Symptoms and diagnosis of anxiety and depression in atopic dermatitis in U.S. adults*

J.I. Silverberg 1, J.M. Gelfand, 2 D.J. Margolis, 2 M. Boguniewicz, 2, 3, 4 L. Fonacier, 5 M.H. Grayson, 6 P.Y. Ong, 7 Z.C. Chiesa Fuxench 2 and E.L. Simpson 8

1 Feinberg School of Medicine, Northwestern University, Chicago, IL, U.S.A.
2 School of Medicine, University of Pennsylvania Perelman, Philadelphia, PA, U.S.A.
3 National Jewish Health, Denver, CO, U.S.A.
4 School of Medicine, University of Colorado, Denver, CO, U.S.A.
5 NYU Winthrop Hospital, Mineola, NY, U.S.A.
6 Nationwide Children’s Hospital, The Ohio State University College of Medicine, Columbus, OH, U.S.A.
7 Children’s Hospital Los Angeles, Keck School of Medicine, University of Southern California, Los Angeles, CA, U.S.A.
8 Oregon Health & Science University, Portland, OR, U.S.A.

Linked Comment: Nicholas and Drucker. Br J Dermatol 2019; 181:442–443.

Correspondence
Jonathan I. Silverberg.
E-mail: JonathanISilverberg@gmail.com

Accepted for publication
21 January 2019

Funding sources
The Atopic Dermatitis in America Study is an independent research project of the Asthma and Allergy Foundation of America in partnership with the National Eczema Association and sponsored by Sanofi Genzyme and Regeneron.

Conflicts of interest
See Appendix.

*Plain language summary available online

DOI 10.1111/bjd.17683

Summary

Background The relationship between atopic dermatitis (AD), anxiety and depression in the U.S. adult population is not well established.

Objectives To determine the relationship of AD and its severity with symptoms and diagnosis of anxiety and depression in U.S. adults.

Methods A cross-sectional, population-based study of 2893 adults was performed. AD was determined using modified U.K. Diagnostic Criteria.

Results Adults with AD vs. those without AD had higher mean Hospital Anxiety and Depression Scale anxiety (HADS-A) (7.7 vs. 5.6) and depression (HADS-D) (6.0 vs. 4.3) scores and higher prevalences of abnormal (≥11) HADS-A (28.6% vs. 15.5%) and HADS-D (13.5% vs. 9.0%) scores. In multivariable linear and logistic regression models controlling for sociodemographics, AD was associated with significantly higher mean HADS-A and HADS-D scores (7.7 and 6.0) and higher odds of abnormal HADS-A [odds ratio (OR) 2.19, 95% confidence interval (CI) 1.65–2.91] and HADS-D (OR 1.50, 95% CI 1.04–2.17) (P ≤ 0.03 for all). Mean and abnormal HADS-A and HADS-D scores were increased in moderate and severe/very severe self-reported global AD severity, Patient-Oriented Eczema Measure (POEM), Patient-Oriented Scoring AD (PO-SCORAD), PO-SCORAD itch and sleep (P < 0.0001 for all). All respondents with severe PO-SCORAD, POEM and PO-SCORAD itch had borderline or abnormal HADS-A and HADS-D scores. Adults with AD vs. those without AD had higher prevalence of self-reported healthcare-diagnosed anxiety or depression in the past year (40.0% vs. 17.5%). Many adults with AD who had borderline and/or abnormal HADS-A or HADS-D scores reported no diagnosis of anxiety or depression.

Conclusions AD is associated with significantly increased anxiety and depression, which may go undiagnosed.

What’s already known about this topic?

- Previous studies found higher rates of anxiety and depression in clinical cohorts of patients with atopic dermatitis.
Atopic dermatitis (AD) is a chronic inflammatory skin disease characterized by itch, skin pain, sleep disturbances and multiple comorbidities, all of which can lead to significant psychosocial distress and mental health burden.1–6 However, previous studies found conflicting results regarding whether AD is associated with increased mental health disorders, e.g. depression or anxiety.7–9 We hypothesized that AD is associated with higher likelihood of anxiety and/or depression.

In addition, there are a number of outstanding questions about the relationship between AD, anxiety and depression. Firstly, the prevalence and severity of anxiety and depression in the U.S. adult population with AD are not well established. Secondly, the relationship of different aspects of AD severity with anxiety and depression requires elucidation. We hypothesized that symptoms of anxiety and depression are very common in AD, especially in moderate-to-severe AD. Finally, anxiety and depression may go undiagnosed in all age groups.10,11 We hypothesized that a large proportion of adults with AD have undiagnosed anxiety and/or depression. In the present study, we sought to determine the relationship of AD and its severity with symptoms and diagnosis of anxiety and depression in U.S. adults.

Materials and methods

Data source

Data were obtained from the Atopic Dermatitis in America survey for which the population was sampled from the long-standing Growth from Knowledge (GfK) Knowledge Panel. The GfK Knowledge Panel is the largest and oldest probability-based web panel in the U.S.A. and contains between 40 000 and 50 000 adult panel members at any given time. The GfK web panel was initially constructed from a national address-based sample of households in the U.S.A. who are recruited to participate and receive small incentives for completing web surveys on a regular basis. This approach uses a single sampling frame via the Delivery Sequence File of the U.S. Postal Service to provide a statistically valid representation of the U.S. population in addition to 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 U.S. population.12–14 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 U.S. adults. In this stage, an initial cross-sectional sample of 2137 adults from the existing GfK Knowledge 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 in order to avoid biasing participation based on respondent interest or disinterest in the subject. A total of 1286 adults completed the survey (response rate 59–80%), of which 1278 qualified for the study (qualification rate 99.4%). Although this sample provided a precise estimate of the prevalence of AD among the adult population, it did not yield a large enough sample of patients with AD and control participants to investigate differences between different levels of disease severity. In stage 2, an additional sample of 13 713 adults from the GfK Knowledge Panel completed screening to identify and interview an additional group of adults with AD and controls. The final cohort consisted of 602 adults who met an adapted U.K. Working Party (UKWP) definition of AD and 2291 controls without AD (Fig. S1; see Supporting Information). Using data from the U.S. Census Bureau, sample weights were created that adjusted for age, sex, 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 U.S. population.

Based on an expected lifetime prevalence of AD of 20%,15 it was determined that a sample size of 500 would provide an adequate estimate with a maximum expected sampling error of ± 4.4% at the 95% confidence level.

Assessment of atopic dermatitis and mental health

An adaptation of the UKWP criteria was selected by the AD in America advisory committee as the screening tool for patient eligibility.16 This included all aspects of the UKWP criteria (having an itchy skin condition during the past 12 months and three or more of the following: (i) history of skin crease...
Mental health was assessed using the Hospital Anxiety and Depression Scale anxiety (HADS-A) and depression (HADS-D) scores (seven items; range 0–21 per score). 12,23 Borderline and abnormal anxiety/depression scores were defined as ≥ 8 and ≥ 11, respectively. Self-reported 1-year history of anxiety or depression was assessed using the question 'Have you been diagnosed by a healthcare provider with any of the following in the past 12 months: Anxiety or depression?' (Yes/No).

