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Atopic Dermatitis in America Study: a cross-sectional study examining the prevalence and disease burden of atopic dermatitis in the US adult population

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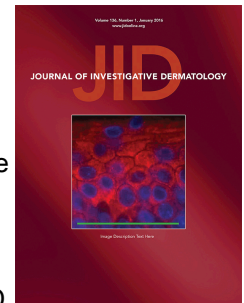
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SHORT TITLE: Prevalence of atopic dermatitis in US adults

List of abbreviations: *Atopic dermatitis, AD; GfK Knowledge Panel, GfK; Health Related Quality of Life, HRQoL; UK Working Party, UKWP; Patient Oriented Eczema Measure, POEM; Dermatology Life Quality Index, DLQI; and Hospital Anxiety and Depression Scale (HADS).*

ABSTRACT

Population-based estimates on the prevalence of atopic dermatitis in adults vary widely. The objectives of the present study were to determine the prevalence of atopic dermatitis in the population of the United States, distribution of disease severity, and assess its impact on health-related quality of life. Among 1,278 participating adults, the prevalence (95%CI) of atopic dermatitis was 7.3% (5.9-8.8). 60.1% (56.1-64.1%) of participants were classified as mild 28.9% (25.3-32.7%) as moderate and 11% as severe (8.6-13.7%). Patients with atopic dermatitis and those with more severe disease had higher scores in the dermatology life quality index (mean [SD] AD: 4.71 [6.44] vs. controls: 0.97 [2.12] (<0.001), and the hospital anxiety (mean [SD] AD: 7.03 [4.80] vs. controls: 4.73 [4.8], and depression (mean (SD) AD: 5.83 [4.54] vs. controls: 3.62 [3.61]) scale indicating a worse impact on quality of life and an increased likelihood of anxiety or depression. Based on our prevalence estimates 16.5 million adults would have a diagnosis of atopic dermatitis with 6.6 million meeting criteria for moderate-to-severe disease. Our study confirms the high prevalence and disease burden of atopic dermatitis in this population.

INTRODUCTION

Atopic dermatitis (AD) is a chronic, inflammatory skin disease of complex etiology.(Weidinger and Novak 2016) While AD is primarily recognized as a disease of children, increasing evidence suggests that it is more common in adults than previously thought.(Flohr and Mann 2014) Prior studies focused primarily on the prevalence of AD in the pediatric population, yet only a handful examined the prevalence in the adult population. Population-based estimates on the prevalence of AD in the adult population of the United States vary between 3.2%-10.2%, with differences in estimates being partially attributed to varying case definitions for AD. In addition, studies examining the distribution of AD disease severity are scarce. (Hanifin and Reed 2007, Garmhausen, Hagemann et al. 2013, Silverberg and Hanifin 2013, Silverberg, Patel et al. 2015)

AD can have detrimental effects on patients' health related quality of life (HRQoL).(Fivenson, Arnold et al. 2002, Hay, Johns et al. 2014, Drucker, Wang et al. 2016, Whiteley, Emir et al. 2016, Drucker, Wang et al. 2017, Eckert, Gupta et al. 2017) However, studies have often not examined the impact of AD disease severity on HRQoL. While Eckert et al. (Eckert, Gupta et al. 2017) observed that AD in adults was associated with a substantial impact on HRQoL like psoriasis; data on the impact of disease severity was not examined. In contrast, Whiteley et al. (Whiteley, Emir et al. 2016) found no differences in patient reported outcomes (PRO) of HRQoL between self-reported AD severity except for greater impairment in work productivity and daily activities among adults with moderate-to-severe disease compared to mild disease. If we are to develop strategies to best allocate resources for the management of AD in adults, more epidemiological studies are needed to better understand its distribution including that of disease severity. As such, the objectives of this study were to examine (1) the prevalence of AD in the

US adult population, (2) the distribution of AD disease severity and, (3) the impact of AD and AD disease severity on HRQoL.

RESULTS

Prevalence of AD and distribution of AD severity

An initial sample of 2,137 adults from the GfK web panel was invited to participate in the survey. A total of 1,278 adults completed the survey (response rate=59.80%). Table 1 summarizes the prevalence of AD based on the UK working party (UKWP) criteria including age of onset. Overall, the prevalence (95%CI) of AD in those with the strictest criteria, which included age of onset < 2 years of age, was 7.3% (5.9-8.8%). When criteria for age of onset were less restricted, allowing for an older age of onset, the prevalence remained similar across groups except when limiting analyses to those with onset ≥ 18 years of age (16.1% [14.1-18.1]). Distribution of disease severity was examined among those subjects who met the strictest UKWP criteria (including age of onset < 2 years of age) using POEM. Based on POEM, 60.1% (56.1-64.1%) had mild disease, whereas 28.9% (25.3-32.7%) and 11.0% (8.6-13.7%) had moderate to severe disease, respectively (Table 1).

