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Depression and psychological distress in US adults with atopic dermatitis

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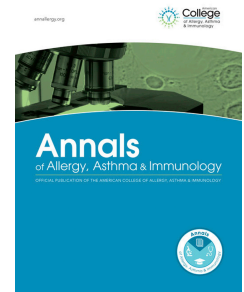
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Title: Depression and psychological distress in US adults with atopic dermatitis
Short Title: Psychological distress in AD

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Abbreviations used: ICD-9-CM=International Classification of Disease 9th edition Clinical Modification; MEPS=Medical Expenditure Panel Survey; FPL=federal poverty level; OR=odds ratio; CI=confidence interval; AD=atopic dermatitis; PHQ-2=Patient Health Questionnaire; K-6=Kessler psychological distress score

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1 Introduction

2 Atopic dermatitis (AD) is a chronic inflammatory skin condition that affects 7% of
3 adults¹⁻³ and 13% of children⁴ in the United States (US). Itch is the most burdensome symptom
4 in AD². However, other symptoms contribute to the burden of AD, including skin pain^{2, 5},
5 oozing/weeping, and sleep disturbance^{2, 6-8}. Previous studies found AD is also associated with
6 greater burden of anxiety and depression⁹⁻¹² and lower physical and social functioning.
7 Symptoms of anxiety and depression appear to contribute to the overall burden of AD^{11, 13, 14}. It
8 is thus important to understand the burden of mental health symptoms in AD. We hypothesized
9 that adults with AD have significantly higher psychosocial distress.

10 Mental health symptoms can occur in many chronic diseases^{15, 16}. However, mental
11 health symptoms may be particularly more likely to occur in AD than other chronic diseases. We
12 hypothesized that AD is associated with greater symptoms of depression and psychological
13 distress than psoriasis and many other chronic diseases. This study examines depressive
14 symptoms and psychological distress among US adults with AD, psoriasis, and other disorders.

Methods

Data source

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Data were analyzed from the 2004-2015 Medical Expenditure Panel Surveys (MEPS), a representative survey of the civilian non-institutionalized population in the US that is published by the Agency for Healthcare Research and Quality. MEPS data included socio-demographic characteristics, clinical diagnosis and procedure codes, and health status of approximately 15,000 US households annually. Surveys were administered in-person using computer-assisted personal interviewing technology. Interviews and surveys were conducted in English and Spanish. Sample weights provided by MEPS allowed for nationally representative estimates of health status across the adult US population. The study was approved by the Institutional Review Board at Northwestern University. This study design complies with all Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) recommendations¹⁷.

Identification of AD and controls

The study cohort comprised adults (age ≥ 18 years). AD and psoriasis were identified using *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)* codes (691 and 696, respectively). Medical conditions reported by interview respondents were recorded and converted by professional coders into ICD-9 codes. The control group for comparison included all MEPS participants without an indicated diagnosis of AD or psoriasis in the medical conditions file.

Variables

The primary outcomes in this study were mental health burden, as assessed by Patient Health Questionnaire (PHQ2) and Kessler Psychological Distress Scale (K6). PHQ2 (2 items, range 0-6) is a clinical screening tool for depression, based on the frequency of depressed mood and anhedonia over the previous two weeks. K6 (6 domains, range 0-24) assesses nervousness, hopelessness, restlessness, depression, effort, and worthlessness over a 30-day period. K6 scores ≥ 13 indicate serious psychological distress¹⁸.

Socio-demographic characteristics analyzed included age (18-39/40-59/60+ years), gender (male/female), race (white/black/multiracial-other), income (poor or negative/near poor/low income/middle income/high income), marital status (married/widowed, separated, or divorced/never married), and type of insurance coverage (private/public/none). Income strata were defined relative to the federal poverty level (FPL): poor/near poor/low income was <200% of FPL, middle income 200-<400% of FPL, and high income $\geq$ 400% of FPL.

Statistical analysis

All statistical analyses were performed using survey procedures that adjusted for sample weights, strata, and clustering in SAS (version 9.4, SAS Institute, Cary, NC). Summary statistics were generated for socio-demographic characteristics in those with vs. without AD or psoriasis. Weighted frequencies, prevalences, 95% confidence intervals (95% CI) were estimated. Rao-Scott χ^2 tests were used to compare categorical variables.

Binary logistic regression models were used to examine the impact of AD and psoriasis (independent variables) on positive screening for depressive symptoms (PHQ-2 $\geq$ 2) (dependent variable). Linear regression models were used to examine the impact of AD, psoriasis and other chronic conditions (independent variables) on overall K6 index (dependent variable). We also assessed two-way interactions of AD or psoriasis with asthma as predictors of K6 scores. Interactions were considered significant if the interaction-term P-value was significant ($P < 0.05$) and there was effect-modification $\geq$ 20%.

