

Association Between Atopic Dermatitis and Suicidality

A Systematic Review and Meta-analysis

Jeena K. Sandhu, BA; Kevin K. Wu, BA; Thanh-Lan Bui, MA; April W. Armstrong, MD, MPH

IMPORTANCE Atopic dermatitis (AD) is a chronic inflammatory skin disease associated with numerous psychiatric comorbidities. However, the association between AD and suicidality has not been well established.

OBJECTIVE To synthesize the available literature to evaluate the association between AD and suicidality.

DATA SOURCE The protocol was prospectively registered in the PROSPERO database (CRD42018105291).

STUDY SELECTION Per PRISMA guidelines, PubMed, Embase, PsycINFO, and Cochrane databases were systematically searched for relevant articles published from 1946 to May 25, 2018. The search criteria for PubMed were as follows: (*dermatitis, atopic* [MeSH] OR *eczema* [MeSH]) AND (*suicidal ideation* [MeSH] OR *suicide, attempted* [MeSH] OR *suicide* [MeSH] OR *suicidality* OR *suicidal behavior*). The search criteria for Embase, PsycINFO, and Cochrane were as follows: (*atopic dermatitis* OR *eczema*) AND (*suicidal ideation* OR *suicide attempt* OR *suicide* OR *suicidality* OR *suicidal behavior*).


DATA EXTRACTION AND SYNTHESIS This systematic review and meta-analysis performed in an academic medical setting included observational studies that evaluated suicidal ideation, suicide attempts, and completed suicide among patients with AD.

MAIN OUTCOME AND MEASURE The quality of included studies was assessed using the Newcastle-Ottawa Scale for observational studies.

RESULTS The analysis identified 15 studies with a total of 4 770 767 participants, of whom 310 681 were patients with AD (52.7% female) and 4 460 086 served as controls (50.9% female). In the meta-analyses, patients with AD were 44% more likely to exhibit suicidal ideation (pooled odds ratio, 1.44; 95% CI, 1.25-1.65) and 36% more likely to attempt suicide (pooled odds ratio, 1.36; 95% CI, 1.09-1.70) compared with patients without AD. Studies investigating completed suicides in patients with AD had inconsistent results.

CONCLUSIONS AND RELEVANCE Results of this study suggest that patients with AD are at significantly increased risk of suicidal ideation and suicide attempts. It is important for dermatology providers to be aware of this risk, screen for suicidality in patients with AD, and make mental health referrals when necessary.

JAMA Dermatol. 2019;155(2):178-187. doi:10.1001/jamadermatol.2018.4566
Published online December 12, 2018.

 CME Quiz at
jamanetwork.com/learning
and CME Questions page 264

Author Affiliations: Currently a medical student at the University of Missouri-Kansas City School of Medicine, Kansas City (Sandhu); currently a medical student at the Frank H. Netter MD School of Medicine at Quinnipiac University, North Haven, Connecticut (Wu); currently a medical student at the University of California, Irvine, School of Medicine, Irvine (Bui); Department of Dermatology, University of Southern California Keck School of Medicine, Los Angeles (Armstrong).

Corresponding Author: April W. Armstrong, MD, MPH, Department of Dermatology, University of Southern California Keck School of Medicine, 1975 Zonal Ave, Keith Administration Room 510, Mail Code 9034, Los Angeles, CA 90089 (aprilarmstrong@post.harvard.edu).

Atopic dermatitis (AD) is an inflammatory skin disease affecting 18 million adults (7.2%) and 9.6 million children (13.0%) in the United States.^{1,2} It is a chronic illness, and patients may have the disease for many years.³ Atopic dermatitis is associated with multiple physical comorbidities, such as asthma, allergic rhinitis, metabolic syndrome, and sleep disturbances, which all contribute to the overall physical burden of the disease.⁴

Many patients with AD have a profound psychosocial burden. Because of the visibility of the disease, patients may experience shame, embarrassment, and stigmatization.⁵ Children with AD perform significantly worse in academics compared with healthy children.⁶ Adults with AD perform significantly worse at work and have fewer job opportunities compared with healthy adults.⁷ Atopic dermatitis has been associated with depression and anxiety.⁸⁻¹⁰ However, the evidence for an association between AD and suicidality is inconclusive.

Suicidality encompasses the following 3 components¹¹: suicidal ideation, suicide attempts, and completed suicides. Suicidal ideation refers to having thoughts of or planning for suicide. Suicide attempts refer to acts of attempting suicide where the individual survives. Completed suicides refer to successful suicide attempts that lead to patient death. Suicidality is a major health concern that requires greater attention. Suicide is the second leading cause of death among adolescents and the tenth leading cause of death among all Americans, with the death toll reaching almost 45 000 annually.^{12,13} Even more concerning is the rising suicide rate,¹² increasing from 11.27 suicides per 100 000 people in 2007 to 13.20 suicides per 100 000 people in 2016. There is a gap in the literature regarding suicidality in patients with AD. This systematic review and meta-analysis performed in an academic medical setting aimed to synthesize the available literature to elucidate the association between AD and suicidality.

Methods

Search Strategy and Study Inclusion

We performed a systematic review and meta-analysis in accord with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) reporting guideline to investigate the association between AD and suicidality. The protocol for this study was registered in the PROSPERO database (CRD42018105291), an international prospective register of systematic reviews. To perform our search, we used PubMed, Embase, PsycINFO, and Cochrane databases. Our search criteria for PubMed were as follows: (*dermatitis, atopic* [MeSH] OR *eczema* [MeSH]) AND (*suicidal ideation* [MeSH] OR *suicide, attempted* [MeSH] OR *suicide* [MeSH] OR *suicidality* OR *suicidal behavior*). Our search criteria for Embase, PsycINFO, and Cochrane were as follows: (*atopic dermatitis* OR *eczema*) AND (*suicidal ideation* OR *suicide attempt* OR *suicide* OR *suicidality* OR *suicidal behavior*).

Our search included all English-language articles from database inception to the date our searches were performed: PubMed was searched from 1946 to May 25, 2018, Embase was searched from 1947 to May 25, 2018, PsycINFO was searched

Key Points

Question Is there an increased risk of suicidality among patients with atopic dermatitis?

Findings In this systematic review and meta-analysis of 15 studies and 310 681 patients with atopic dermatitis, patients with atopic dermatitis had a 44% increased odds of suicidal ideation and a 36% increased odds of suicide attempts compared with patients without atopic dermatitis.

Meaning According to the results of this study, patients with atopic dermatitis are at significantly greater risk of suicidal ideation and suicide attempts. It is important for dermatology providers to be aware of this increased risk in patients with atopic dermatitis, monitor for suicidality, and make appropriate referrals to mental health professionals.