Subject demographic characteristics

Subject demographics are summarized in tables 2 and 3. The distribution of demographic characteristics was similar with no statistically significant differences observed except for sex, race and income level when comparing subjects with AD versus controls (Table 2). Among AD severity groups, only level of education showed a statistically significant difference among groups (Table 3).

Association between demographic variables and AD

Tables 2 and 3 also summarize the associations between demographic variables and presence of AD, and AD disease severity. In the adjusted model, statistically significant associations were

seen only for sex, race (i.e. multiracial, Non-Hispanic) and income. Subjects who were female had an increase adjusted odds ratio (95%CI) of AD compared to males (1.65 [1.05-2.61]). Compared to White, non-Hispanic subjects, those who described themselves as multiracial, non-Hispanic had an increased odds of AD (3.36 [1.31-8.58]). Lower odds of AD were observed for those subjects who reported an income level between \$50,000-\$99,999 (0.45[0.20-0.99]) and $\geq$ \$100,000 (0.28 [0.11-0.70]) versus those who reported an income level of less than \$15,000 (Table 2). When examining the association between demographic variables and AD disease severity, only marital status and level of education showed a statistically significant association in the adjusted model (Table 3). Subjects that reported living with a partner had a 2-fold increased risk of having moderate-to-severe disease compared to those who were married (2.14 [1.02-4.51]). In addition, subjects that reported a higher level of education had a decreased risk of having moderate-to-severe disease compared to those that reported having completed less than a high school level of education (0.44 [0.21-0.91]) (Table 3).

Anxiety, Depression and Health-related quality of life (HRQoL): HADS and DLQI

The mean (SD) DLQI score in patients with AD was 4.71 (6.44) vs. 0.97 (2.12) in controls ($p<0.001$) (Table 4). The proportion of subjects with AD that reported a moderate-to-large effect on QoL using established thresholds was higher compared to controls (24.37 vs. 4.66; $p<0.001$). A similar trend was observed for both components of the HADS scale. The mean (SD) HADS-anxiety score in the AD group was 7.03 (4.80) vs. 4.73 (4.8) in the control group. 24.73% of subjects with AD met clinical criteria for anxiety compared to 9.20% in the control group ($p<0.001$). The mean (SD) HADS-depression score was 5.83 (4.54) among those with AD and 3.62 (3.61) in the control group. The proportion of subjects that met clinical criteria for depression was 13.98% in the AD group vs. 5.99% in the control group ($p<0.003$).

68.8% of subjects classified as having severe disease reported a moderate-to-large effect on QoL compared to 10.50% and 37.36% in the mild and moderate group, respectively ($p < 0.001$). Similarly, a greater proportion of subjects in the severe group met clinical criteria for anxiety compared to subjects in the mild or moderate group based on their HADS-A score (54.55% vs. 16.02% vs. 32.18%). Lastly, while the proportion of AD subjects with moderate or severe disease who met clinical criteria for depression using HADS-D score was similar (19.54% vs. 19.70%), this was higher compared to those with mild disease (8.84%; $p = 0.001$).

Association between AD disease severity with HRQoL, anxiety and depression:

Results of the unadjusted and adjusted models examining the association between AD disease and impact on HRQoL are summarized in table 5. In the unadjusted model (uOR), patients with AD were more than six-times more likely to report a moderate-to-severe impact on DLQI compared to controls (6.73 [3.41-13.24]). These results were similar for both the age and sex adjusted models and the fully adjusted model. In unadjusted and fully adjusted models, subjects with AD had approximately a 3-fold and 2.5-fold increased risk of having a clinical diagnosis of anxiety or depression, respectively, when compared to controls. Similarly, increased odds of worse quality of life, anxiety and depression based on the DLQI and HADS-scales scores were observed with increasing AD severity (Table S1). Again, these results were similar for both the age and sex-adjusted, and fully adjusted model.