Statistical analyses

All data analyses and statistical processes were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC, U.S.A.) and included representative sample weights. Baseline respondent characteristics were determined. Rao-Scott χ²-test was used to test the association between AD and responses to individual

---

Table 1 Participant characteristics

| Variable                          | Overall Frequency (n = 2893) | Weighted percentage | Atopic dermatitis (AD) No Frequency (n = 2291) | Weighted percentage | Yes Frequency (n = 602) | Weighted percentage |
|-----------------------------------|-----------------------------|---------------------|-----------------------------------------------|---------------------|------------------------|---------------------|
| Age, years                        |                             |                     |                                               |                     |                        |                     |
| 18–39                             | 775                         | 38.5%               | 602                                           | 38.6%               | 173                    | 38.0%               |
| 40–59                             | 1069                        | 36.7%               | 833                                           | 35.8%               | 236                    | 40.5%               |
| 60–100                            | 1049                        | 24.8%               | 856                                           | 25.6%               | 195                    | 21.5%               |
| Female sex                        | 1551                        | 52.5%               | 1202                                          | 52.5%               | 349                    | 58.0%               |
| Race/ethnicity                    |                             |                     |                                               |                     |                        |                     |
| White                             | 2080                        | 62.9%               | 1684                                          | 73.5%               | 396                    | 65.8%               |
| African-American/black            | 269                         | 11.6%               | 195                                           | 8.5%                | 74                     | 12.3%               |
| Hispanic                          | 341                         | 17.6%               | 264                                           | 11.5%               | 77                     | 12.8%               |
| Multiracial/other                 | 203                         | 7.8%                | 148                                           | 6.5%                | 55                     | 9.1%                |
| Level of education                |                             |                     |                                               |                     |                        |                     |
| Less than high school             | 188                         | 16.0%               | 140                                           | 6.1%                | 48                     | 8.0%                |
| High school or equivalent         | 832                         | 26.7%               | 668                                           | 29.2%               | 164                    | 27.2%               |
| Some college                      | 889                         | 30.2%               | 703                                           | 30.7%               | 186                    | 30.9%               |
| Bachelor’s degree or higher       | 984                         | 28.1%               | 780                                           | 34.1%               | 204                    | 33.9%               |
| Poverty Income Ratio              |                             |                     |                                               |                     |                        |                     |
| < 1.00                            | 366                         | 13.8%               | 260                                           | 12.6%               | 106                    | 18.6%               |
| 1.00–1.99                        | 451                         | 14.5%               | 349                                           | 14.1%               | 102                    | 15.9%               |
| 2.00–3.99                        | 796                         | 25.8%               | 649                                           | 26.6%               | 147                    | 22.7%               |
| ≥ 4.00                           | 1280                        | 46.0%               | 1033                                          | 46.7%               | 247                    | 42.9%               |
| Region                            |                             |                     |                                               |                     |                        |                     |
| Northeast                         | 533                         | 18.2%               | 422                                           | 18.1%               | 111                    | 18.6%               |
| Midwest                           | 723                         | 20.3%               | 571                                           | 20.1%               | 152                    | 21.0%               |
| South                             | 956                         | 36.4%               | 743                                           | 35.5%               | 213                    | 40.4%               |
| West                              | 681                         | 25.0%               | 555                                           | 26.3%               | 126                    | 20.0%               |
| Prescription AD treatment (ever)  |                             |                     |                                               |                     |                        |                     |
| Topical therapy                   | –                           | –                   | –                                             | –                   | –                      | –                   |
| Systemic antihistamines           | –                           | –                   | –                                             | –                   | –                      | –                   |
| Systemic corticosteroids          | –                           | –                   | –                                             | –                   | –                      | –                   |
| Systemic immunosuppressants       | –                           | –                   | –                                             | –                   | –                      | –                   |
| Self-reported AD severity         |                             |                     |                                               |                     |                        |                     |
| Mild                              | –                           | –                   | –                                             | –                   | 289                    | 59.4%               |
| Moderate                          | –                           | –                   | –                                             | –                   | 172                    | 34.8%               |
| Severe                            | –                           | –                   | –                                             | –                   | 34                     | 6.9%                |
items from HADS. Bivariable linear regression models were used to test the associations of AD and AD severity with continuous HADS-A and HADS-D scores. Bivariable binary logistic regression models were used to test the associations of AD and AD severity with abnormal HADS-A and HADS-D scores ($\geq 11$). Multivariable models included age (continuous), sex (male/female), race/ethnicity (white, black, Hispanic, multiracial or other), level of education [less than high school (HS), HS or equivalent, more than HS], household size (continuous), and poverty income ratio (PIR) ($<1, 1–1.9, 2–3.9, \geq 4$). Crude and adjusted beta, odds ratios (ORs) and 95% confidence intervals (CIs) were estimated. A two-sided $P$-value $<0.05$ was taken to indicate statistical significance for all estimates.

**Results**

**Respondent characteristics**

Overall, the prevalence of AD was 7.3% (95% CI 5.9–8.8). A total of 602 participants met AD criteria and 2291 controls without AD were included in the final cohort. In total 58.0% of respondents with AD were female and 65.8% were white, with a weighted mean age of 46.6 years (95% CI 45.1–48.1). Sociodemographics of the cohort and AD characteristics are presented in Table 1. The weighted mean duration of AD was 16.7 years (95% CI 14.7–18.7), PO-SCORAD was 27.5 (95% CI 25.7–29.3), POEM was 7.5 (95% CI 6.8–8.1) and DLQI was 4.9 (95% CI 4.2–5.5).

**Hospital Anxiety and Depression Scale anxiety and depression scores**

Significantly higher proportions of adults with AD endorsed being affected by all individual items from the HADS questionnaire (Rao-Scott $\chi^2$-test, $P < 0.001$ for all) when compared with adults without AD (Fig. 1).

Adults with AD also had higher weighted mean HADS, HADS-A and HADS-D scores and higher weighted prevalences of borderline (8–10) and/or abnormal ($\geq 11$) HADS-A and HADS-D scores (Table 2) when compared with adults without AD. Borderline or abnormal HADS-A, HADS-D or both HADS-A and HADS-D scores were present in 48.4%, 34.5% and 26.6% of adults with AD, respectively; this included severe scores for 9.9% (HADS-A) and 4.1% (HADS-D).

In bivariable linear regression and multivariable models controlling for sociodemographics, AD was associated with significantly higher mean HADS-A and HADS-D scores (Table 3). There were stepwise and significantly increased HADS-A and HADS-D scores in patients with moderate and severe/very severe self-reported global AD severity, POEM, PO-SCORAD, PO-SCORAD itch and PO-SCORAD sleep ($P < 0.0001$ for all).

Similarly, in bivariable logistic regression and multivariable models controlling for sociodemographics, AD was associated with significantly higher odds of abnormal HADS-A or HADS-D scores (scores $\geq 11$) (Table 4). In multivariable models, abnormal HADS-A scores were also associated with female sex (1.32, 95% CI 1.01–1.73), < HS education (1.60 95% CI
and were inversely associated with age (0.97, 95% CI 0.96–0.98) and PIR (0.91, 95% CI 0.86–0.97), but not with race/ethnicity (0.86, 95% CI 0.65–1.14) or household size (0.99, 95% CI 0.90–1.08). HADS-D was inversely associated with age (0.99, 0.98–0.99), nonwhite race/ethnicity (0.69, 0.48–0.99) and PIR (0.82, 0.75–0.90), but not with female sex (0.99, 0.71–1.37), < HS education (1.58, 0.99–2.53) or household size (1.03, 0.91–1.16).

In addition, there were stepwise and significantly increased HADS-A and HADS-D scores in patients with moderate and severe/very severe self-reported global AD severity, POEM, PO-SCORAD, PO-SCORAD itch and PO-SCORAD sleep (P ≤ 0.02 for all). In multivariable models, HADS-A and HADS-D scores were not significantly associated with any covariables in the model other than AD severity assessments, except for inverse associations of HADS-A with age and HADS-D with nonwhite race/ethnicity.