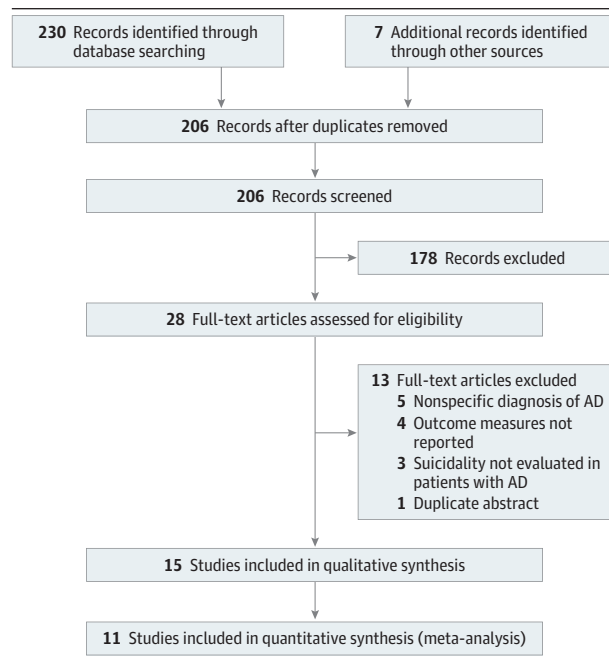
from 1967 to May 25, 2018, and Cochrane databases were searched from 1996 to May 25, 2018. The initial search resulted in a total of 230 articles (Figure 1). Duplicate articles were eliminated, resulting in a total of 206 articles. Two of us (J.K.S. and K.K.W.) independently reviewed the titles and abstracts of the 206 articles to determine eligibility for our systematic review and meta-analysis. Inclusion criteria were as follows: English-language articles; primary investigations; observational or controlled studies; patients of any age; study population identified as having a specific diagnosis of AD, atopic eczema, or eczema; suicidality as a primary or secondary end point; documentation of suicidality via medical records, survey, or questionnaire; suicidality studied in relation to AD; and outcome measures reported. Case reports and case series were excluded. In the process of reviewing these titles and abstracts, we identified an additional 7 articles by manually searching the reference lists. There were 28 articles that met our criteria based on their titles and abstracts.

After reviewing titles and abstracts, 2 of us (J.K.S. and K.K.W.) independently reviewed the entirety of the 28 full-text articles to further assess eligibility. A total of 13 studies were excluded for the following reasons: nonspecific diagnosis of AD (n = 5), outcome measures not reported (n = 4), suicidality not evaluated in patients with AD (n = 3), and conference paper with duplicate abstract (n = 1). At the conclusion of our search, we identified 15 eligible studies to include in our systematic review and meta-analysis.

Data Extraction

Two of us (J.K.S. and K.K.W.) independently extracted data and performed the systematic review and meta-analysis. Any discrepancies were reviewed with another of us (A.W.A.) and resolved among 3 of us (J.K.S., K.K.W., and A.W.A.). For each study, the reviewers recorded study year, study setting, country of study origin, study design, number of individuals with AD, number of individuals with AD with suicidality, number of controls, number of controls with suicidality, and the demographic characteristics (age and sex) for both the AD and control groups (Table 1 and Table 2). The reviewers recorded data on suicidal ideation, suicide attempts, and completed suicides among patients with AD. In addition, the reviewers recorded the

Figure 1. Selection Process for Study Inclusion in the Systematic Review and Meta-analysis



AD indicates atopic dermatitis.

instruments used to measure suicidality and the measure of association (hazard ratio [HR], odds ratio [OR], or risk ratio [RR]) for the association between AD and suicidality. The reviewers performed quality assessment using the Newcastle-Ottawa Scale (NOS) for observational studies.²⁹

Meta-analyses

The following 2 meta-analyses were conducted to assess 2 aspects of suicidality in patients with AD: (1) suicidal ideation and (2) suicide attempts. We were unable to perform a separate meta-analysis for completed suicides because of the paucity of available data. A total of 11 studies were included in the suicidal ideation meta-analysis, and a total of 3 studies were included in the suicide attempts meta-analysis. Studies were excluded from the pooled analysis if an unadjusted OR was unable to be attained from the article itself or through calculation using the study data. One study¹⁶ was excluded from the meta-analysis because the suicidality data of the control group were not representative of the general population.

For the meta-analyses, we calculated the pooled ORs for suicidal ideation and suicide attempts using the unadjusted ORs that were either provided by the study or calculated using data from the study. We used the random-effects model by DerSimonian and Laird to obtain the pooled ORs and account for any study heterogeneity. To further assess heterogeneity of each study, we calculated the I^2 statistic. We evaluated for possible publication bias via visual inspection of a funnel plot showing precision vs measure of association for each study. Egger regression test was performed to provide a quantitative value for further assessment of publication bias. A software program (STATA, version 13.1; StataCorp LP) was used for the meta-analyses. The threshold for statistical significance was 2-sided $P < .05$.

Results

This systematic review and meta-analysis incorporated 15 studies that reported the prevalence of suicidality among patients with AD. Among a total of 4 770 767 participants, 310 681 were patients with AD (52.7% female) and 4 460 086 served as controls (50.9% female) (Table 1). Seven articles^{18,20,23,24,26-28} studied only adults, 2 articles^{22,25} studied only children (<18 years old), 3 articles^{16,17,21} studied both adults and children, and 3 articles^{14,15,19} did not report the age of the participants. The study locations included North America ($n = 1$), Europe ($n = 6$), Africa ($n = 1$), and Asia ($n = 7$) (Table 1). There were 13 cross-sectional studies and 2 cohort studies. Of a maximum of 10 points for cross-sectional studies, NOS scores ranged from 5 to 8. Of a maximum of 9 points for cohort studies, NOS scores ranged from 6 to 8 (Table 1). Suicidality was evaluated using a variety of assessment tools, including the Carroll Rating Scale for Depression, *Diagnostic and Statistical Manual of Mental Disorders* (Fifth Edition) (DSM-5) Questionnaire, German Pöldinger Scale, Beck Depression Inventory, Primary Care Evaluation of Mental Disorders, medical records, mortality records, and various other questionnaires.

In 5 of the studies that did not report any measure of association, we calculated the unadjusted ORs using the data provided by the study. Measures of association for each study are listed in Table 2.

Suicidal Ideation

Based on our meta-analysis pooling data from 11 of 14 studies investigating suicidal ideation, we found that patients with AD were significantly more likely to experience suicidal ideation than those without AD (Figure 2A) (pooled OR, 1.44; 95% CI, 1.25-1.65). Three studies were excluded from the meta-analysis for the following reasons: (1) suicidality data of the control group were not representative of the general population ($n = 1$)¹⁶ and (2) the unadjusted ORs could not be calculated with the data provided ($n = 2$).^{19,23} A symmetrical funnel plot (Figure 3A) and an insignificant Egger regression test ($P = .23$) suggest limited publication bias among these studies.

Suicide Attempts

Based on our meta-analysis pooling data from 3 of 5 studies investigating suicide attempts, we found that patients with AD were significantly more likely to attempt suicide than patients without AD (Figure 2B) (pooled OR, 1.36; 95% CI, 1.09-1.70). Two studies^{21,23} were excluded because an unadjusted OR could not be calculated with the data provided. A symmetrical funnel plot (Figure 3B) and an insignificant Egger regression test ($P = .90$) suggest limited publication bias among these studies.