DISCUSSION

Population-based studies on the prevalence of AD are limited and variations in study design, objective assessment of AD and disease severity limit comparison. A recent study found that the prevalence of AD in adults in the US was 4.9% (95%CI: 4.6-5.2%). (Barbarot, Auziere et al. 2018) In contrast, our study found a higher prevalence of AD (7.3% [5.9-8.8%]), similar to a prior study describing a prevalence of 7.2%.(Silverberg, Garg et al. 2015). The observed decreased prevalence in this study could be attributable to use of different criteria for study inclusion including stricter diagnostic criteria and limiting participation to subjects between the ages of 18-65 y/o, which could have potentially resulted in an underestimation of the true prevalence. A different US study, observed a higher prevalence of AD in adults (10.2%), yet the authors acknowledged this could have been the result of misclassification of AD cases by using less stringent criteria for definition of AD leading to a higher reported prevalence.(Silverberg and Hanifin 2013). With respect to prevalence of disease severity, we found that while most adult patients with AD had either mild (60.1%, [56.1-64.1%]) or moderate (28.9%, [25.3-32.7%]) disease based on POEM score, almost 11% (8.6-13.17%) would be classified as severe. Hanifin et al. (Hanifin and Reed 2007) examined the prevalence of symptom severity in both children and adults and found that 30% reported mild symptoms while 18% reported severe symptoms. A different study observed that 49.7% of adult respondents rated their AD as mild, 40.4% moderate, and 9.8% severe.(Whiteley, Emir et al. 2016) Using POEM, Barbarot et al. reported a higher prevalence of severe disease among adult patients with AD in the US (17% versus 35% and 48%, for mild and moderate disease, respectively). (Barbarot, Auziere et al. 2018) Because these studies used varying strata for POEM, it is likely that these differences can be attributed to varying case definition between both studies.

In our study, identifying as female was associated with a 70% increased odds of AD as compared to men. Prior studies have shown that females have a higher prevalence of eczema or AD when compared to men (Silverberg and Hanifin 2013). To the best of our knowledge, it remains unclear as to why eczema or AD seems to be more prevalent in adult women compared to men. With respect to income, our study showed a decrease risk of AD with increasing income level. Hanifin et al. (Hanifin and Reed 2007) also showed a decreased prevalence of AD among those with higher income, whereas a study in the adult Korean population found no association between AD and income level.(Lee, Kim et al. 2017) Patients who reported being multi-racial, non-Hispanic, also had a higher risk of AD (3.36 [1.31-8.58]). Silverberg et al. (Silverberg and Hanifin 2013) reported a higher prevalence of eczema among those who described themselves as multiracial compared to white or African American/black subjects (14.6% versus 10.5% and 7.7%, respectively). With respect to Ethnicity, Silverberg et al. (Silverberg and Hanifin 2013) also found a lower prevalence of eczema among Hispanics however this was not observed in the present study. Marital status and level of education were the only statistically significant associations observed with increasing disease severity, with those who replied living with partner having higher odds for moderate-to-severe disease compared to those with mild disease, and those with a higher level of education demonstrating lower odds for moderate-to-severe disease. These results require additional confirmation, as to the best of our knowledge; prior studies have not explored the association with AD disease severity. For example, in the study by Silverberg et al. (Silverberg and Hanifin 2013)a higher risk for eczema was observed for those having a greater than high school level of education but these findings were not stratified by disease severity. With respect to marital status, and like our findings, this same study also showed no statistically significant associations with eczema. However, when stratified by disease severity,

we found that living with a partner was more likely to be associated with moderate-to-severe disease compared to mild disease (2.14 [1.02-4.51]). Lee et al. (Lee, Kim et al. 2017), also found that separated/divorce and never married adult subjects had a higher prevalence of AD compared to married subjects. Because AD is a disease associated with a high physical and psychological burden, it would not be surprising that it would result in impaired social relationships. While varying case definitions for AD, as well as stratification of demographic variables, limit comparisons between both studies, future research in this area would benefit from a more uniform approach.

