted mean ± SD EQ-5D: 0·88 ± 0·16 vs. 0·70 ± 0·26; DLQI: 2·0 ± 2·0 vs. 7·9 ± 6·2; POEM 4·2 ± 4·2 vs. 10·9 ± 6·8 ($P < 0·001$ for all)]. Similar results were observed in the European and U.S. populations.

Discussion

This real-world, internet-based survey on self-reported outcomes assessed the impact of disease severity on HRQoL in adults with moderate-to-severe AD in Europe (France, Germany and the U.K.) and the U.S.A. The results demonstrate that the level of AD severity has a significant impact on HRQoL in adults with moderate-to-severe AD in both regions (European and U.S. populations). A higher AD severity was correlated with poorer HRQoL, assessed with the EQ-5D and DLQI (a dermatology-specific HRQoL index). The correlation between AD severity and HRQoL was stronger for the DLQI than for the EQ-5D. Two real-world studies in the U.S. adult population have also assessed the relationship between AD severity and HRQoL, showing that a more severe AD had a higher impact on HRQoL.[4,12] One of these studies reported that participants with severe AD were eight times more likely to have had a moderate-to-severe effect on DLQI than those with mild AD.[4]

In addition, self-reported AD severity was correlated with the symptoms of AD perceived by the patient (assessed using the POEM). As expected and seen in previous studies, self-reported AD severity was highly correlated with POEM score (Spearman's correlation coefficient $r \geq 0·70$).[22] Similar results for correlations of PO-SCORAD with EQ-5D, DLQI and POEM assessments were observed in the European and U.S. populations.

The EQ-5D scores in this study were in line with the EQ-5D scores reported in previous studies for patients with AD.[23,24] It should be noted that the EQ-5D scores in the

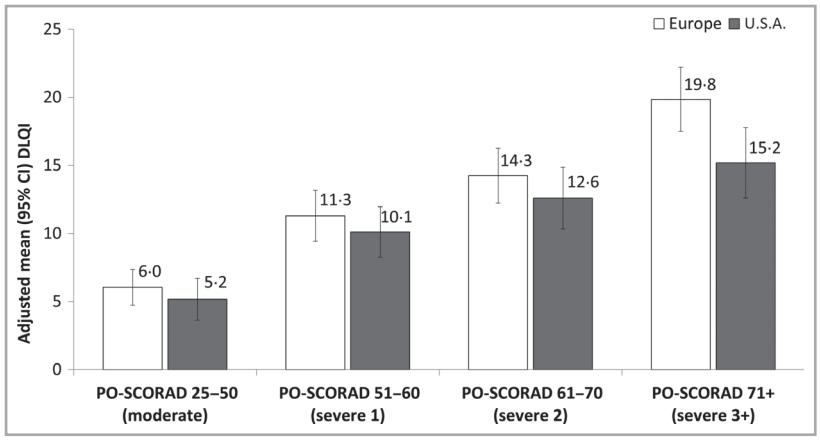

Fig 2. Mean Dermatology Life Quality Index (DLQI) score by Patient-Oriented SCORing of Atopic Dermatitis (PO-SCORAD) severity, adjusted for covariates The mean was adjusted for country, age, sex, alcohol use, smoking, body mass index category, household income, Charlson Comorbidity Index and years since atopic dermatitis diagnosis. DLQI score can range from 0 to 30. The higher the score, the more severe the patient's health-related quality of life impairment. CI, confidence interval.

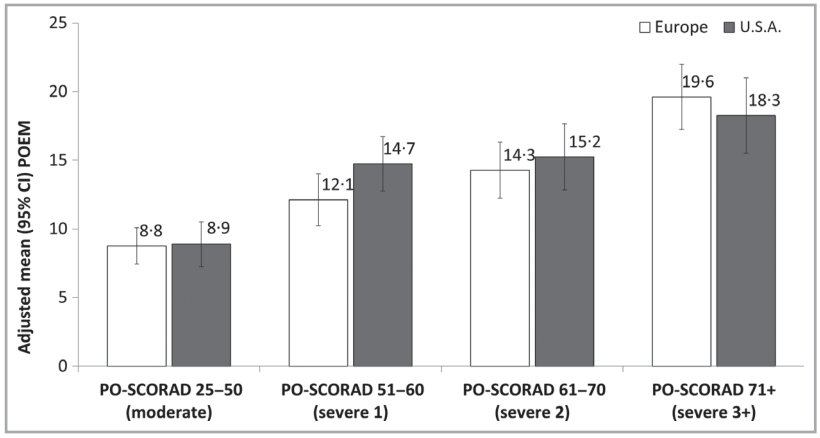

Fig 3. Mean Patient-Oriented Eczema Measure (POEM) score by Patient-Oriented SCORing of Atopic Dermatitis (PO-SCORAD) severity, adjusted for covariates. The mean was adjusted for country, age, sex, alcohol use, smoking, body mass index category, household income, Charlson Comorbidity Index and years since atopic dermatitis diagnosis. The POEM score can range from 0 to 30. A higher score indicates more severe eczema. CI, confidence interval.