Binary logistic regression models were constructed to determine associations of AD or psoriasis with individual items from the PHQ-2, as the proportional odds assumption was not met for either item. Ordinal logistic regression models were constructed to determine associations of AD or psoriasis with individual items from the K6, as the proportional odds assumption was met for all models of K-6 items. Multivariable models adjusted for age (continuous) and sex (m/f). Adjusted odds ratios (aOR) and 95% CI were estimated. Multivariable linear regression models invoking stepwise variable selection ($\alpha=0.10$) were used to determine socio-demographic predictors of K6 index scores among adults with AD or psoriasis.

72 Complete case analysis was performed. A two-sided P-value ≤ 0.05 was considered
73 statistically significant.

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Results

Population characteristics

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The study cohort comprised a weighted frequency of 2,341,285,705 adults between 2004-2015, of which 436,918 reported a diagnosis of AD. Adults with vs. without AD were significantly younger (Rao-Scott Chi Square, $P=0.02$) (Table 1). Whereas, a diagnosis of psoriasis was associated with older age, higher income, white race, being married, and privately insured ($P\leq0.003$) (Table 2).

PHQ2 screening in AD and psoriasis

Adults with vs. without AD had a higher proportion (44.3% [21.1, 67.5%] vs 21.9% [21.5, 22.2%]) and odds (binary logistic regression; aOR [95% CI]: 2.86 [1.14, 7.16], $P=0.02$) of screening positive for depressive symptoms (PHQ2 ≥ 2). In particular, adults with AD were more likely to report depressed mood (aOR [95% CI]: 2.94 [1.05, 8.24], $P=0.04$) and anhedonia (2.47 [1.00, 6.12], $P=0.05$). Whereas, psoriasis was associated with no significant differences of prevalence (20.6% [17.6, 23.6%] vs 21.9% [21.5, 22.3%]) or odds (binary logistic regression; aOR [95% CI]: 0.92 [0.76, 1.10], $P=0.35$) of screening positive for depressive symptoms overall, or depressed mood (aOR [95% CI]: 0.90 [0.75, 1.07], $P=0.23$) or anhedonia (0.93 [0.78, 1.11], $P=0.42$) in particular. Adults with AD compared to psoriasis had significantly higher likelihood of screening positive for depression (aOR [95% CI]: 3.81 [1.49, 9.75], $P=0.006$).

K6 scores in AD and psoriasis

Adults with vs without AD had increased psychological distress (weighted mean [95% CI] K6 scores (6.5 [3.8, 9.1] vs 3.6 [3.5, 3.6]; linear regression: $P=0.04$). Further, adults with vs. without AD had higher prevalence [95% CI] (25.9% [7.0, 44.8%] vs 5.5% [5.3, 5.7%]) and odds (binary logistic regression, aOR [95% CI]: 6.04 [2.28, 15.99], $P=0.0003$) of severe psychological distress (K6 score ≥ 13). Whereas, psoriasis was not significantly associated with K6 scores overall (3.6 [3.2, 3.9] vs 3.6 [3.5, 3.6]), or severe psychological distress in particular (5.8% [4.0, 7.6%] vs 5.5% [5.3, 5.7%]; aOR [95% CI]: 1.06 [0.77, 1.45], $P=0.74$). Moreover, adults with AD were more likely to have severe psychological distress compared to those with psoriasis (aOR

[95% CI]: 6.92 [2.60, 18.41], $P=0.0001$). Similarly, other disorders were associated with higher K6 scores, including asthma, autoimmune disorders, urticaria, diabetes, hypertension, anxiety, depression, and other atopic disorders ($P\leq 0.02$) (Figure 1).

There were no significant two-way interactions of either AD or psoriasis with asthma ($P=0.35$ and 0.45) as predictors of K6 index scores.

In multivariable linear regression models invoking stepwise selection among adults with AD, K6 index scores were higher in those with poor/near poor/low income (adjusted beta [95% CI]: 6.22 [0.88, 11.56], $P=0.02$) and middle income (4.49 [0.39, 8.59], $P=0.03$), but lower in those of black (-7.36 [-11.70, -3.03], $P=0.002$) and other/multiple (-2.85 [-5.67, -0.03], $P=0.05$) race/ethnicity. Whereas, K6 scores were higher among adults with psoriasis who had poor/near poor/low (2.48 [1.76, 3.20], $P<0.0001$) and middle income (1.27 [0.56, 1.98], $P=0.0005$), public (2.01 [0.94, 3.08], $P=0.0003$) or no (1.24 [0.35, 2.14], $P=0.007$) insurance, but lower in those with black race (-1.26 [-2.18, -0.33], $P=0.008$).