Our results confirm the high burden of AD on HRQoL and mental health. Findings from Simpson et al. (Simpson, Bieber et al. 2016) showed that nearly 22% of adult patients with AD had clinical symptoms of depression or anxiety with higher burden of anxiety compared to depression. Eckert et al. (Eckert, Gupta et al. 2017) also found a high disease burden in adult patients with AD, which was comparable to that of psoriasis patients, as well as higher rates of depression and anxiety. In our study, the mean DLQI score for our overall AD population was 4.71 (6.44), which would indicate a small effect on QoL, but, when stratified by disease severity, subjects with severe disease were 8 times more likely to report a moderate-to-severe effect on DLQI as compared to those with mild disease (8.33 [3.72-18.65]). In the study by Simpson et al. (Simpson, Bieber et al. 2016) the mean (SD) total DLQI score was 14.3 (7.0) indicating a large effect on QoL. Simpson et al. (Simpson, Bieber et al. 2016) also found a higher risk for a clinical diagnosis of anxiety and depression (HADS score ≥ 11) in AD patients and in those with more severe disease compared to those with mild disease. Thus, our results confirm that disease burden in AD is higher in those with more severe disease.

Our study has certain limitations. Misclassification or recall bias could have resulted in wrongly estimating the prevalence of AD. We sought to mitigate these risks by using strict diagnostic criteria for AD. On the other hand, this attempt could have also resulted in an underestimation of the prevalence of AD by limiting inclusion to only those patients who developed symptoms early in childhood and excluding those who start to present symptoms during adulthood. Interestingly, the prevalence of AD remains similar when criteria for age of onset were relaxed, but increased when age of onset was limited to those who presented symptoms for the first time after 18 years of age (16.5% [14.1-18.1]). Likewise, a recent systematic review found that 26.5% (16.5-37.2%) reported onset of AD after 16 years of age. (Lee, Patel et al. 2018) However, these results must be interpreted with caution as childhood AD may be more persistent than previously thought and would contribute to the higher prevalence seen in adults.(Margolis, Abuabara et al. 2014, Kosse, Bouvy et al. 2018) Due to the study design, we are also unable to prove causality with respect to risk factors for AD. Nonetheless, our study has several strengths. We used a large population-based sample as well as strict diagnostic criteria for AD. There is no clear consensus on how to best define disease severity in AD. However, by using POEM, we could evaluate the impact of AD-specific symptoms and obtain a more accurate representation of disease severity.

In summary, it is important that we put our findings into perspective. For example, it is estimated that the prevalence of psoriasis varies between 2-3% of the population, which translates to 7-9 million patients with psoriasis.(Gelfand, Stern et al. 2005) In contrast, using US census estimates, based on the findings from our study, 16.5 million adults would have a diagnosis of AD with 6.6 million meeting criteria for moderate-to-severe disease. Yet, the widely-held dogma that AD is primarily a disease of children often results in a lack of appreciation of the true impact of this disease in adults. Increasing awareness that AD is a

prevalent disease in this population could lead to more timely diagnosis and treatment. In addition, there is a need to establish better criteria for the diagnosis of AD in adults as current criteria often lack sensitivity and specificity. Lastly, an increasing number of studies provide evidence that AD is associated with marked QoL impairment and increased health care costs with higher burden and costs in those with more severe disease.(Eckert, Gupta et al. 2017, Drucker, Qureshi et al. 2018) Additional studies should center on exploring those factors associated with AD, and AD disease severity, which lead to increased disease burden in this population.

MATERIALS AND METHODS

Data Source

Data was obtained from the *Atopic Dermatitis in America* survey sampled from the GfK Knowledge Panel. This panel is a large probability-based web panel in the US and contains between 40,000 to 50,000 adult members at any given time. The GfK panel is constructed from a national address-based sample of households in the US who are recruited to join and who receive small incentives for participating in web surveys. This panel also provides internet access, as well as computer hardware, to households without existing internet access and has been previously used in other large, population-based, epidemiological studies. (Heckman, Darlow et al. (2013), (Hays, Liu et al. 2015, Lantz, Evans et al. 2016)

Study design

This was a cross-sectional study which involved a two-stage sampling process. An initial cross-sectional sample of 2,137 adults was drawn from the GfK panel to develop the prevalence estimate. The focus of the survey was not disclosed in the invitation to avoid biasing participation based on respondent interest or disinterest in the subject. Although the cross-sectional 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. Based on the initial prevalence estimate, an additional, national over-sample of 8,127 adults was screened to identify and interview a total of 602 adult patients with AD from both samples who met the UKWP definition of AD, including age of onset < 2 years of age (N=602).