As AD severity can be defined by different constructs, weighted mean HADS-A and HADS-D scores were stratified by the lesional severity and extent (PO-SCORAD), frequency of symptoms (POEM) and intensity of itch (PO-SCORAD itch) (Fig. 2). When compared with mild-to-moderate POEM and PO-SCORAD itch scores alone, as judged by existing interpretability bands, severe scores on these assessments were associated with significantly higher mean HADS-A and HADS-D scores, and higher prevalence of borderline and abnormal HADS-A and HADS-D scores (P < 0.0001). Concurrent severe PO-SCORAD, POEM and/or PO-SCORAD itch were associated with even higher HADS-A and HADS-D scores compared with severe scores for only one of these assessments (P < 0.0001). Overall, 100% (100–100%) of respondents with severe scores for all three assessments had borderline or abnormal HADS-A and HADS-D scores.

**Diagnosis of anxiety or depression**

Overall, adults with AD vs. those without AD had higher prevalence of self-reported healthcare-diagnosed anxiety or depression.
depression in the past year (40.0% vs. 17.5%) (Table 2). In combination, 50.3% (45.5–55.2) of adults with AD and 27.3% (25.1–29.6) of adults without AD had abnormal HADS-A or HADS-D scores or reported a healthcare diagnosis of anxiety or depression.

However, substantial proportions of adults with AD who had borderline and/or abnormal HADS-A or HADS-D scores reported no diagnosis of anxiety or depression (Table 2). Adults with both abnormal HADS-A and HADS-D scores were more likely to be diagnosed with anxiety or depression compared with those with either score being abnormal, or those who had a borderline score for either or both.

### Discussion

Using a U.S. population-based sample, we found that adults with AD had significantly higher mean HADS-A and HADS-D scores, and that among adults with AD there were higher proportions of respondents with borderline and/or abnormal HADS-A and HADS-D scores, and higher proportions of self-reported healthcare-diagnosed anxiety or depression in the past year, all of which indicate a significant mental health burden of AD. All of these outcomes were associated with AD severity, such that those with moderate and severe AD had significantly worse mental health than those with mild AD. Importantly, 100% of respondents with severe POEM, PO-SCORAD and PO-SCORAD-itch scores vs. those with mild/moderate scores were found to have borderline and/or abnormal HADS-A and HADS-D scores. Of note, HADS-A scores were consistently higher than HADS-D scores. Of note, HADS-A and HADS-D scores were associated only with AD severity, but not with any other sociodemographic covariables. This finding suggests that AD severity is the major driver of anxiety and depression in adults with AD. Taken together, it appears that AD, particularly moderate-to-severe AD, is associated with profound symptoms of anxiety and depression.

The HADS is a multidimensional mental health assessment that is not specific to skin disease, and has been studied extensively in many medical disorders. The mean HADS, HADS-A and HADS-D scores for AD (13.6, 7.7 and 6.0, respectively), are similar to previous observational clinical studies in Germany (HADS-A 8.2, HADS-D 4.9) and Singapore (HADS-A 7.2, HADS-D 5.0).

---

**Table 2** Prevalence of borderline and/or abnormal Hospital Anxiety and Depression Scale (HADS) anxiety and/or depression scores and 1-year history of anxiety or depression

| Variable                        | No (a = 2291) | Yes (a = 602) | 1-year diagnosis of anxiety or depression |
|---------------------------------|---------------|---------------|------------------------------------------|
|                                 | Frequency, n  | Prevalence, % (95% CI) | Frequency, n  | Prevalence, % (95% CI) | Frequency, n  | Prevalence, % (95% CI) |
| HADS anxiety Borderline         | 308           | 13.9 (12.1–15.7) | 112           | 19.8 (15.9–23.7) | 51           | 45.6 (34.4–56.8) |
| Abnormal                        | 303           | 15.5 (13.6–17.5) | 150           | 28.6 (24.0–33.2) | 104          | 70.6 (61.8–79.3) |
| Moderate                        | 216           | 10.8 (9.2–12.5)  | 102           | 18.7 (14.7–22.7) | 63           | 61.5 (50.0–73.0) |
| Severe                          | 87            | 4.7 (3.6–5.8)    | 48            | 9.9 (6.7–13.1)   | 41           | 87.8 (77.1–98.5) |
| Borderline or abnormal          | 611           | 29.4 (27.1–31.8) | 262           | 48.4 (43.5–53.3) | 155          | 60.4 (53.2–67.5) |
| HADS depression Borderline      | 236           | 10.5 (8.9–12.0)  | 115           | 21.0 (16.8–25.2) | 73           | 66.6 (56.0–77.2) |
| Abnormal                        | 185           | 9.0 (7.5–10.6)   | 79            | 13.5 (10.0–17.0) | 52           | 71.9 (60.3–83.4) |
| Moderate                        | 138           | 7.0 (5.6–8.3)    | 54            | 9.4 (6.3–12.4)   | 34           | 73.2 (60.4–86.0) |
| Severe                          | 47            | 2.1 (1.4–2.8)    | 25            | 4.1 (2.1–6.2)    | 18           | 68.8 (45.2–92.5) |
| Borderline or abnormal          | 421           | 19.5 (17.5–21.6) | 194           | 34.5 (29.7–39.3) | 125          | 68.7 (60.7–76.6) |
| HADS anxiety and depression     |               |                |               |                |               |                |
| Borderline                      |               |                |               |                |               |                |
| One                             | 414           | 18.7 (16.7–20.7) | 163           | 30.6 (25.9–35.2) | 84           | 52.5 (43.1–61.9) |
| Both                            | 65            | 2.9 (2.0–3.6)    | 32            | 5.1 (3.0–7.2)    | 20           | 67.9 (48.4–87.4) |
| Abnormal                        |               |                |               |                |               |                |
| One                             | 258           | 12.6 (10.9–14.4) | 135           | 24.5 (20.2–28.8) | 82           | 64.9 (55.4–74.4) |
| Both                            | 115           | 6.0 (4.7–7.3)    | 47            | 8.8 (5.7–11.8)   | 37           | 79.5 (65.4–93.7) |
| Borderline or abnormal          |               |                |               |                |               |                |
| One                             | 462           | 20.8 (18.7–22.9) | 162           | 29.6 (25.0–34.1) | 70           | 45.4 (36.0–54.7) |
| Both                            | 285           | 14.1 (12.3–15.9) | 147           | 26.6 (22.1–31.2) | 105          | 74.0 (65.4–82.7) |