Analysis of individual K6 items demonstrated that adults with AD had higher odds of feeling more hopeless (adjusted OR [95% CI]: 2.51 [1.10, 5.75]), restless (2.88 [1.03, 8.05]), apathy (3.20 [1.34, 7.64]), and worthless (3.06 [1.20, 7.80]) in multivariable models that adjusted for age and sex (Table 3). However, psoriasis was only associated with nervousness in multivariable models (1.17 [1.00, 1.36], $P=0.05$). When compared to psoriasis, AD was associated with higher odds of hopelessness (3.23 [1.36, 7.65]), restlessness (2.60 [1.17, 5.78]), sadness (2.57 [1.05, 6.27]), apathy (3.50 [1.60, 7.65]), and worthlessness (3.94 [1.56, 9.98]).

Discussion

This study found increased prevalence and severity of depression and/or psychological distress in US adults with AD, but not for psoriasis. In particular, this study found significant differences in domains of hopelessness, restlessness, depression, apathy, worthlessness, and social interactions. Psychological distress, as judged by K6 scores, was comparable in those with AD to those with anxiety and depression, and higher than those with psoriasis, urticaria, asthma, other atopic disease, autoimmune disease, diabetes, hypertension.

This study adds to previous studies that found increased mental health burden in adults with vs without AD. Two systematic reviews and meta-analyses examined the relationship of AD with depression, suicidality and/or anxiety. The first found significantly higher odds of AD with depression and anxiety in adults, depression in children, and suicidality in adults and adolescents¹⁹. The second included 36 studies with sufficient data for meta-analysis and found that 1 in 5 persons (20.1%) with AD had depression compared to only 14.8% in non-AD controls²⁰. In the US particularly, two studies found that approximately 1 in 5 adults with AD either met the SIGECAPS criteria for major depressive disorder or reported a healthcare diagnosis of depression in the previous year¹². AD patients had higher rates of clinical depression, antidepressant use, and suicidality in adults²⁰. A US population-based study of 2893 adults with vs. without AD found higher prevalences of abnormal (≥ 11) Hospital Anxiety and Depression - anxiety (28.6% vs. 15.5%) and depression (13.5% vs. 9.0%) subscores¹⁴. Mean and abnormal anxiety and depression scores were increased in moderate and severe AD, in particular¹⁴. The results of this study further show evidence of depressive symptoms, negative impacts on multiple aspects of mental health, and severe psychological distress in AD patients. Moreover, they suggest that the mental health burden of AD is greater than in psoriasis and many other chronic diseases. The mechanism underlying the association of AD with mental health burden is not fully elucidated. However, there is likely a cyclical relationship where AD worsens mental health symptoms, and mental health symptoms exacerbate AD. Chronic itch, pain, self-consciousness, and sleep disturbance negatively impact quality of life (QOL) and may worsen psychosocial distress^{21, 22}. In addition, elevated pro-inflammatory cytokines may affect neurotransmitter synthesis and metabolism, potentially contributing to the pathogenesis of mental disorders in AD²³. Differential activation of immune pathways in AD may explain why AD had a greater mental health burden than psoriasis and other chronic diseases. Future studies

are needed to elucidate the mechanisms of mental health disturbance in AD. In addition, the lower mental health burden observed in psoriasis and/or other chronic diseases than AD may be due to the availability of more effective therapeutic options. Future studies are needed to determine how the evolving therapeutic landscape in AD impacts the mental health of AD patients and societal burden of AD.

The high mental health burden of AD suggests a need for clinicians to screen for mental health when assessing and managing AD. Certainly, primary care and mental health providers should screen AD patients for symptoms of depression and anxiety. Allergists, dermatologists, and other specialists should also consider incorporating mental health screening into the assessment of AD patients. Multiple different screening assessments were used in clinical research studies, including the patient health questionnaire 9, Hamilton depression scale, Beck depression index, etc²⁰. Currently, Hospital Anxiety and Depression Scale is the only mental health scale that has specifically been validated in adults with AD¹¹. All of these assessments are feasible and can fairly easily be incorporated into almost any clinical practice setting. A recent US population-based study found that even adults with mild AD had increased odds of depression and anxiety; moderate-severe AD was associated with even higher odds of depression and anxiety¹⁴. Thus, while all AD patients may benefit from mental health screening, those with moderate-severe AD would most likely benefit from mental screening in clinical practice. Given the likely bidirectional relationship of AD and mental health symptoms, positive screening for psychological distress may warrant mental health intervention to ameliorate the symptoms and severity of AD. Previous reports showed some benefit for exposure-based cognitive behavior therapy²⁴ and mindfulness-based cognitive hypnotherapy²⁵ in AD. Previous studies found that AD treatments also can improve mental health symptoms. A case-control study found that conventional treatments, including emollients, topical corticosteroids, and anti-histamines, improved depressive symptoms (Hamilton Depression Scale)²⁶. A Japanese study found that “tight control” of AD using topical corticosteroids, calcineurin inhibitors, and oral cyclosporine improved depressive symptoms (Hopkins Symptoms Checklist for depression) in adults with severe²⁷. A phase 3, randomized, placebo-controlled trial found that dupilumab improved symptoms of depression and anxiety (Hospital Anxiety and Depression Scale) in adults with moderate-severe²⁸. AD patients might also benefit from multidisciplinary assessment and management with a care team that includes dermatologists, allergists, and mental health