Completed Suicides

Two studies^{17,27} in our systematic review and meta-analysis investigated the prevalence of completed suicides among patients with AD. Singhal et al¹⁷ reported a higher risk of completed suicides in their AD group compared with a control group (RR, 1.4; 95% CI, 1.1-1.8). The number of completed suicides in the control group was not reported; therefore, an unadjusted OR could not be calculated for the meta-analysis. In contrast to the findings

Table 1. Study Population Characteristics for Atopic Dermatitis and Suicidality

| Source | Setting | Study Design (Years) | Age of Study Participants Included, y | No. of Patients | | Age, Mean (\pm SD or %), y | | Female, No. (%) | | Quality Assessment (No. of Stars) |
|-------------------------------------|---|----------------------------------|---------------------------------------|--|--|---|---|---|--|---|
| | | | | AD Group | Control Group | AD Group | Control Group | AD Group | Control Group | |
| Gupta and Gupta, ¹⁴ 1998 | United States and Canada; inpatient and outpatient (dermatology department) | Cross-sectional (NR) | NR | 146 | Total: 334 Psoriasis: 217; acne: 72; alopecia areata: 45 | 42 (\pm 16) | Psoriasis: 48 (\pm 16); acne: 24 (\pm 7); alopecia areata: 45 (\pm 12) | 94 (64.4) | Psoriasis: 106 (48.8); acne: 58 (80.6); alopecia areata: 34 (75.6) | 5/10 ^a Selection: 3 Comparability: 0 Outcome: 2 |
| Zachariae et al, ¹⁵ 2004 | Denmark; outpatient and inpatient (dermatology clinics, university hospitals) | Cross-sectional (NR) | NR | Total: 95 Inpatient: 56; outpatient: 39 | 293 | 30.1 Inpatient: 29.8; outpatient: 30.6 | 44.2 | 59 (62.1) Inpatient: 37 (66.1); outpatient: 22 (56.4) | 187 (63.8) | 6/10 ^a Selection: 2 Comparability: 2 Outcome: 2 |
| Kimata et al, ¹⁶ 2006 | Japan; outpatient (hospital clinic) | Cross-sectional (NR) | 15-49 | Total: 6748 Mild AD: 2348; moderate AD: 2617; severe AD: 1783 | 3575 | NR | NR | Total: 3440 (51.0) Mild AD: 1213 (51.7); moderate AD: 1328 (50.7); severe AD: 899 (50.4) | 1846 (51.6) | 5/10 ^a Selection: 4 Comparability: 0 Outcome: 1 |
| Singhal et al, ¹⁷ 2014 | England; inpatient (English Hospital Episode and mortality data) | Retrospective cohort (1999-2011) | 10 to \leq 65 | 267 788 | NR | NR | NR | 139 250 (52.0) | NR | 8/9 ^b Selection: 4 Comparability: 2 Outcome: 2 |
| Halvorsen et al, ¹⁸ 2014 | Norway; schools | Cross-sectional (NR) | 18-19 | 342 | 2521 | NR | NR | 231 (67.5) | 1263 (50.1) | 7/10 ^a Selection: 3 Comparability: 2 Outcome: 2 |
| Mina et al, ¹⁹ 2015 | India; outpatient (tertiary care center) | Cross-sectional (NR) | NR | 81 | 0 | 34.94 (\pm 15.89) | NA | 45 (55.6) | 0 | 6/10 ^a Selection: 4 Comparability: 0 Outcome: 2 |
| Dalgard et al, ²⁰ 2015 | Belgium, Denmark, France, Germany, Hungary, Italy, Norway, the Netherlands, Poland, Russia, Spain, Turkey, United Kingdom; outpatient (dermatology clinics) | Cross-sectional (NR) | \geq 18 | 162 | 1359 | NR | 41.1 (\pm 13.6) | NR | 903 (66.4) | 8/10 ^a Selection: 4 Comparability: 2 Outcome: 2 |
| Sorour et al, ²¹ 2017 | Egypt; outpatient (clinics in 3 major hospitals) | Cross-sectional (2014-2015) | 17-60 | 110 | Total: 932 Psoriasis: 300; alopecia areata: 208; acne: 206; vitiligo: 108; chronic urticaria: 110 | NR | NR | 61 (55.5) | Psoriasis: 133 (44.3); alopecia areata: 86 (41.3); acne: 103 (50.0); vitiligo: 60 (55.6); chronic urticaria: 61 (55.5) | 5/10 ^a Selection: 4 Comparability: 0 Outcome: 1 |
| Noh et al, ²² 2016 | South Korea; middle schools and high schools | Cross-sectional (2005-2012) | 12-17 | 17 971 | 56 215 | NR | NR | 9938 (55.3) | 26 027 (46.3) | 7/10 ^a Selection: 3 Comparability: 2 Outcome: 2 |

(continued)

by Singhal et al,¹⁷ Thyssen et al²⁷ reported no significant difference in risk of completed suicides in both patients with mild AD (HR, 0.81; 95% CI, 0.33-1.96) and patients with moderate to severe AD (HR, 0.73; 95% CI, 0.27-1.97) compared with controls.

Table 1. Study Population Characteristics for Atopic Dermatitis and Suicidality (continued)

| Source | Setting | Study Design (Years) | Age of Study Participants Included, y | No. of Patients | | Age, Mean (\pm SD or %), y | | Female, No. (%) | | Quality Assessment (No. of Stars) |
|---|--|--|---------------------------------------|-----------------|---|---|--|---------------------|--|---|
| | | | | AD Group | Control Group | AD Group | Control Group | AD Group | Control Group | |
| Dieris-Hirche et al, ²³ 2017 | Germany; outpatient (dermatology department, clinics, and general community) | Cross-sectional (NR) | 18-65 | 181 | 64 | 27.6 (\pm 8.3) | 29.7 (\pm 10.0) | 137 (75.7) | 41 (64.1) | 7/10 ^a Selection: 3 Comparability: 2 Outcome: 2 |
| Kwak and Kim, ²⁴ 2017 | South Korea; general community | Cross-sectional (2010-2012) | \geq 19 | 157 | 11 756 | 35.2 (\pm 1.3) | 45.3 (\pm 0.3) | 76 (48.4) | 5960 (50.7) | 7/10 ^a Selection: 3 Comparability: 2 Outcome: 2 |
| Lee and Shin, ²⁵ 2017 | South Korea; middle schools and high schools | Cross-sectional (2013) | 12-17 | 4904 | 67 531 | Middle school (12-14 y): 2509 (51.2%) High school (15-17 y): 2395 (48.8%) | Middle school (12-14 y): 34 021 (50.4%) High school (15-17 y): 33 510 (49.6%) | 2804 (57.2) | 32 976 (48.8) | 7/10 ^a Selection: 3 Comparability: 2 Outcome: 2 |
| Kye and Park, ²⁶ 2017 | South Korea; general community | Cross-sectional (2010-2012) | \geq 19 | 237 | Patients with other diseases: 10 536 | NR | NR | NR | NR | 7/10 ^a Selection: 3 Comparability: 2 Outcome: 2 |
| Thyssen et al, ²⁷ 2018 | Denmark; general community; DanFunD and DPNR | Cohort DanFunD (2011-2015); DPNR (1997-2012) | \geq 18 | DanFunD: 1044 | DanFunD: questionnaire participants without AD: 8612 DPNR: Total AD: 10 038 (mild AD: 5766; moderate to severe AD: 4272) | DanFunD: 49.8 (\pm 13.8) DPNR: Mild AD: 38.3 (\pm 13.0); Moderate to severe AD: 42.8 (\pm 15.0) | DanFunD: 52.9 (\pm 13.1) DPNR: 48.0 (\pm 17.9) | DanFunD: 678 (64.9) | DanFunD: 4525 (52.5) DPNR: 2 171 073 (51.0) | 6/9 ^b Selection: 4 Comparability: 0 Outcome: 2 |
| Lee et al, ²⁸ 2018 | South Korea; general community | Cross-sectional (2008-2013) | \geq 19 | 677 | 36 901 | 36.1 (\pm 0.6) | 45.4 (\pm 0.2) | 324 (47.9) | 18 746 (50.8) | 6/10 ^a Selection: 2 Comparability: 2 Outcome: 2 |