Definition of AD and controls

An adaptation of the UK working party (UKWP) criteria was selected by the *AD in America* advisory committee as the screening tool for patient eligibility.(Williams, Burney et al. 1996) These include (1) having and itchy skin condition during the past 12 months and 3 or more of the following: (2) history of skin crease involvement; (3) a personal history of asthma and/or hay fever; (4) a history of general dry skin during the past year; or (5) onset under the age of two. However, because recall of AD in childhood among adults is low (Naleway, Belongia et al. 2003) and considering the growing number of patients with adult-onset AD, patients were initially not screened out of the survey if they failed to meet the stricter criteria of AD onset under age 2 years of age. The control group was comprised of participants from the initial, cross-sectional sample who did not meet criteria for AD.

Definition of AD Severity

AD severity was classified based on the Patient Oriented Eczema Measure (POEM).(Charman, Venn et al. 2004) POEM is a validated, self-administered tool, primarily used in clinical trials, to assess patient-reported symptoms in AD. The Harmonizing Outcome Measures for Eczema initiative, which seeks to develop consensus on best measures to use when assessing AD disease severity, recently agreed that POEM should be the chosen instrument when assessing symptoms of AD in future clinical trials.(Spuls, Gerbens et al. 2017) By allowing stratification of disease severity based on self-assessment, POEM has potential applications for use in larger, epidemiological studies.(Charman, Venn et al. 2013) POEM measures the frequency in the past week of seven symptoms related to AD. For this study, a score of 0-7 was considered mild, 8-16 as moderate, and 17-28 as severe, based on published strata for POEM. (Vakaharia, Chopra et al. 2018)

The impact of AD on HRQoL and the distribution of anxiety and depressive symptoms were assessed using the Dermatology Life Quality Index (DLQI) and the Hospital and Anxiety Depression scale (HADS). The DLQI is self-administered and consists of 10 questions, with higher scores indicating a worse impact on HRQoL.(Finlay and Khan 1994) The HADS is also self-administered and consists of 2 subscales with a score of 0-7 (normal); 8-10 (borderline) and, 11-21 (clinical diagnosis of anxiety or depression) for either scale.(Zigmond and Snaith 1983)

Sample Size calculation

Based on an expected lifetime prevalence of atopic dermatitis of 20% (Hanifin and Reed 2007), it was determined that a sample size of 500 would provide an adequate estimate with a maximum expected sampling error of +/- 4.4 percentage points at the 95% confidence level.

Statistical analyses

Descriptive statistics were used to summarize and compare demographic and health characteristics between subjects with vs. without AD, and between AD severity groups (i.e. clear/mild vs. moderate vs. severe). The *t*-test or its nonparametric equivalent was used for continuous variables. χ^2 test was used for comparisons between categorical variables. For ordered categorical variables (i.e. income) a test for trend was used. Unadjusted logistic regression models were used to examine differences in HRQoL between AD and the control group as well as between AD disease severity groups. The overall models were adjusted for age and sex, and were also adjusted for additional covariates using a purposeful selection modeling approach. Covariates with plausible relationship to the exposure and outcome, and those that resulted in a change in the point estimates of the main effects by >10-15% were kept in the final model. As this was an exploratory analysis no pre-specified hypothesis was determined a priori. Correction

for multiple comparisons was considered to decrease the possibility of committing a type I error (i.e. rejection of the null hypothesis when this is true). However, as the primary purpose of this analysis was exploratory, we opted not to correct for multiple testing as this is a more conservative approach that could potentially result in not detecting potentially meaningful comparisons (i.e. Type II error) that would serve as basis for future research. Analyses were performed using STATA 13 (College Station, TX).

Ethics

This study was approved by ICF Institutional Review Board. Participants in the patient survey provided electronic consent at the start of the survey. Participants were informed that their answers were voluntary and confidential, and that responses were not identified by individual responder. All responses were compiled and analyzed as a group. Study design and reporting were done in accordance with STROBE guidelines.

Conflicts of Interest

The following authors' state conflicts of interest: Dr. Chiesa has served as a consultant for the Asthma and Allergy Foundation of America and the National Eczema Associations. Dr. Chiesa has also received research grants from Regeneron, Sanofi, Tioga and Vanda pharmaceuticals for work related to atopic dermatitis and has received honoraria for CME work in atopic dermatitis sponsored by educational grants from Regeneron and Sanofi pharmaceuticals. Dr. Boguniewicz, MD has received research grants from Regeneron and served on advisory boards and speakers bureau for Regeneron and Sanofi-Genzyme. Dr. Gelfand served as a consultant for BMS, Boehringer Ingelheim, GSK, Janssen Biologics, Menlo Therapeutics, Novartis Corp, Regeneron, Dr Reddy's labs, UCB (DSMB), Sanofi and Pfizer Inc., receiving honoraria; and receives