CI, confidence interval.
Table 3 Association of atopic dermatitis and atopic dermatitis severity with Hospital Anxiety and Depression Scale (HADS) scores, and anxiety and depression subscores

| Variable | Weighted mean (95% CI)* | Crude beta (95% CI) | P-valueb | Adjusted beta (95% CI) | P-valueb |
|----------|-------------------------|---------------------|----------|------------------------|----------|
| **HADS score** | | | | | |
| Atopic dermatitis | | | | | |
| No | 9.9 (9.5–10.3) | 0.00 (ref) | – | 0.00 (ref) | – |
| Yes | 13.6 (12.8–14.5) | 3.72 (2.81–4.63) | < 0.0001 | 3.47 (2.60–4.34) | < 0.0001 |
| **Self-reported global atopic dermatitis severity** | | | | | |
| Mild | 10.7 (9.8–11.7) | 0.00 (ref) | – | 0.00 (ref) | – |
| Moderate | 16.6 (15.0–18.2) | 5.84 (3.98–7.70) | < 0.0001 | 4.89 (3.08–6.72) | < 0.0001 |
| Severe | 20.3 (17.3–23.3) | 9.54 (6.53–12.56) | < 0.0001 | 8.63 (5.38–11.89) | < 0.0001 |
| **Patient-Oriented Eczema Measure (PO-SCORAD)** | | | | | |
| Clear/almost clear/mild | 11.4 (10.5–12.3) | 0.00 (ref) | – | 0.00 (ref) | – |
| Moderate | 16.0 (14.5–17.5) | 4.60 (2.85–6.36) | < 0.0001 | 4.10 (2.56–5.65) | < 0.0001 |
| Severe/very severe | 18.5 (15.6–21.4) | 7.12 (4.14–10.09) | < 0.0001 | 6.44 (3.63–9.24) | < 0.0001 |
| **Patient-Oriented Scoring Atopic Dermatitis (PO-SCORAD)** | | | | | |
| Mild | 10.4 (9.5–11.3) | 0.00 (ref) | – | 0.00 (ref) | – |
| Moderate | 15.5 (14.2–16.8) | 5.09 (3.49–6.68) | < 0.0001 | 4.21 (2.72–5.69) | < 0.0001 |
| Severe | 22.2 (20.5–23.9) | 11.78 (9.90–13.66) | < 0.0001 | 10.31 (8.01–12.61) | < 0.0001 |
| **PO-SCORAD itch** | | | | | |
| Clear/almost clear/mild | 10.5 (9.4–11.6) | 0.00 (ref) | – | 0.00 (ref) | – |
| Moderate | 14.6 (13.1–16.1) | 4.11 (2.27–5.94) | < 0.0001 | 3.98 (2.30–5.67) | < 0.0001 |
| Severe/very severe | 17.3 (15.7–18.9) | 6.79 (4.85–8.73) | < 0.0001 | 6.18 (4.35–8.02) | < 0.0001 |
| **PO-SCORAD sleep** | | | | | |
| Clear/almost clear/mild | 9.6 (8.7–10.6) | 0.00 (ref) | – | 0.00 (ref) | – |
| Moderate | 15.6 (14.6–16.8) | 5.92 (4.36–7.49) | < 0.0001 | 5.48 (3.90–7.06) | < 0.0001 |
| Severe/very severe | 18.2 (16.6–19.8) | 8.58 (6.77–10.40) | < 0.0001 | 7.81 (6.1–9.5) | < 0.0001 |
| **HADS anxiety score** | | | | | |
| Atopic dermatitis | | | | | |
| No | 5.6 (5.4–5.8) | 2.05 (1.51–2.59) | < 0.0001 | 1.92 (1.41–2.43) | < 0.0001 |
| Yes | 7.7 (7.2–8.2) | 2.05 (1.51–2.59) | < 0.0001 | 1.92 (1.41–2.43) | < 0.0001 |
| **Self-reported global atopic dermatitis severity** | | | | | |
| Mild | 6.1 (5.5–6.7) | 0.00 (ref) | – | 0.00 (ref) | – |
| Moderate | 9.2 (8.2–10.2) | 3.10 (1.96–4.25) | < 0.0001 | 2.64 (1.52–3.75) | < 0.0001 |
| Severe | 11.2 (9.2–13.1) | 5.07 (3.11–7.02) | < 0.0001 | 4.67 (2.57–6.76) | < 0.0001 |
| **Patient-Oriented Eczema Measure (PO-SCORAD)** | | | | | |
| Clear/almost clear/mild | 6.4 (5.9–6.9) | 0.00 (ref) | – | 0.00 (ref) | – |
| Moderate | 8.9 (8.0–9.8) | 2.49 (1.43–3.54) | < 0.0001 | 2.29 (1.37–3.20) | < 0.0001 |
| Severe/very severe | 10.6 (8.8–12.3) | 4.16 (2.37–5.96) | < 0.0001 | 3.90 (2.19–5.61) | < 0.0001 |
| **Patient-Oriented Scoring Atopic Dermatitis (PO-SCORAD)** | | | | | |
| Mild | 5.9 (5.3–6.4) | 0.00 (ref) | – | 0.00 (ref) | – |
| Moderate | 8.7 (7.9–9.4) | 2.78 (1.83–3.73) | < 0.0001 | 2.23 (1.35–3.12) | < 0.0001 |
| Severe | 12.5 (11.0–14.0) | 6.61 (5.09–8.14) | < 0.0001 | 5.88 (4.23–7.53) | < 0.0001 |
| **PO-SCORAD itch** | | | | | |
| Clear/almost clear/mild | 6.0 (5.4–6.7) | 0.00 (ref) | – | 0.00 (ref) | – |
| Moderate | 7.8 (7.0–8.7) | 1.78 (0.70–2.86) | 0.001 | 1.75 (0.75–2.75) | 0.006 |
| Severe/very severe | 9.9 (8.9–10.9) | 3.88 (2.70–5.07) | < 0.0001 | 3.57 (2.43–4.70) | < 0.0001 |
| **PO-SCORAD sleep** | | | | | |
| Clear/almost clear/mild | 5.5 (4.9–6.1) | 0.00 (ref) | – | 0.00 (ref) | – |
| Moderate | 8.2 (7.4–9.0) | 2.69 (1.71–3.66) | < 0.0001 | 2.47 (1.49–3.44) | < 0.0001 |
| Severe/very severe | 10.5 (9.6–11.4) | 5.02 (3.94–6.10) | < 0.0001 | 4.57 (3.54–5.59) | < 0.0001 |
| **HADS depression score** | | | | | |
| Atopic dermatitis | | | | | |
| No | 4.3 (4.1–4.5) | 0.00 (ref) | – | 0.00 (ref) | – |
| Yes | 6.0 (5.6–6.4) | 1.67 (1.20–2.13) | < 0.0001 | 1.55 (1.01–2.00) | < 0.0001 |
| **Self-reported global atopic dermatitis severity** | | | | | |
| Mild | 4.6 (4.1–5.2) | 0.00 (ref) | – | 0.00 (ref) | – |
| Moderate | 7.4 (6.6–8.2) | 2.74 (1.79–3.69) | < 0.0001 | 2.26 (1.33–3.19) | < 0.0001 |
| Severe | 9.1 (7.8–10.5) | 4.48 (3.09–5.86) | < 0.0001 | 3.97 (2.50–5.43) | < 0.0001 |

(continued)
The observed mean HADS, HADS-A and HADS-D scores in adults with moderate AD (14.6–16.6, 7.8–9.2 and 6.8–7.4, respectively) and severe AD (17.3–22.2, 9.9–12.5 and 7.4–9.7, respectively) were slightly higher than scores observed at baseline in a clinical trial of adults with moderate-to-severe AD (HADS 12.2, HADS-A 7.0, HADS-D 5.2).2 The HADS-A and HADS-D scores were also higher than previously reported in other chronic skin disorders, e.g. patients enrolled in clinical trials of biologics for moderate-to-severe psoriasis (6.8–7.2 and 5.3–5.7, respectively),26,27 and other medical disorders such as diabetes (5.7 and 5.0, respectively) and HIV (6.5 and 5.5, respectively).28 A cross-sectional study that used HADS scores of 1519 adults with AD from six U.S. medical centres found that approximately one-quarter of patients with mild AD and one-half of patients with moderate-to-severe AD had symptoms of anxiety or depression, with even more severe HADS scores among those with uncontrolled AD.29 These results suggest that moderate-to-severe AD has an equal or even greater mental health burden than many other health disorders. The mental health burden of AD should be an important consideration in disease awareness, prioritizing appropriate resource allocation and clinical decision making.