Abbreviations: AD, atopic dermatitis; DanFunD, Danish Study of Functional Disorders; DPNR, Danish National Patient Register; NA, not applicable; NR, not reported.

^a Calculated using the modified Newcastle-Ottawa Scale for cross-sectional studies.

^b Calculated using the Newcastle-Ottawa Scale for cohort studies.

Suicidality in Children With AD

Two studies^{22,25} in our systematic review and meta-analysis investigated only pediatric patients (<18 years old). Lee and Shin²⁵ found that Korean children with AD were at significantly higher risk of suicidal ideation (adjusted OR, 1.23; 95% CI, 1.13-1.35) and suicide attempts (adjusted OR, 1.31; 95% CI, 1.12-1.52). Another study²² examining pediatric patients with AD failed to identify an overall increased risk compared with the general pediatric population. Among that group, only female pediatric patients with AD appeared to have increased risk of suicidal ideation (adjusted OR, 1.114; 95% CI, 1.046-1.186) and suicide attempts (adjusted OR, 1.188; 95% CI, 1.065-1.325) compared with healthy controls.

Suicidality With Greater Disease Severity

Two studies in our systematic review and meta-analysis investigated differences in suicidality with greater AD severity. Kimata¹⁶ reported that patients with severe AD exhibited higher suicidal ideation (19.60%) than those with mild AD

(0.21%). However, in regard to completed suicides, Thyssen et al²⁷ found no difference when comparing incidence rates per 1000 person-years in those with mild AD (0.12; 95% CI, 0.05-0.33 per 1000 person-years) vs those with moderate to severe AD (0.11; 95% CI, 0.04-0.24 per 1000 person-years).

Discussion

Our systematic review and meta-analysis found that patients with AD have a significantly greater risk of suicidal ideation and suicide attempts. Our findings were most pronounced in regard to suicidal ideation. Specifically, patients with AD had a 44% higher likelihood of suicidal ideation and a 36% higher likelihood of suicide attempts than patients without AD. Data on completed suicides are limited and had inconsistent results: Singhal et al¹⁷ reported a higher risk of completed suicides in patients with AD compared with healthy controls, while Thyssen et al²⁷ reported no difference in risk of completed

Table 2. Study Outcomes for Atopic Dermatitis and Suicidality

| Source | Outcome Ascertainment | Aspects of Suicidality Assessed | Patients With Suicidality, No./Total No. (%) | | Measure of Association Between AD and Suicidality |
|---|---|---------------------------------|--|---|--|
| | | | AD Group | Control Group | |
| Gupta and Gupta, ¹⁴ 1998 | Carroll Rating Scale for Depression | Suicidal ideation | "I feel that life is not still worth living": 5/146 (3.4) | "I feel that life is not still worth living": Total: 20/331 (6.0) Psoriasis: 18/214 (8.4); acne: 1/72 (1.4); alopecia areata: 1/45 (2.2) | OR, 0.55; 95% CI, 0.20-1.50 ^a |
| Zachariae et al, ¹⁵ 2004 | Beck Depression Inventory | Suicidal ideation | 18/95 (18.9) | 20/293 (6.8) | OR, 3.19; 95% CI, 1.61-6.33 ^a |
| Kimata et al, ¹⁶ 2006 | Qualitative questionnaire (investigator-designed) | Suicidal ideation | Total AD: 501/6748 (7.4) Mild AD: 5/2348 (0.2); moderate AD: 157/2617 (6.0); severe AD: 339/1783 (19.0) | 3/3575 (0.1) | Total AD: OR, 95.5; 95% CI, 30.7-297.3 ^a |
| Singhal et al, ¹⁷ 2014 | ICD-9 Codes; Mortality data from hospital records and death registrations supplied by Office for National Statistics in England | Completed suicides | 67/267 788 (0.0) | NR | RR, 1.4; 95% CI, 1.1-1.8 |
| Halvorsen et al, ¹⁸ 2014 | Qualitative questionnaire (investigator-designed) | Suicidal ideation | 53/342 (15.5) | 230/2521 (9.1) | Adjusted OR, 1.87; 95% CI, 1.31-2.68 Adjusted for race/ethnicity, family income, and sex |
| Mina et al, ¹⁹ 2015 | Primary Care Evaluation of Mental Disorders (includes PHQ-9) | Suicidal ideation | 13/81 (16.0) | NR | NR |
| Dalgard et al, ²⁰ 2015 | Qualitative questionnaire (investigator-designed) | Suicidal ideation | 25/162 (15.4) | 88/1359 (6.5) | Adjusted OR, 1.32; 95% CI, 0.75-2.33 Adjusted for sex, age, socioeconomic status, stress, comorbidities, and depression |
| Sorour et al, ²¹ 2017 | DSM-5 Questionnaire plus diagnosis confirmed by psychiatric professor | Suicidal ideation | 21/110 (19.1) | Total: 182/932 (19.5) Psoriasis: 30 (16.5); alopecia areata: 80 (44.0); acne: 24 (13.2); vitiligo: 27 (14.8); chronic urticaria: 21 (11.5) | OR, 0.97; 95% CI, 0.59-1.61 ^a |
| | | Suicide attempts | 0/110 | Total: 31/932 (3.3) Psoriasis: 13 (41.9); alopecia areata: 9 (29.0); acne: 5 (16.1); vitiligo: 4 (12.9); chronic urticaria: 0 | NR |
| Noh et al, ²² 2016 | Korea Youth Risk Behavior Web-Based Survey | Suicidal ideation | Total: 3717/17 971 (20.7) Girls: 2504/9938 (25.2); boys: 1213/8033 (15.1) | Total: 9892/56 215 (17.6) Girls: 5726/26 027 (22.0); boys: 4166/30 188 (13.8) | Boys: Adjusted OR, 1.042; 95% CI, 0.961-1.130 Girls: Adjusted OR, 1.114; 95% CI, 1.046-1.186 Adjusted for school year, academic achievement, socioeconomic status, family structure, distorted weight perception, sleep satisfaction, perceived stress, and depressed mood |
| | | Suicide attempts | Total: 859/17 971 (4.8) Girls: 626/9938 (6.3); boys: 233/8033 (2.9) | Total: 2172/56 215 (3.9) Girls: 1327/26 027 (5.1); boys: 845/30 188 (2.8) | Boys: Adjusted OR, 0.949; 95% CI, 0.800-1.124 Girls: Adjusted OR, 1.188; 95% CI, 1.065-1.325 Adjusted for school year, academic achievement, socioeconomic status, family structure, distorted weight perception, sleep satisfaction, perceived stress, and depressed mood |
| Dieris-Hirche et al, ²³ 2017 | German Pöldinger Scale | Suicidal ideation | "Have you thought about taking your own life lately?": 39/181 (21.5) | "Have you thought about taking your own life lately?": 0/64 | Adjusted OR, 35.75; 95% CI, 2.16-590.85 |
| | | Suicide attempts | "Have you ever tried to commit suicide?": 12/181 (6.6) | "Have you ever tried to commit suicide?": 0/64 | Adjusted OR, 9.51; 95% CI, 0.55-163.03 |