present study were within the range for other dermatological diseases such as psoriasis (mean 0·5–0·9, results from a systematic literature review)[25] and pemphigus (mean 0·8),[26] as well as for other chronic diseases [mean 0·2 (type 2 diabetes mellitus) to 0·9 (cancer)].[25] Moreover, the EQ-VAS scores were also similar to the range for psoriasis (mean 50·7–75·1) and for pemphigus (mean of 68·0).[25,26] By contrast, DLQI scores were slightly different from those published by Holm *et al.*,[27] who reported mean adjusted DLQI scores by physician-assessed disease severity (SCORAD) of 5·3 for mild AD (score < 15), 8·6 for moderate AD (score 15–40) and 11·9 for severe AD (score > 40) in patients from Denmark. These DLQI scores are higher than those reported in the present study for patients with mild or moderate AD. However, they are lower for those with severe AD, specifically those with severe 2 and severe 3+ AD. These differences in DLQI scores across severity levels might partially be due to the difference in age (mean age 26 vs. 48 years) and sex distribution (proportion of females 59% vs. 69%) between Holm *et al.* and this study.[27] External factors such as age and sex, as well as geography, have previously been associated with differences in DLQI.[28,29] This, along with the identified discrepancies between DLQI scores and health utility values,[30] the number of 'not relevant' response options in the questionnaire affecting the DLQI score and several sociodemographic factors,[31,32] point to the inherent limitations of the DLQI and caution should be exercised when making a comparison across study populations.

Comparisons between the European and the U.S. populations (without categorization by AD severity) showed a younger age at AD diagnosis and a high prevalence of current smokers in the European vs. the U.S. population. Related to this, Lee *et al.* reported a significant association between

current smoking and the development of adult-onset AD.[33] Therefore, the higher percentage of current smokers in the European population could partially explain the earlier age at AD diagnosis in this population vs. the U.S. population. In addition to these differences, a higher prevalence of obesity in the U.S.A. vs. the European population was also observed. These data are according to the higher global prevalence of obesity reported in the U.S.A. vs. European countries. Therefore, the results of the present study are consistent with external data (i.e. they imply that our sample is as expected).[34] In terms of AD treatment, the European population showed a more frequent immunosuppressant treatment than in the U.S. population, which could be explained by the fact that the immunosuppressant treatment (ciclosporin) is approved for short-term treatment of severe refractory AD in many European countries but not in the U.S.A.[35]

The results of the exploratory analysis that compared adults with moderate-to-severe AD and adults with mild AD showed a higher negative impact on HRQoL in the moderate-to-severe group than in the mild group, as expected. These results are consistent with those reported by Whiteley *et al.*,[36] and support the relative validity of the moderate-to-severe group as a set of participants representing this population.

The study outcomes for the total sample (France, Germany, the U.K. and the U.S.A.) are consistent with the aforementioned patterns observed for the separate regions (European and U.S. populations), which provides support for the generalizability of our findings.

The fact that the diagnoses and other clinical variables were not verified using patient medical charts owing to the self-reported nature of the data is a limitation of this study. Moreover, although the NHWS was designed to be representative of the U.S.A. and the European countries in general, it is possible that age, technology-related limitations, willingness to participate in a follow-up survey and/or severity of AD may have resulted in the under-representation of some subgroups of the overall AD population.

The strengths of the present study include the use of up-to-date, previously validated instruments to assess AD severity and HRQoL. The use of both generic and dermatology-specific HRQoL questionnaires provided information on the impact of moderate-to-severe AD within dermatology and nondermatology settings. Moreover, the use of the NHWS survey sample allowed the efficient targeting/screening of patients with AD in a wide geographic sample. We implemented a thorough and specific AD definition based on multiple survey questions to identify respondents with a current physician diagnosis of clearly stated AD and seen recently by a dermatologist or allergist/immunologist. This study also included a thorough assessment of current severity level using the PO-SCORAD, adding greater detail across the moderate–severe AD subgroup.

In conclusion, the present study shows that higher self-reported AD severity is associated with poorer HRQoL from the patient's perspective, with similar observations across European and U.S. populations.

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Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher's website:

Fig S1. Scatter plots and regression line illustrating the correlation between the Patient-Oriented SCORing of Atopic Dermatitis total score and EQ-5D scores.

Fig S2. Scatter plots and regression lines illustrating the correlation between Patient-Oriented SCORing of Atopic Dermatitis total score and Dermatology Life Quality Index score.

Fig S3. Scatter plots and regression lines illustrating the correlation between Patient-Oriented SCORing of Atopic Dermatitis total score and Patient-Oriented Eczema Measure score.

Table S1 Sociodemographic and clinical characteristics of adults with mild and moderate-to-severe atopic dermatitis, by level of severity (total population).

Table S2 Sociodemographic and clinical characteristics of adults with moderate-to-severe atopic dermatitis, by region (Europe and U.S.A.) and total population.