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Table 1. Prevalence of atopic dermatitis in US adults based on UKWP criteria and age of onset and prevalence of disease severity based on POEM score

Prevalence of Atopic Dermatitis in US Adults based on UKWP criteria and age of onset¹			
Primary analysis			
	No.	Prevalence	95% CI
Onset of disease < 2 y/o	93	7.3	5.9-8.8
Sensitivity Analyses			
	No.	Prevalence	95% CI
Onset of disease < 6 y/o	98	7.7	6.3-9.3
Onset of disease < 10 y/o	99	7.7	6.3-9.4
Onset of disease < 18 y/o	114	8.9	7.4-10.6
Onset of disease ≥18 or older	206	16.1	14.1-18.1
Prevalence of disease severity based on POEM score²			
	No.	Prevalence	95% CI
Clear or mild disease	362	60.13	56.1-64.1
Moderate disease	174	28.9	25.3-32.7
Severe disease	66	10.96	8.6-13.7

¹Based on a cross-sectional sample N=1278. UKWGUKWP criteria includes past year history of itchy skin + 3 or more of the following conditions: skin fold involvement and/or history of asthma or hay fever and/or past year dry skin and/or age of onset criteria

²Based on a cross-sectional and over-sample of N=602 adult patients with AD

Table 2. Demographics¹ and measure of association² with Atopic Dermatitis for US adults without and with atopic dermatitis¹

	Controls	Atopic Dermatitis	p-value	OR ²	95% CI	p-value
N (%)	1,185 (92.72)	93 (7.28)	n/a	n/a	n/a	n/a
Sex, N (%)						
male	596 (50.30)	35 (37.63)		1 (ref)	n/a	n/a
female	589 (49.70)	58 (62.37)	0.02	1.65	1.05-2.61	0.03
Age						
mean (SD)	51.25 (16.97)	51.81 (18.17)	0.63	1.00	0.98-1.02	0.76
Race/Ethnicity, N (%)						
White, Non-Hispanic	883 (74.51)	57 (61.29)		1 (ref)	n/a	n/a
Black, Non-Hispanic	101 (8.52)	10 (10.75)		1.20	0.56-2.54	0.63
Other, Non-Hispanic	37 (3.12)	6 (6.45)		2.08	0.81-5.34	0.13
Hispanic	138 (11.65)	13 (13.98)		1.29	0.65-2.55	0.46
Multiracial, Non-Hispanic	26 (2.19)	7 (7.53)	0.004	3.36	1.31-8.58	0.01
Marital status						
Married	692 (58.40)	51 (54.84)		1 (ref)	n/a	n/a
Widowed	61 (5.15)	5 (5.38)		0.62	0.22-1.79	0.38
Divorced	134 (11.31)	10 (10.75)		0.72	0.34-1.53	0.40
Separated	20 (1.69)	5 (5.38)		2.05	0.68-6.18	0.20
Never married	212 (17.89)	18 (19.35)		0.80	0.40-1.60	0.53
Living with partner	66 (5.57)	4 (4.30)	0.33	0.53	0.16-1.70	0.29
Level of Education						
< High School	104 (8.78)	12 (12.90)		1 (ref)	n/a	n/a
Completed High School	345 (29.11)	17 (18.28)		0.50	0.22-1.15	0.10
Some college education or higher education	347 (29.28)	35 (37.63)		1.23	0.56-2.66	0.61
Bachelor's degree or higher	389 (32.83)	29 (31.18)	0.06	1.34	0.57-3.12	0.50
Income						
<\$15,000	111 (9.37)	15 (16.13)		1 (ref)	n/a	n/a
\$15,000-\$29,999	106 (8.95)	15 (16.13)		1.06	0.47-2.41	0.88
\$30,000-\$49,999	193 (16.29)	21 (22.58)		0.80	0.36-1.76	0.57
\$50,000-\$99,999	405 (34.18)	26 (27.96)		0.45	0.20-0.99	0.05
\$100,000+	370 (31.22)	16 (17.20)	0.002	0.28	0.11-0.70	0.01
Employment status						
Currently employed	718 (60.59)	45 (48.39)		1 (ref)	n/a	n/a
Not currently	54 (4.56)	9 (9.68)		1.95	0.84-4.51	0.12

employed						
Retired	289 (24.39)	28 (30.11)		1.56	0.79-3.07	0.20
Disabled	46 (3.88)	5 (5.38)		1.42	0.50-4.08	0.51
Other	78 (6.58)	6 (6.45)	0.08	0.89	.34-2.30	0.81

^{1,2}Based on a cross-sectional sample N=1278 subjects. M (SD) = Mean (standard deviation); OR=odds ratio; 95%CI=95% Confidence Interval

Table 3. Demographics¹ and measure of association according to disease severity (clear/mild vs. moderate/severe)² for US adults with atopic dermatitis.