(continued)

Table 2. Study Outcomes for Atopic Dermatitis and Suicidality (continued)

| Source | Outcome Ascertainment | Aspects of Suicidality Assessed | Patients With Suicidality, No./Total No. (%) | | Measure of Association Between AD and Suicidality |
|--|---|---------------------------------|--|---------------------------|---|
| | | | AD Group | Control Group | |
| Kwak and Kim, ²⁴ 2017 | Korea National Health and Nutrition Examination Survey | Suicidal ideation | 34/157 (21.7) | 1669/11 756 (14.2) | Adjusted OR, 1.87; 95% CI, 1.15-3.02 Adjusted for age and gender Adjusted OR, 1.61; 95% CI, 0.99-2.62 Adjusted for BMI, residential area, smoking, alcohol consumption, marital status, economic status, occupation, and education Adjusted OR, 1.66; 95% CI, 1.02-2.69 Adjusted for diabetes and hypertension |
| | | Suicide attempts | 300/4904 (6.1) | 2721/67 531 (4.0) | Adjusted OR, 1.31; 95% CI, 1.12-1.52 Adjusted for sex, age, residence, family affluence, father's education attainment, mother's education attainment, alcohol consumption, sleep duration, sleep satisfaction, and violence |
| Lee and Shin et al, ²⁵ 2017 | Korean Youth Risk Behavior Survey | Suicidal ideation | 1044/4904 (21.3) | 11 026/67 531 (16.3) | Adjusted OR, 1.23; 95% CI, 1.13-1.35 Adjusted for sex, age, residence, family affluence, father's education attainment, mother's education attainment, alcohol consumption, sleep duration, sleep satisfaction, and violence |
| | | Suicide attempts | 300/4904 (6.1) | 2721/67 531 (4.0) | Adjusted OR, 1.31; 95% CI, 1.12-1.52 Adjusted for sex, age, residence, family affluence, father's education attainment, mother's education attainment, alcohol consumption, sleep duration, sleep satisfaction, and violence |
| Kye and Park et al, ²⁶ 2017 | Korea National Health and Nutrition Examination Survey | Suicidal ideation | 41/237 (17.3) | Total: 2204/10 536 (20.9) | Adjusted OR, 0.94; 95% CI, 0.58-1.51 Adjusted for age, sex, marital status, household income, education, depression, depressive mood, physical discomfort, stress perception, high-risk drinking, and other diseases |
| | | Suicide attempts | 1/237 (0.4) | Total: 135/10 536 (1.3) | Adjusted OR, 0.40; 95% CI, 0.05-3.45 Adjusted for age, sex, marital status, household income, education, depression, depressive mood, physical discomfort, stress perception, high-risk drinking, and other diseases |
| Thyssen et al, ²⁷ 2018 | DanFunD questionnaire DNPR (Danish version of the ICD codes) | Suicidal ideation | 34/1044 (3.3) | 144/8612 (1.7) | OR, 1.98; 95% CI, 1.35-2.89 ^a |
| | | Completed suicides | Total: 9/10 038 (0.1) Mild AD: 5 (55.6); moderate to severe AD: 4 (44.4) | 5821/4 259 457 (0.1) | OR, 0.6558; 95% CI, 0.34-2.26 ^a Mild AD: adjusted HR, 0.81; 95% CI, 0.33-1.96 Moderate to severe AD: adjusted HR, 0.73; 95% CI, 0.27-1.97 Adjusted for age, sex, socioeconomic status, and health care consumption |
| Lee et al, ²⁸ 2018 | Korea National Health and Nutrition Examination Survey | Suicidal ideation | 133/677 (19.6) | 4907/36 901 (13.3) | Adjusted OR, 1.67; 95% CI, 1.31-2.14 Adjusted for age, sex, monthly income, region of residency, education level, smoking status, and drinking habits |

Abbreviations: AD, atopic dermatitis; BMI, body mass index; *DSM-5*, *Diagnostic and Statistical Manual of Mental Disorders* (Fifth Edition); DanFunD, Danish Study of Functional Disorders; DNPR, Danish National Patient Register; HR, hazard ratio; ICD, *International Classification of Diseases*; NR, not reported;

OR, odds ratio; PHQ, Patient Health Questionnaire; RR, risk ratio.

^a Measurement of association was calculated because the study did not report measures of association.

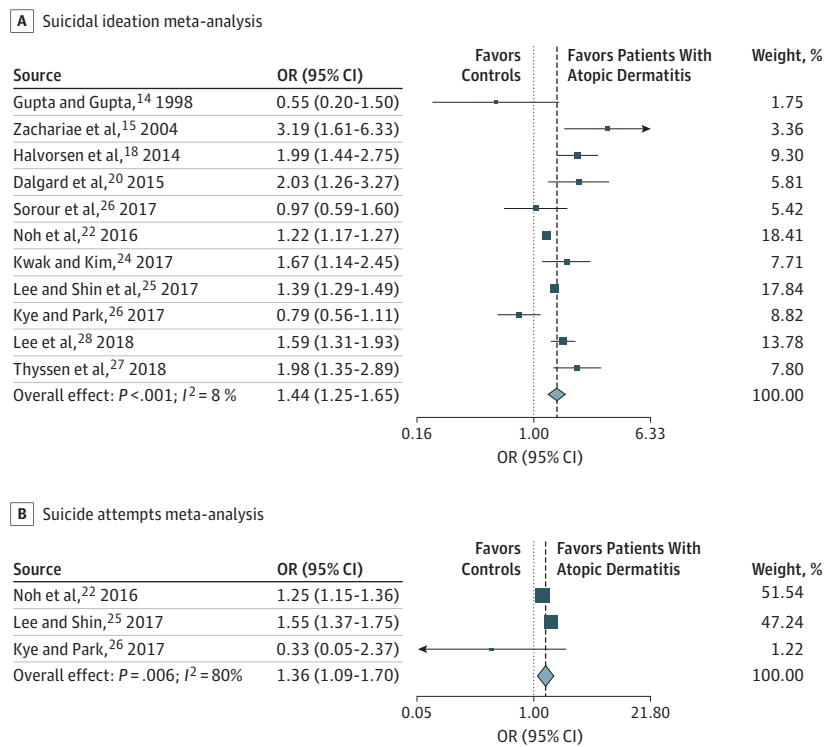
suicides in patients with AD compared with healthy controls. The inconsistency of these results may be because of the large difference in sample sizes of the 2 studies: Singhal et al¹⁷ had a study population of 267 788 patients with AD, while Thyssen et al²⁷ had a study population of 10 038 patients with AD (Table 1). Because of the rarity of suicides, sufficiently large sample sizes followed up over long periods may be needed to detect differences in suicide rates between patients with and without AD.