The present study is consistent with a previous study that found higher rates of depression among U.S. adults with AD vs. those without AD.10 However, there are some notable differences. We found that 40% of adults with AD reported being diagnosed with depression and/or anxiety, which is higher than the 19.9% of adults with AD who had depression in the past year according to the National Health Interview Survey.10 The differences are likely related to the question used in our study that included both anxiety and depression. In addition, we found that 21.0% of adults with AD had borderline HADS-D scores and 13.5% had abnormal HADS-D scores, including 9.4% with moderate and 4.1% with severe HADS-D scores, which differs from the 17.5% of adults with AD who met SIGECAPS (Sleep, Interest, Guilt, Energy, Concentration, Appetite, Psychomotor function, Suicidal ideation) criteria for major depressive disorder and those with moderate (5.4%) and severe (5.8%) Patient Health Questionnaire-9 scores in the National Health and Nutrition Examination Survey.10 These differences are likely attributable to different definitions of depression and its severity. Regardless of the differences, these studies and others demonstrate markedly increased symptoms of anxiety and depression in adult AD. Of note, the prevalences of borderline and abnormal HADS-A and HADS-D scores were consistently higher than prevalences of self-reported diagnosed anxiety or depression. Furthermore, a substantial proportion of respondents with AD who had marked elevations of their HADS-A and HADS-D scores were not diagnosed with anxiety or depression. This suggests that the mental health burden of AD is underappreciated, and that patients with AD would benefit from routine screening for symptoms of anxiety and depression.

Depressive and anxiety disorders can be classified in several ways according to the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV), including classification as Axis I disorders (primary disorders) or Axis III disorders (secondary to a medical condition). It is important to recognize that depression and anxiety are symptoms of the AD per se in many patients, i.e. DSM-IV Axis III disorders. In many patients, HADS-A and HADS-D scores significantly improve with

| Variable | Weighted mean (95% CI)* | Crude beta (95% CI) | P-valueb | Adjusted beta (95% CI) | P-valueb |
|----------|--------------------------|---------------------|---------|------------------------|---------|
| Patient-Oriented Eczema Measure (POEM) |  |  |  |  |  |
| Clear/almost clear/mild | 5.0 (4.5–5.5) | 0.00 (ref) | – | 0.00 (ref) | – |
| Moderate | 7.1 (6.3–7.9) | 2.12 (1.19–3.05) | < 0.0001 | 1.82 (0.96–2.68) | < 0.0001 |
| Severe/very severe | 7.9 (6.6–9.3) | 1.95 (1.58–4.33) | < 0.0001 | 2.54 (1.26–3.82) | < 0.0001 |
| Patient-Oriented Scoring Atopic Dermatitis (PO-SCORAD) |  |  |  |  |  |
| Mild | 4.5 (4.0–5.0) | 0.00 (ref) | – | 0.00 (ref) | – |
| Moderate | 6.8 (6.2–7.5) | 2.31 (1.48–3.15) | < 0.0001 | 1.97 (1.19–2.76) | < 0.0001 |
| Severe | 9.7 (8.7–10.6) | 5.17 (4.13–6.20) | < 0.0001 | 4.44 (3.25–5.62) | < 0.0001 |
| PO-SCORAD itch |  |  |  |  |  |
| Clear/almost clear/mild | 4.5 (3.9–5.0) | 0.00 (ref) | – | 0.00 (ref) | – |
| Moderate | 6.8 (6.0–7.6) | 2.33 (1.36–3.30) | < 0.0001 | 2.24 (1.33–3.14) | < 0.0001 |
| Severe/very severe | 7.4 (6.6–8.2) | 2.91 (1.94–3.88) | < 0.0001 | 2.61 (1.70–3.53) | < 0.0001 |
| PO-SCORAD sleep |  |  |  |  |  |
| Clear/almost clear/mild | 4.1 (3.6–4.6) | 0.00 (ref) | – | 0.00 (ref) | – |
| Moderate | 7.4 (6.6–8.1) | 3.24 (2.35–4.11) | < 0.0001 | 3.02 (2.13–3.90) | < 0.0001 |
| Severe/very severe | 7.7 (6.9–8.5) | 3.56 (1.63–4.50) | < 0.0001 | 3.24 (2.38–4.10) | < 0.0001 |

*Weighted mean [95% confidence interval (CI)] are presented including sample weights. Bold indicates P-values with statistical significance. Linear regression models were created with short form-12 mental or physical health scores or Dermatology Life Quality Index as the dependent variables. The independent variable was having atopic dermatitis as defined by modified U.K. Working Party criteria or atopic dermatitis severity using self-reported global atopic dermatitis severity, POEM, PO-SCORAD, PO-SCORAD itch and PO-SCORAD sleep scores. Crude beta and 95% CI were estimated. Multivariable models 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 ratio income (continuous). Adjusted beta and 95% CI were estimated.
### Table 4 Association of atopic dermatitis and atopic dermatitis severity with definite anxiety and depression