	Clear or Mild	Moderate	Severe	p-value	OR ²	95% CI	p-value
N (%)	362 (60.13)	174 (28.90)	66 (10.96)	n/a	n/a	n/a	n/a
Sex, N (%)							
male	149 (41.16)	76 (43.68)	28 (42.42)				
female	213 (58.84)	98 (56.32)	38 (57.58)	0.86			
Age							
mean (SD)	51.45 (15.5)	51.2 (16.37)	48.08 (15.33)	0.27	1.00	0.99-1.02	0.70
Race/Ethnicity, N (%)							
White, Non-Hispanic	241 (66.57)	110 (63.22)	45 (68.18)		1 (ref)	n/a	n/a
Black, Non-Hispanic	47 (12.98)	20 (11.49)	7 (10.61)		0.78	0.45-1.36	0.39
Other, Non-Hispanic	13 (3.59)	10 (5.75)	3 (4.55)		1.81	0.79-4.11	0.16
Hispanic	46 (12.71)	23 (13.22)	8 (12.12)		1.01	0.60-1.72	0.96
Multiracial, Non-Hispanic	15 (4.14)	11 (6.32)	3 (4.55)	0.93	1.54	0.70-3.37	0.28
Marital status							
Married	210 (58.01)	88 (50.57)	35 (53.03)		1 (ref)	n/a	n/a
Widowed	16 (4.42)	9 (5.17)	3 (4.55)		1.30	0.57-2.98	0.53
Divorced	55 (15.19)	28 (16.09)	11 (16.67)		1.08	0.64-1.81	0.77
Separated	9 (2.49)	9 (5.17)	2 (3.03)		1.59	0.60-4.22	0.35
Never married	56 (15.47)	24 (13.79)	11 (16.67)		0.99	0.57-1.70	0.96
Living with partner	16 (4.42)	16 (9.2)	4 (6.06)	0.54	2.14	1.02-4.51	0.05
Level of Education							
< High School	20 (5.52)	15 (8.62)	13 (19.7)		1 (ref)	n/a	n/a
Completed High School	99 (27.35)	49 (28.16)	16 (24.24)		0.57	0.29-1.13	0.11
Some college education or higher	112 (30.94)	59 (33.91)	15 (22.73)		0.56	0.28-1.12	0.10
Bachelor's degree or higher	131 (36.19)	51 (29.31)	22 (33.33)	0.03	0.44	0.21-0.91	0.03
Income							
<\$15,000	45 (12.43)	34 (19.54)	11 (16.67)		1 (ref)	n/a	n/a
\$15,000-\$29,999	50 (13.81)	21 (12.07)	15 (22.73)		0.80	0.42-1.50	0.48
\$30,000-\$49,999	69 (19.06)	26 (14.94)	11 (16.67)		0.69	0.36-1.31	0.26
\$50,000-\$99,999	117 (32.32)	59 (33.91)	14 (21.21)		0.77	0.42-1.42	0.40
\$100,000+	81 (22.38)	34 (19.54)	15 (22.73)	0.10	0.83	0.41-1.68	0.61
Employment status							
Currently employed	208 (57.46)	95 (54.6)	37 (56.06)		1 (ref)	n/a	n/a
Not currently employed	19 (5.25)	11 (6.32)	3 (4.55)		1.05	0.49-2.25	0.90
Retired	94 (25.97)	40 (22.99)	12 (18.18)		0.81	0.46-1.41	0.45

Disabled	25 (6.91)	19 (10.92)	10 (15.15)		1.38	0.71-2.66	0.34
Other	16 (4.42)	9 (5.17)	4 (6.06)	0.46	1.28	0.58-2.86	0.54

^{1,2} Based on a cross-sectional and over-sample of N=602 adult patients with AD. UKWP criteria includes past year history of itchy skin + 3 or more of the following conditions: skin fold involvement and/or history of asthma or hay fever and/or part year dry skin and/or age of onset criteria <2y/o. Mean (SD)= mean (standard deviation); OR=odds ratio; 95%CI=95% Confidence Interval.