The physical and psychosocial burden of AD may contribute to the observed increased risk of suicidality. Patients with uncontrolled AD may experience debilitating symptoms of pruritus, burning, and pain of the skin.³⁰ Furthermore, sleep loss caused by pruritus has been shown to increase risk of suicidality in patients with AD.³¹⁻³⁴ Psychosocial factors, such as the stigmatization and shame experienced from their disease,⁵ and impairment of school⁶ or

work⁷ performance may also contribute to the increased risk of suicidality seen in patients with AD.

Atopic dermatitis is associated with an increase in proinflammatory cytokines, which may have a role in the pathogenesis of suicidality in patients with AD.³⁵ Higher levels of proinflammatory cytokines in the central nervous system may alter serotonin metabolism, thereby disrupting the balance of neurotransmitters in the brain.^{36,37} In a study³⁸ of cytokine levels in the cerebrospinal fluid, higher levels of proinflammatory cytokines were detected in the cerebrospinal fluid of patients who attempted suicide, further implicating cytokines in the pathogenesis of suicidality. Treatments targeting cytokines, such as interleukin 4 and interleukin 13, have been shown to decrease symptoms of depression and anxiety in patients with AD.³⁹ By addressing the physical burden, psychosocial burden, and chronic inflammatory state of AD, we can work toward reducing suicidality in patients with AD.

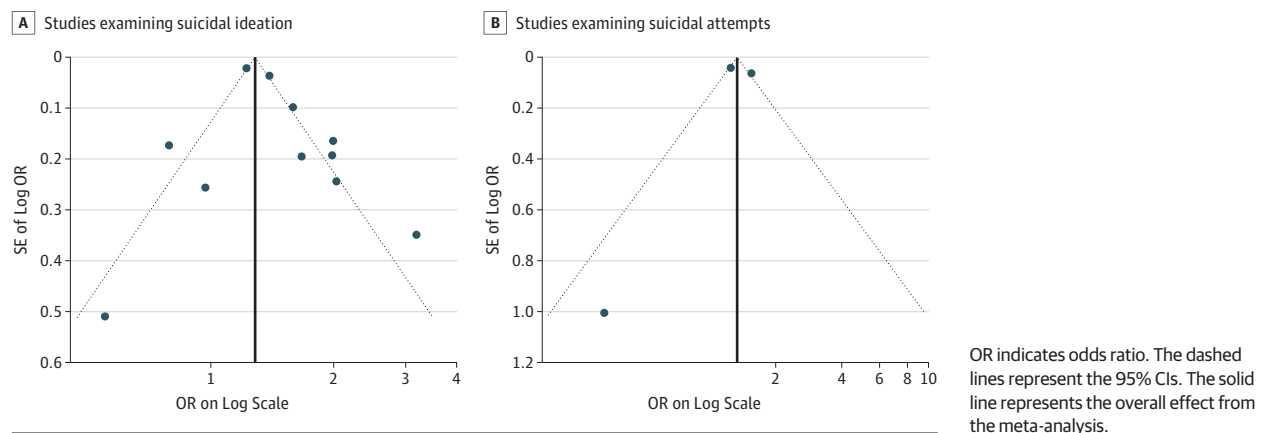
Figure 2. Forest Plots of Random-Effects Meta-analyses Among Patients With Atopic Dermatitis



A and B, Shown are 11 studies^{14,15,18,20-22,24-28} on suicidal ideation and 3 studies^{22,25,26} on suicide attempts. The diamond represents the exact estimate from the study. The width of the line extending from each diamond represents the 95% CI. The dashed line represents the estimated pooled

effect size. The open diamond represents a visual summary of the overall 95% CI of the effect estimate. Weights are from random-effects analysis. OR indicates odds ratio. Data on the left side of the solid line favor controls, and data on the right side of the solid line favor patients with atopic dermatitis.

Figure 3. Funnel Plots With 95% CIs Among Patients With Atopic Dermatitis



Some studies in our systematic review and meta-analysis assessed subpopulations of patients with AD, including children (<18 years old) and patients with greater disease severity. The results of one study²⁵ investigating pediatric patients with AD suggested a significantly higher risk of suicidal ideation and suicide attempts compared with healthy pediatric patients. In another study,²² higher risk of suicidal ideation and suicide attempts was only seen in female pediatric patients after sex stratification. Young girls tend to report greater dis-

satisfaction with appearance and lower self-esteem than young boys, which can contribute to the risk of suicidality seen specifically in female pediatric patients with AD.^{40,41} In studies^{16,27} comparing patients with mild AD vs patients with moderate to severe AD, patients with moderate to severe AD were found to have a higher prevalence of suicidal ideation but not completed suicides. Greater disease severity of AD is associated with increased sleep loss, more severe pruritus, and higher depression and anxiety rates, which can all contribute to more

suicidal ideation.⁴² Despite these findings, there is a shortage of studies investigating subpopulations, and more studies are needed to better understand these associations.

Strengths and Limitations

This systematic review and meta-analysis should be interpreted in the context of the strengths and limitations of the studies reviewed. While true differences among individual studies likely introduced heterogeneity, additional heterogeneity was likely evident because of the use of a multitude of instruments. Such instrument-related heterogeneity may be larger in studies using less validated questionnaires in contrast to studies using validated and more psychometrically sound instruments. The random-effects model by DerSimonian and Laird was used in our meta-analyses to account for heterogeneity. However, because a large number of different instruments was used among a small number of studies, we were unable to discern the amount of heterogeneity that resulted from the differences in study instrumentation and the amount of heterogeneity that resulted from true differences in individual study results. Some studies included control groups of patients with other medical conditions, which may have confounded their results. A number of studies were uncontrolled or did not report values of their control group, which prevented us from including these data in our meta-analyses. In addition, few studies investigated the prevalence of completed suicides among patients with AD vs controls.