| Variable | Weighted prevalence, % (95% CI) | Crude OR (95% CI) | P-value<sup>b</sup> | Adjusted OR (95% CI) | P-value<sup>b</sup> |
|----------|---------------------------------|-------------------|---------------------|---------------------|---------------------|
| **HADS anxiety score ≥ 11** |                                  |                   |                     |                     |                     |
| Atopic dermatitis |                                  |                   |                     |                     |                     |
| No | 15.5 (13.6–17.5) | 1.00 (ref) | – | 1.00 (ref) | – |
| Yes | 28.6 (24.0–33.2) | 2.17 (1.66–2.85) | **<0.0001** | 2.19 (1.65–2.91) | 0.01 |
| Self-reported global atopic dermatitis severity |                                  |                   |                     |                     |                     |
| Mild | 16.3 (10.8–21.8) | 1.00 (ref) | – | 1.00 (ref) | – |
| Moderate | 39.1 (29.7–48.5) | 3.30 (1.87–5.81) | **<0.0001** | 2.75 (1.52–4.95) | 0.0008 |
| Severe | 62.7 (43.6–81.8) | 8.62 (3.46–21.51) | **<0.0001** | 8.34 (3.01–23.12) | **<0.0001** |
| Patient-Oriented Eczema Measure (POEM) |                                  |                   |                     |                     |                     |
| Clear/almost clear/Mild | 17.2 (12.3–22.0) | 1.00 (ref) | – | 1.00 (ref) | – |
| Moderate | 38.9 (29.7–48.2) | 3.07 (1.83–5.16) | **<0.0001** | 3.11 (1.80–5.39) | **<0.0001** |
| Severe | 56.3 (41.9–70.7) | 6.21 (3.15–12.22) | **<0.0001** | 6.67 (3.27–13.60) | **<0.0001** |
| Patient-Oriented Scoring Atopic Dermatitis (PO-SCORAD) |                                  |                   |                     |                     |                     |
| Mild | 12.9 (8.7–17.1) | 1.00 (ref) | – | 1.00 (ref) | – |
| Moderate | 39.1 (31.1–47.2) | 4.35 (2.63–7.20) | **<0.0001** | 3.56 (2.09–6.05) | **<0.0001** |
| Severe | 63.0 (45.9–80.1) | 11.50 (5.04–26.26) | **<0.0001** | 9.75 (3.99–23.86) | **<0.0001** |
| PO-SCORAD itch |                                  |                   |                     |                     |                     |
| Mild | 13.0 (7.7–18.3) | 1.00 (ref) | – | 1.00 (ref) | – |
| Moderate | 31.0 (22.4–39.7) | 3.01 (1.62–5.61) | 0.0005 | 3.12 (1.63–5.97) | 0.0006 |
| Severe | 49.3 (39.6–58.9) | 6.50 (3.53–11.97) | **<0.0001** | 6.33 (3.35–11.99) | **<0.0001** |
| PO-SCORAD sleep |                                  |                   |                     |                     |                     |
| Mild | 12.9 (8.0–17.9) | 1.00 (ref) | – | 1.00 (ref) | – |
| Moderate | 30.0 (20.2–39.8) | 2.89 (1.51–5.50) | **<0.0001** | 2.57 (1.29–5.11) | 0.007 |
| Severe | 50.9 (41.9–60.0) | 6.99 (3.94–12.40) | **<0.0001** | 6.30 (3.46–11.46) | **<0.0001** |
| **HADS depression score ≥ 11** |                                  |                   |                     |                     |                     |
| Atopic dermatitis |                                  |                   |                     |                     |                     |
| No | 9.0 (7.5–10.6) | 1.00 (ref) | – | 1.00 (ref) | – |
| Yes | 13.5 (10.0–17.0) | 1.57 (1.10–2.24) | 0.01 | 1.50 (1.04–2.17) | 0.03 |
| Self-reported global atopic dermatitis severity |                                  |                   |                     |                     |                     |
| Mild | 7.8 (4.0–11.7) | 1.00 (ref) | – | 1.00 (ref) | – |
| Moderate | 18.0 (10.6–25.4) | 2.58 (1.24–5.40) | 0.01 | 2.26 (1.04–4.89) | 0.03 |
| Severe | 29.5 (9.9–49.2) | 4.92 (1.66–14.65) | 0.004 | 4.33 (1.44–13.05) | 0.009 |
| Patient-Oriented Eczema Measure (POEM) |                                  |                   |                     |                     |                     |
| Clear/almost clear/mild | 8.3 (4.8–11.8) | 1.00 (ref) | – | 1.00 (ref) | – |
| Moderate | 20.4 (12.6–28.2) | 2.83 (1.46–5.48) | **<0.0001** | 2.58 (1.32–5.01) | 0.005 |
| Severe | 21.2 (8.4–34.0) | 2.97 (1.21–7.25) | **<0.0001** | 2.31 (0.96–5.54) | 0.06 |
| Patient-Oriented Scoring Atopic Dermatitis (PO-SCORAD) |                                  |                   |                     |                     |                     |
| Mild | 7.6 (4.3–11.0) | 1.00 (ref) | – | 1.00 (ref) | – |
| Moderate | 15.3 (9.6–21.1) | 2.19 (1.14–4.19) | 0.02 | 1.82 (0.92–3.61) | 0.08 |
| Severe | 35.7 (17.6–53.8) | 6.71 (2.67–16.87) | **<0.0001** | 4.14 (1.60–10.67) | 0.003 |
| PO-SCORAD itch |                                  |                   |                     |                     |                     |
| Mild | 6.0 (2.7–9.2) | 1.00 (ref) | – | 1.00 (ref) | – |
| Moderate | 18.1 (10.8–25.4) | 3.49 (1.62–7.50) | **<0.0001** | 3.53 (1.54–8.11) | 0.003 |
| Severe | 19.9 (11.8–27.9) | 3.91 (1.81–8.47) | **<0.0001** | 3.69 (1.61–8.47) | 0.002 |
| PO-SCORAD sleep |                                  |                   |                     |                     |                     |
| Mild | 6.0 (3.1–8.9) | 1.00 (ref) | – | 1.00 (ref) | – |
| Moderate | 18.9 (10.7–27.1) | 3.62 (1.72–7.62) | **<0.0001** | 3.41 (1.50–7.73) | 0.003 |
| Severe | 20.7 (12.5–28.9) | 4.05 (1.98–8.30) | **<0.0001** | 3.52 (1.72–7.19) | 0.006 |

<sup>a</sup>Weighted prevalence [95% confidence interval (CI)] are presented including sample weights. <sup>b</sup>P-values in bold indicate statistical significance. Logistic regression models were created with definite anxiety (HADS anxiety ≥ 11 vs. 0–10) and depression (HADS depression ≥ 11 vs. 0–10) as the dependent variables. The independent variable was having atopic dermatitis as defined by modified U.K. Working Party criteria or atopic dermatitis severity using self-reported global atopic dermatitis severity, POEM, PO-SCORAD, PO-SCORAD itch and PO-SCORAD sleep scores. Crude odds ratios (ORs) and 95% CI were estimated. Multivariable models 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). Adjusted ORs and 95% CI were estimated. HADS, Hospital Anxiety and Depression Scale.
adequate treatment of AD signs and symptoms. However, some patients experiencing symptoms of anxiety and depression may have Axis I depressive or anxiety disorders and/or benefit from additional referral to a mental health specialist.

The strengths of this study include the following: it was a large-scale population-based study with a diverse sample and sample weights that adjusted for multiple sociodemographics and allowed for generalization of results that are representative of the U.S. population; it used multiple and well-validated assessments of AD severity and controlled for multiple confounding variables in multivariable models. POEM, PO-SCORAD and self-reported global AD severity have all been studied in patients with AD and are considered to have good overall face validity, construct validity, internal consistency, reliability and/or responsiveness; POEM is the preferred assessment of AD symptoms for clinical trials by the Harmonising Outcome Measures in Eczema group. There is some debate regarding the optimal cut-off to use for a case definition of anxiety or depression. Initially, a cut-off of ≥ 11 was considered optimal for case definitions. However, a recent review highlighted that in most studies an optimal balance between sensitivity and specificity was achieved when cases were defined by a score of ≥ 8 on both HADS-A and HADS-D. Therefore, we analysed both cut-offs of ≥ 8 and ≥ 11.

This study has some limitations. We used an internet panel, which may be subject to false answers, answering too fast, giving the same answer repeatedly (also known as straight-lining), and receiving multiple surveys completed by the same respondent. However, we do not believe these to be major concerns, given that there were < 0.05% missing values for AD and HADS questions, > 95% of surveys took 10 min or longer to complete, < 0.5% had the same responses for all HADS questions, and internet protocol and e-mail address verification was used for the panel. We used an adaptation of the extensively validated UKWP criteria to establish the diagnosis of AD, which lacked one criterion based on physical examination. The validity of this case definition of AD has not yet been prospectively studied. However, the prevalence estimate for AD using this UKWP-like criteria is remarkably similar to the 2012 National Health Interview Survey that found the prevalence of adult AD to be 4.9%, using a single self-reported question about eczema. These nearly identical estimates, despite using different cohorts and definitions of AD, support the validity of the definition used for AD. An international, cross-sectional, web-based survey found the U.S. prevalence of adult AD to be 4-9%. AD was defined using UKWP-like criteria plus self-report of ever having an AD diagnosis by a physician. That definition was not validated and is likely excessively rigorous given numerous previous studies showing the validity of UKWP criteria alone for identifying AD. Requiring a diagnosis of AD is problematic given the lack of use of the terminology ‘AD’ by clinicians and patients during clinical encounters, health disparities and poor access to specialty care in the U.S.A. Had that study employed UKWP-like criteria alone, the prevalence would have likely been approximately 7%. The effects of past and present treatment were not examined. Given the cross-sectional design of the study, we are unable to ascertain the directionality of the associations observed, although we hypothesize that the relationships are bidirectional. Future studies are warranted to address these points.