Table 4. Health-Related Quality of Life: DLQI, HADS-A and HADS-D scores amongst subjects with and without atopic dermatitis¹ and according to atopic dermatitis disease severity²

	Control	AD	p-value	Clear or mild (<i>POEM</i> score=0-7)	Moderate (<i>POEM</i> score=8-16)	Severe (<i>POEM</i> score=17-28)	p-value ³
N (%)	1,185 (92.72)	93 (7.28)		362 (60.13)	174 (28.90)	66 (10.96)	
DLQI total score							
mean (SD)	0.97 (2.12)	4.71 (6.44)	<0.001	2.04 (2.79)	5.87 (6.26)	11.44 (8.48)	<0.001
DLQI categories, N (%)							
No effect or small effect on QoL (<i>DLQI</i> score=0-5)	348 (95.34)	70 (75.27)	<0.001	324 (89.5)	109 (62.64)	21 (31.82)	<0.001
Moderate-to-large effect on QoL (<i>DLQI</i> score=6-30)	17 (4.66)	23 (24.37)		38 (10.50)	65 (37.36)	45 (68.18)	
HADS-A total score							
mean (SD)	4.73 (3.98)	7.03 (4.80)	<0.001	6.09 (4.22)	8.22 (4.81)	10.45 (5.22)	<0.001
HADS-A category, N (%)							
Normal/ borderline (<i>HADS-A</i> score=0-8)	1,076 (90.80)	109 (9.20)	<0.001	304 (83.98)	118 (67.82)	30 (45.45)	<0.001
Abnormal (<i>HADS-A</i> score=11-21)	109 (9.20)	23 (24.73)		58 (16.02)	56 (32.18)	36 (54.55)	
HADS-D total score							
mean (SD)	3.62 (3.61)	5.83 (4.54)	<0.001	4.86 (3.99)	6.7 (4.33)	8.11 (3.84)	<0.001
HADS-D category, N (%)							
Normal/ borderline (<i>HADS-D</i> score=0-7)	1,114 (94.01)	80 (86.02)	0.003	330 (91.16)	140 (80.46)	53 (80.30)	0.001
Abnormal (<i>HADS-D</i> score=11-21)	71 (5.99)	13 (13.98)		32 (8.84)	34 (19.54)	13 (19.70)	

¹Based on a cross-sectional sample N=1278.

²Based on a cross-sectional and oversample of patients with AD N=602. UKWP criteria includes past year history of itchy skin + 3 or more of the following conditions: skin fold involvement and/or history of asthma or hay fever and/or part year dry skin and/or age of onset criteria <2y/o. POEM=Patient Oriented Eczema Measure; Mean (SD)= mean (standard deviation); DLQI=Dermatology Life Quality Index; HADS-A=Hospital Anxiety and Depression Scale-Anxiety; HADS-D=Hospital Anxiety and Depression Scale-Depression

³p-values were calculated based on subject's POEM score

Table 5. Association between AD and HRQoL in US adult patients with Atopic Dermatitis compared to controls

Risk of worse HrQoL, Anxiety and Depression in AD vs. controls (<i>reference group</i>)			
DLQI			
	OR	95% Confidence Interval	p-value
Model 1 ¹	6.73	3.42-13.24	<0.001
Model 2 ²	7.24	3.61-14.50	<0.001
Model 3 ³	8.33	3.72-18.65	<0.001
HADS-Anxiety scale			
	OR	95% Confidence Interval	p-value
Model 1 ¹	3.24	1.95-5.40	<0.001
Model 2 ²	3.54	2.07-6.05	<0.001
Model 3 ³	3.29	1.85-5.84	<0.001
HADS-Depression scale			
	OR	95% Confidence Interval	p-value
Model 1 ¹	2.55	1.35-4.80	0.004
Model 2 ²	2.70	1.42-5.13	0.002
Model 3 ³	2.33	1.16-4.66	0.02

¹Unadjusted model; ²Age and sex adjusted model; ³Adjusted model 2 + adjusted for income, level of education, employment and marital status.

DLQI=Dermatology Life Quality Index; HADS=Hospital Anxiety and Depression Scale; OR=odds ratio