Monitoring for suicidality in patients with AD is crucial to improving patient outcomes. Dermatology providers may use several tools to screen patients with AD for suicidality. Asking patients about suicidal ideation with a question (eg, “Do you have any thoughts of killing yourself?”) may be integrated into a patient visit. In addition, the Patient Health

Questionnaire-2 is a validated questionnaire that can be used to screen for dysphoria and anhedonia with the following question: “Over the past 2 weeks, how often have you been bothered by any of the following problems? (1) little interest or pleasure in doing things and (2) feeling down, depressed, or hopeless.”⁴³ If the patient screens positive on the Patient Health Questionnaire-2, dermatology providers should subsequently ask the following 2 questions to assess for suicidality: “Do you ever think about ending your own life?” and “Do you currently have a plan to commit suicide?”⁴⁴ More comprehensive questionnaires, such as the Columbia-Suicide Severity Rating Scale,⁴⁵ may also be administered, but the length of that questionnaire may limit its use in clinical practice.

If a patient screens positive for suicidality, the dermatology provider should send a referral to the patient’s primary care or mental health provider for follow-up care. If the patient reports an orchestrated plan to commit suicide, this patient should be urgently referred to the emergency department for further assessment. In nonemergent situations, dermatology providers may provide resources to the patient, such as suicide awareness brochures and the US National Suicide Prevention Lifeline phone number (1-800-273-8255), a hotline providing emotional support to people in suicidal crises.

Conclusions

This systematic review and meta-analysis found that patients with AD are at a significantly increased risk of suicidal ideation and suicide attempts. It is important for dermatology providers to be aware of this increased risk in patients with AD, monitor for suicidality, and make appropriate referrals to mental health professionals.

ARTICLE INFORMATION

Accepted for Publication: October 14, 2018.

Published Online: December 12, 2018.
doi:10.1001/jamadermatol.2018.4566

Author Contributions: Ms Sandhu and Mr Wu contributed equally to this article and are co-first authors. Ms Sandhu and Mr Wu had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: Sandhu, Wu, Armstrong.
Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: Sandhu, Wu, Armstrong.
Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: All authors.

Obtained funding: Armstrong.

Administrative, technical, or material support: Wu, Armstrong.

Supervision: Armstrong.

Conflict of Interest Disclosures: Dr Armstrong reported serving as investigator and advisor to AbbVie, Janssen, Lilly, Pfizer, UCB, Dermira, Ortho Dermatologics, Sanofi, Regeneron, Science 37, and Modernizing Medicine. No other disclosures were reported.

Funding/Support: The data analysis in this study was partially funded by the Southern California Clinical and Translational Science Institute with grants UL1TR001855 and UL1TR000130 from the National Center for Advancing Translational Science of the National Institutes of Health (Dr Armstrong).

Role of the Funder/Sponsor: The funding source had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Disclaimers: The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. Dr Armstrong is an Associate Editor of *JAMA Dermatology* but was not involved in any of the decisions regarding review of the manuscript or its acceptance.

Additional Contributions: Wendy Mack, PhD, Department of Preventive Medicine, University of Southern California Keck School of Medicine, Los Angeles, assisted with and guided the statistical design of our study. No compensation was received.

REFERENCES

1. Silverberg JI. Public health burden and epidemiology of atopic dermatitis. *Dermatol Clin*. 2017;35(3):283-289. doi:10.1016/j.det.2017.02.002
2. Silverberg JI, Simpson EL. Associations of childhood eczema severity: a US population-based study. *Dermatitis*. 2014;25(3):107-114. doi:10.1097/DER.0000000000000034
3. Kim JP, Chao LX, Simpson EL, Silverberg JI. Persistence of atopic dermatitis (AD): A systematic review and meta-analysis. *J Am Acad Dermatol*. 2016;75(4):681-687.e11. doi:10.1016/j.jaad.2016.05.028
4. Simpson EL. Comorbidity in atopic dermatitis. *Curr Dermatol Rep*. 2012;1(1):29-38. doi:10.1007/s13671-011-0003-5
5. Chernyshov PV. Stigmatization and self-perception in children with atopic dermatitis. *Clin Cosmet Investig Dermatol*. 2016;9:159-166. doi:10.2147/CCID.S91263
6. Absolon CM, Cottrell D, Eldridge SM, Glover MT. Psychological disturbance in atopic eczema: the extent of the problem in school-aged children. *Br J Dermatol*. 1997;137(2):241-245. doi:10.1046/j.1365-2133.1997.18121896.x