In conclusion, AD is associated with increased symptoms of anxiety and depression, higher proportions of borderline and/or abnormal anxiety and depression scores, and higher proportions of diagnosed anxiety or depression in the U.S. population. Moderate and severe AD were particularly associated with markedly worse mental health. These data support the heavy mental health burden that AD places on patients. It is important for clinicians to recognize that virtually all patients with moderate-to-severe AD have symptoms of anxiety and depression. We recommend that clinicians incorporate assessment of mental health symptoms in clinical practice to determine disease burden and screen for patients with symptoms of anxiety and depression.

References

1. Vakharia PP, Chopra R, Sacotte R et al. Burden of skin pain in atopic dermatitis. Ann Allergy Asthma Immunol 2017; 119(5):48–52.e3.
2. Simpson EL, Bieber T, Eckert I et al. Patient burden of moderate to severe atopic dermatitis (AD): insights from a phase 2b clinical trial of dupilumab in adults. J Am Acad Dermatol 2016; 74:491–8.
3. Brunner PM, Silverberg JJ, Guttman-Yassky E et al. Increasing comorbidities suggest that atopic dermatitis is a systemic disorder. J Invest Dermatol 2017; 137:18–25.
4. Silverberg J, Garg N, Silverberg NB. New developments in comorbidities of atopic dermatitis. Curr Allergy Asthma Rep 2014; 14:222–4.
5. Silverberg JJ, Gelfand JM, Margolis DJ et al. Association of atopic dermatitis with allergic, autoimmune and cardiovascular comorbidities in US adults. Ann Allergy Asthma Immunol 2018; 121(6):610–6.
6. Silverberg JJ, Gelfand JM, Margolis DJ et al. Patient burden and quality of life in atopic dermatitis in US adults: a population-based cross-sectional study. Ann Allergy Asthma Immunol 2018; 121:340–7.
7. Zachariae R, Zachariae C, Ibsen HH et al. Psychological symptoms and quality of life of dermatology outpatients and hospitalized dermatology patients. Acta Derm Venereol 2004; 84:205–12.
8. Gupta MA, Gupta AK. Depression and suicidal ideation in dermatology patients with acne, alopecia areata, atopic dermatitis and psoriasis. Br J Dermatol 1998; 139:846–50.
9. Dieris-Hirche J, Gieler U, Kupfer JP, Milch WE. [Suicidal ideation, anxiety and depression in adult patients with atopic dermatitis]. Hautarzt 2009; 60:641–6 (in German).
10. Downey VA, Zun LS. Identifying undiagnosed pediatric mental illness in the emergency department. Pediatr Emerg Care 2018; 34:e21–3.
11. Koychev I, Ehmeier KP. Anxiety in older adults often goes undiagnosed. Practitioner 2016; 260(17–20):2–3.
12. Rowen TS, Gaither TW, Awad MA et al. Public hair grooming prevalence and motivation among women in the United States. JAMA Dermatol 2016; 152:1106–13.
13. Hays RD, Liu H, Kapteyn A. Use of Internet panels to conduct surveys. Behav Res Methods 2015; 47:685–90.
14. Heckman CJ, Darlow S, Manne SL et al. Correspondence and correlates of couples’ skin cancer screening. JAMA Dermatol 2013; 149:825–30.
15. Hanifin JM, Reed ML. Eczema Prevalence and Impact Working Group. A population-based survey of eczema prevalence in the United States. Dermatitis 2007; 18:82–91.
16 Williams HC, Burney PG, Pembroke AC, Hay RJ. The U.K. Working Party’s diagnostic criteria for atopic dermatitis. III. Independent hospital verification. Br J Dermatol 1994; 131:406–16.
17 Vakharia PP, Chopra R, Sacotte R et al. Validation of patient-reported global severity of atopic dermatitis in adults. Allergy 2018; 73:451–8.
18 Stalder JF, Barbatro S, Wollenberg A et al. Patient-Oriented SCORAD (PO-SCORAD): a new self-assessment scale in atopic dermatitis validated in Europe. Allergy 2011; 66:1114–21.
19 Charman CR, Venn AJ, Ravenscroft JC et al. Translating Patient-Oriented Eczema Measure (POEM) scores into clinical practice by suggesting severity strata derived using anchor-based methods. Br J Dermatol 2013; 169:1326–32.
20 Basra MK, Fenech R, Gat RM et al. The Dermatology Life Quality Index 1994–2007: a comprehensive review of validation data and clinical results. Br J Dermatol 2008; 159:997–1035.
21 Rogers A, DeLong LK, Chen SC. Clinical meaning in skin-specific quality of life instruments: a comparison of the Dermatology Life Quality Index and Skindex banding systems. DERMATOL Clin 2012; 30:x.
22 Winnikowski A, Richards HL, Griffiths CE, Main CJ. The impact of psychological and clinical factors on quality of life in individuals with atopic dermatitis. J Psychosom Res 2004; 57:195–200.
23 Zigmond AS, Snith RP. The hospital anxiety and depression scale. Act Psychand Sund 1983; 67:361–70.
24 Derris-Hirche J, Gieler U, Petrik F et al. Suicidal ideation in adult patients with atopic dermatitis: a German cross-sectional study. Act Derm Venereol 2017; 97:1189–95.
25 Lim VZ, Ho RC, Tee SI et al. Anxiety and depression in patients with atopic dermatitis in a Southeast Asian tertiary dermatological centre. Ann Acad Med Singapore 2016; 45:451–5.
26 Gordon KB, Armstrong AW, Han C et al. Anxiety and depression in patients with moderate-to-severe psoriasis and comparison of change from baseline after treatment with guselkumab vs. adalimumab: results from the phase 3 VOYAGE 2 study. J Eur Acad Dermatol Venereol 2018; 32:1940–9.
27 Deiden E, Griffiths CE, Ortonne JP et al. Improvements in patient-reported outcomes in moderate-to-severe psoriasis patients receiving continuous or paused etanercept treatment over 54 weeks: the CRISTEL study. J Eur Acad Dermatol Venereol 2009; 23:1374–82.
28 Ronel J, Dunkel A, Wolf E et al. Anxiety, depression, and health-related quality of life in aging people living with HIV compared to diabetes patients and patients with minor health conditions: a longitudinal study. Psychol Health Med 2018; 23:823–30.
29 Simpson EL, Guttmann-Yassky E, Margolis DJ et al. Association of inadequately controlled disease and disease severity with patient-reported disease burden in adults with atopic dermatitis. JAMA Dermatol 2018; 154:903–12.
30 Yu SH, Silverberg JI. Association between atopic dermatitis and depression in US adults. J Invest Dermatol 2015; 135:3183–6.
31 Simpson EL, Bieber T, Guttmann-Yassky E et al. Two phase 3 trials of dupilumab versus placebo in atopic dermatitis. N Engl J Med 2016; 375:2335–48.
32 Kataoka YN, Nakajima S. Is coping of atopic dermatitis patients originated from their own character or secondarily remodelled by disease suffering? Obvious improvement of coping and psychiatric symptoms after ‘light eczema control’. Acta Derm Venereol 2017; 97:880–1.
33 Vinnik T, Kirby M, Bairchayna M et al. Seasonality and BDNF polymorphism influences depression outcome in patients with atopic dermatitis and psoriasis. World J Biol Psychiatry 2017; 18:604–14.
34 Kawana S, Kato Y, Omi T. Efficacy of a 5-HT1a receptor agonist in atopic dermatitis. Clin Exp Dermatol 2010; 35:835–40.
35 Badia X, Mascaro JM, Lozano R. Measuring health-related quality of life in patients with mild to moderate eczema and psoriasis: clinical validity, reliability and sensitivity to change of the DLQI. The Cavide Research Group. Br J Dermatol 1999; 141:698–702.
36 Coutanceau C, Stalder JF. Analysis of correlations between patient-oriented SCORAD (PO-SCORAD) and other assessment scores of atopic dermatitis severity and quality of life. Dermatology 2014; 229:248–55.
37 Holm EA, Wulf HC, Stegmann H, Jemec GB. Life quality assessment among patients with atopic eczema. Br J Dermatol 2006; 154:719–25.
38 Herd RM, Tidman MJ, Ruta DA, Hunter JA. Measurement of quality of life in atopic dermatitis: correlation and validation of two different methods. Br J Dermatol 1997; 136:502–7.
39 Finlay AV, Khan GK. Dermatology Life Quality Index (DLQI)–a simple practical measure for routine clinical use. Clin Exp Dermatol 1994; 19:210–16.
40 Jobanputra R, Bachmann M. The effect of skin diseases on quality of life in patients from different social and ethnic groups in Cape Town, South Africa. Int J Dermatol 2000; 39:826–31.
41 Holm EA, Esman S, Jemec GB. Does visible atopic dermatitis affect quality of life more in women than in men? Gend Med 2004; 1:125–30.
42 Twiss J, Meads DM, Preston EP et al. Can we rely on the Dermatology Life Quality Index as a measure of the impact of psoriasis or atopic dermatitis? J Invest Dermatol 2012; 132:76–84.
43 Chalmers JR, Schmitz J, Apfelbacher C et al. Report from the third international consensus meeting to harmonise core outcome measures for atopic eczema/dermatitis clinical trials (HOME initiative). Br J Dermatol 2014; 171:1318–25.
44 Chalmers JR, Simpson E, Apfelbacher CJ et al. Report from the fourth international consensus meeting to harmonise core outcome measures for atopic eczema/dermatitis clinical trials (HOME initiative). Br J Dermatol 2016; 175:69–79.
45 Gerbens LA, Chalmers JR, Rogers NK et al. Reporting of symptoms in randomized controlled trials of atopic eczema treatments: a systematic review. Br J Dermatol 2016; 175:678–86.
46 Gerbens LA, Prinsen CA, Chalmers JR et al. Evaluation of the measurement properties of symptom measurement instruments for atopic eczema: a systematic review. Allergy 2017; 72:146–63.
47 Heinl D, Chalmers J, Nankervis H, Apfelbacher CJ. Eczema trials: quality of life instruments used and their relation to patient-reported outcomes. A systematic review. Acta Derma Venereol 2016; 96:596–601.
48 Heinl D, Prinsen CA, Deckert S et al. Measurement properties of adult quality-of-life measurement instruments for eczema: a systematic review. Allergy 2016; 71:358–70.
49 Heinl D, Prinsen CA, Sach T et al. Measurement properties of quality-of-life measurement instruments for children, infants and adolescents with eczema: a systematic review. Br J Dermatol 2016; 176:878–89.
50 Schmitz J, Williams H. HOME Development Group. Harmonising Outcome Measures for Eczema (HOME). Report from the First International Consensus Meeting (HOME 1), 24 July 2010, Munich, Germany. Br J Dermatol 2010; 163:1166–8.
51 Bjelland I, Dahl AA, Haug TT, Neckelmann D. The validity of the Hospital Anxiety and Depression Scale. An updated literature review. J Psychosom Res 2002; 52:69–77.
52 Silverberg JI, Garg NK, Paller AS et al. Sleep disturbances in adults with eczema are associated with impaired overall health: a US population-based study. J Invest Dermatol 2015; 135:56–66.
53 Barbarot S, Azziere S, Gadhari A et al. Epidemiology of atopic dermatitis in adults: results from an international survey. Allergy 2018; 73:1284–93.
Appendix