7. Nørreslet LB, Ebbenhøj NE, Ellekilde Bonde JP, Thomsen SF, Agner T. The impact of atopic dermatitis on work life: a systematic review. *J Eur Acad Dermatol Venereol*. 2018;32(1):23-38. doi:10.1111/jdv.14523
8. Ahmar H, Kurban AK. Psychological profile of patients with atopic dermatitis. *Br J Dermatol*. 1976;95(4):373-377. doi:10.1111/j.1365-2133.1976.tb00838.x
9. Hashiro M, Okumura M. Anxiety, depression and psychosomatic symptoms in patients with atopic dermatitis: comparison with normal controls and among groups of different degrees of severity. *J Dermatol Sci*. 1997;14(1):63-67. doi:10.1016/S0923-1811(96)00555-1
10. Lim VZ, Ho RC, Tee SI, et al. Anxiety and depression in patients with atopic dermatitis in a Southeast Asian tertiary dermatology centre. *Ann Acad Med Singapore*. 2016;45(10):451-455.
11. Meyer RE, Salzman C, Youngstrom EA, et al. Suicidality and risk of suicide: definition, drug safety concerns, and a necessary target for drug development: a consensus statement. *J Clin Psychiatry*. 2010;71(8):e1-e21. doi:10.4088/JCP.10cs06070blu
12. Centers for Disease Control and Prevention. Suicide rising across the US. <https://www.cdc.gov/vitalsigns/suicide/>. Published June 6, 2018. Accessed June 8, 2018.
13. Heron M. Deaths: leading causes for 2015. *Natl Vital Stat Rep*. 2017;66(5):1-76.
14. Gupta MA, Gupta AK. Depression and suicidal ideation in dermatology patients with acne, alopecia areata, atopic dermatitis and psoriasis. *Br J Dermatol*. 1998;139(5):846-850. doi:10.1046/j.1365-2133.1998.02511.x
15. Zachariae R, Zachariae C, Ibsen HH, Mortensen JT, Wulf HC. Psychological symptoms and quality of life of dermatology outpatients and hospitalized dermatology patients. *Acta Derm Venereol*. 2004;84(3):205-212. doi:10.1080/00015550410023284
16. Kimata H. Prevalence of suicidal ideation in patients with atopic dermatitis. *Suicide Life Threat Behav*. 2006;36(1):120-124. doi:10.1521/suli.2006.36.1.120
17. Singhal A, Ross J, Seminog O, Hawton K, Goldacre MJ. Risk of self-harm and suicide in people with specific psychiatric and physical disorders: comparisons between disorders using English national record linkage. *J R Soc Med*. 2014;107(5):194-204. doi:10.1177/0141076814522033
18. Halvorsen JA, Lien L, Dalgard F, Bjertness E, Stern RS. Suicidal ideation, mental health problems, and social function in adolescents with eczema: a population-based study. *J Invest Dermatol*. 2014;134(7):1847-1854. doi:10.1038/jid.2014.70
19. Mina S, Jabeen M, Singh S, Verma R. Gender differences in depression and anxiety among atopic dermatitis patients. *Indian J Dermatol*. 2015;60(2):211.
20. Dalgard FJ, Gieler U, Tomas-Aragones L, et al. The psychological burden of skin diseases: a cross-sectional multicenter study among dermatology out-patients in 13 European countries. *J Invest Dermatol*. 2015;135(4):984-991. doi:10.1038/jid.2014.530
21. Sorour F, Abdelmoaty A, Bahary MH, El Birqdar B. Psychiatric disorders associated with some chronic dermatologic diseases among a group of Egyptian dermatology outpatient clinic attendants. *J Egypt Womens Dermatol Soc*. 2017;14(1):31-36. doi:10.1097/01.EWX.0000503397.22746.bd
22. Noh HM, Cho JJ, Park YS, Kim JH. The relationship between suicidal behaviors and atopic dermatitis in Korean adolescents. *J Health Psychol*. 2016;21(10):2183-2194. doi:10.1177/1359105315572453
23. Dieris-Hirce J, Gieler U, Petrak F, et al. Suicidal ideation in adult patients with atopic dermatitis: a German cross-sectional study. *Acta Derm Venereol*. 2017;97(10):1189-1195. doi:10.2340/00015555-2741
24. Kwak Y, Kim Y. Health-related quality of life and mental health of adults with atopic dermatitis. *Arch Psychiatr Nurs*. 2017;31(5):516-521. doi:10.1016/j.apnu.2017.06.001
25. Lee S, Shin A. Association of atopic dermatitis with depressive symptoms and suicidal behaviors among adolescents in Korea: the 2013 Korean Youth Risk Behavior Survey. *BMC Psychiatry*. 2017;17(1):3. doi:10.1186/s12888-016-1160-7
26. Kye SY, Park K. Suicidal ideation and suicidal attempts among adults with chronic diseases: a cross-sectional study. *Compr Psychiatry*. 2017;73:160-167. doi:10.1016/j.comppsych.2016.12.001
27. Thyssen JP, Hamann CR, Linneberg A, et al. Atopic dermatitis is associated with anxiety, depression, and suicidal ideation, but not with psychiatric hospitalization or suicide. *Allergy*. 2018;73(1):214-220. doi:10.1111/all.13231
28. Lee SH, Lee SH, Lee SY, Lee B, Lee SH, Park YL. Psychological health status and health-related quality of life in adults with atopic dermatitis: a nationwide cross-sectional study in South Korea. *Acta Derm Venereol*. 2018;98(1):89-97. doi:10.2340/00015555-2797
29. Stang A. Critical evaluation of the Newcastle-Ottawa Scale for the assessment of the quality of nonrandomized studies in meta-analyses. *Eur J Epidemiol*. 2010;25(9):603-605. doi:10.1007/s10654-010-9491-z
30. Silverberg JI. Atopic dermatitis. *JAMA Dermatol*. 2014;150(12):1380. doi:10.1001/jamadermatol.2014.2757
31. Chang YS, Chou YT, Lee JH, et al. Atopic dermatitis, melatonin, and sleep disturbance. *Pediatrics*. 2014;134(2):e397-e405. doi:10.1542/peds.2014-0376
32. Bender BG, Ballard R, Canono B, Murphy JR, Leung DY. Disease severity, scratching, and sleep quality in patients with atopic dermatitis. *J Am Acad Dermatol*. 2008;58(3):415-420. doi:10.1016/j.jaad.2007.10.010
33. Kong TS, Han TY, Lee JH, Son SJ. Correlation between severity of atopic dermatitis and sleep quality in children and adults. *Ann Dermatol*. 2016;28(3):321-326. doi:10.5021/ad.2016.28.3.321
34. Halvorsen JA, Dalgard F, Thoresen M, Bjertness E, Lien L. Itch and pain in adolescents are associated with suicidal ideation: a population-based cross-sectional study. *Acta Derm Venereol*. 2012;92(5):543-546. doi:10.2340/00015555-1251
35. Brandt EB, Sivaprasad U. Th2 cytokines and atopic dermatitis. *J Clin Cell Immunol*. 2011;2(3):110. doi:10.4172/2155-9899.1000110
36. Koo J, Marangell LB, Nakamura M, et al. Depression and suicidality in psoriasis: review of the literature including the cytokine theory of depression. *J Eur Acad Dermatol Venereol*. 2017;31(12):1999-2009. doi:10.1111/jdv.14460
37. Davami MH, Baharlou R, Ahmadi Vasmehjani A, et al. Elevated IL-17 and TGF- β serum levels: a positive correlation between T-helper 17 cell-related pro-inflammatory responses with major depressive disorder. *Basic Clin Neurosci*. 2016;7(2):137-142.
38. Lindqvist D, Janelidze S, Hagell P, et al. Interleukin-6 is elevated in the cerebrospinal fluid of suicide attempters and related to symptom severity. *Biol Psychiatry*. 2009;66(3):287-292. doi:10.1016/j.biopsych.2009.01.030
39. Simpson EL, Akinlade B, Ardeleanu M. Two phase 3 trials of dupilumab versus placebo in atopic dermatitis. *N Engl J Med*. 2017;376(11):1090-1091. doi:10.1056/NEJMc1700366
40. Jiménez Flores P, Jiménez Cruz A, Bacardi Gascón M. Body-image dissatisfaction in children and adolescents: a systematic review [in Spanish]. *Nutr Hosp*. 2017;34(2):479-489.
41. Delfabbro PH, Winefield AH, Anderson S, Hammarström A, Winefield H. Body image and psychological well-being in adolescents: the relationship between gender and school type. *J Genet Psychol*. 2011;172(1):67-83. doi:10.1080/O0221325.2010.517812
42. Simpson EL, Guttman-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(8):903-912. doi:10.1001/jamadermatol.2018.1572
43. Kroenke K, Spitzer RL, Williams JB. The Patient Health Questionnaire-2: validity of a two-item depression screener. *Med Care*. 2003;41(11):1284-1292. doi:10.1097/01.MLR.0000093487.78664.3C
44. McDonald K, Shelley A, Jafferany M. The PHQ-2 in dermatology: standardized screening for depression and suicidal ideation. *JAMA Dermatol*. 2018;154(2):139-141. doi:10.1001/jamadermatol.2017.5540
45. Posner K, Brown GK, Stanley B, et al. The Columbia-Suicide Severity Rating Scale: initial validity and internal consistency findings from three multisite studies with adolescents and adults. *Am J Psychiatry*. 2011;168(12):1266-1277. doi:10.1176/appi.ajp.2011.10111704