Conflicts of interest

J.I.S. served as a consultant and/or advisory board member for AbbVie, Asana, Eli Lilly, Galderma, GlaxoSmithKline, Glenmark, Kiniksa, Leo, Menlo, Pfizer, Regeneron-Sanofi, Realm and Roivant, receiving honoraria. He has been a speaker for Regeneron-Sanofi and received research grants from GlaxoSmithKline and Regeneron-Sanofi. J.I.S. is supported by the Dermatology Foundation. J.M.G. served as a consultant for BMS, Boehringer Ingelheim, GSK, Janssen Biologics, Menlo Therapeutics, Novartis Corp, Regeneron, Dr Reddy’s Laboratories, UCB (DSMB), Sanofi and Pfizer Inc., receiving honoraria. J.M.G. receives research grants (to the Trustees of the University of Pennsylvania) from AbbVie, Janssen, Novartis Corp, Sanofi, Celgene, Ortho Dermatologics and Pfizer Inc. and received payment for continuing medical education work related to psoriasis that was supported indirectly by Lilly and Ortho Dermatologics. J.M.G. is a copatent holder of resiquimod for treatment of cutaneous T-cell lymphoma. J.M.G. is a Deputy Editor for the Journal of Investigative Dermatology, receiving honoraria from the Society for Investigative Dermatology. Z.C.C.F. has served as a consultant for the National Eczema Association and the Allergy and Asthma Foundation of America (AAFA), receiving honoraria, and receives or has received research grants (to the Trustees of the University of Pennsylvania) from Regeneron, Sanofi, Tioga and Vanda pharmaceuticals and Realm Therapeutics for work in atopic dermatitis. Z.C.C.F. has received payment for continuing medical education work related to atopic dermatitis, which was supported indirectly by Regeneron and/or Sanofi. D.J.M. is the chair of the data monitoring committee for many Sanofi clinical trials of dupilumab, and, with respect to atopic dermatitis, has received independent research funding to his institution from the National Institutes of Health and Valeant. M.B. has received research funding from Anacor and Regeneron and consulted for Regeneron, Sanofi Genzyme and Pfizer. L.F. has served as a consultant for Regeneron, receiving honoraria. L.F. has also been a speaker for Regeneron and has received research and educational grants from Genentech, Baxter and Pfizer. M.H.G. is a board member of the AAFA and chair for the AAFA Medical Scientific Council, and has served as a consultant for AstraZeneca. E.L.S. has served as a consultant and/or advisory board member for Regeneron-Sanofi. P.Y.O. is a coinvestigator of the Atopic Dermatitis Research Network. He has consulted for Pfizer and Theravance, and has received research funding from Regeneron.

Author contributions

J.I.S. had full access to all the data in the study and takes responsibility for the integrity of the data and accuracy of the data analysis. J.I.S. was responsible for the study concept and design. J.I.S., J.M.G., D.J.M., M.B., L.F, M.H.G., P.Y.O. and Z.C.C.F. were involved in the acquisition of data, analysis and interpretation of data and critical revision of the manuscript for important intellectual content. J.I.S. carried out the statistical analysis and drafted the manuscript. The study was supervised by Allergy and Asthma Foundation of America.

Supporting Information

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

Fig S1. Flowchart of study design.