providers in the outpatient and/or inpatient setting. However, additional research is needed to determine the optimal strategies for reducing psychological distress in AD. In addition, profound mental health burden may be an indicator of poorly controlled AD and prompt stepping up therapy.

Interestingly, K6 scores were lower among adults with AD who were black or multiracial/other race. This finding may be related to differences in the measurement properties of K6 across differential racial/ethnic groups; though, it is unknown if K6 performs differently across different race/ethnicities. Alternatively, there may be racial/ethnic and/or healthcare disparities in racial/ethnic minorities that drive poor mental health thereby mitigating the effects of AD on mental health. Future studies are needed to confirm and elucidate these findings.

Strengths of this study include the use of a nationally representative cohort of adults over a 12 year time-period. However, there are limitations. Data were unavailable for AD severity and phenotypes, which precluded a more detailed analysis of how different aspects of AD impact QOL. This cross-sectional study was unable to evaluate this directionality of the association between AD and mental distress. Future prospective studies are needed to determine the impact of clinical characteristics and global severity on AD humanistic burden.

In conclusion, this study found that AD is associated with more depressive symptoms and psychological distress overall, and even worse than many other chronic diseases. These findings highlight the need for clinicians to consider screening for and monitoring mental health symptoms in the assessment and management of AD patients. Future studies are needed to develop interventions to reduce psychological distress in AD.

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Table 1. Socio-demographic associations of clinical diagnosis of atopic dermatitis and psoriasis among US adults (n=212,071).

Characteristic	AD					Psoriasis				
	No		Yes			No		Yes		
	Wtd Freq	% Prev [95% CI]	Wtd Freq	% Prev [95% CI]	P*	Wtd Freq	% Prev [95% CI]	Wtd Freq	% Prev [95% CI]	P*
Sex					0.55					0.17
Male	1,068,542,114	45.6 [45.4, 45.9]	164,174	37.6 [11.6, 63.5]		1,060,878,378	45.6 [45.3, 45.9]	7,827,909	48.7 [44.3, 53.2]	
Female	1,272,743,592	54.4 [54.1, 54.6]	272,744	62.4 [36.5, 88.4]		1,264,784,453	54.4 [54.1, 54.7]	8,231,883	51.3 [46.8, 55.7]	
Age (years)					0.02					<0.0001
18-39	814,307,874	34.8 [34.1, 35.4]	298,422	68.3 [44.6, 92.0]		810,726,546	34.9 [34.2, 35.5]	3,879,751	24.2 [20.5, 27.8]	
40-59	861,724,470	36.8 [36.4, 37.3]	74,375	17.0 [0.0, 36.9]		855,932,904	36.8 [36.4, 37.3]	5,865,941	36.5 [32.9, 40.2]	
60+	665,253,361	28.4 [27.7, 29.1]	64,121	14.7 [0.0, 31.6]		659,003,382	28.3 [27.6, 29.0]	6,314,100	39.3 [35.1, 43.5]	
Income					0.25					<0.0001
Poor, near poor, low	666,716,849	28.5 [27.8, 29.2]	100,268	22.9 [3.3, 42.6]		663,679,076	28.5 [27.8, 29.2]	3,138,041	19.5 [16.8, 22.3]	
Middle income	700,801,610	29.9 [29.5, 30.4]	70,935	16.2 [0.0, 33.7]		696,395,136	29.9 [29.5, 30.4]	4,477,409	27.9 [24.6, 31.2]	
High income	973,767,246	41.6 [40.7, 42.5]	265,715	60.8 [36.0, 85.6]		965,588,620	41.5 [40.7, 42.4]	8,444,342	52.6 [48.7, 56.5]	
Race					0.19					<0.0001
White	1,919,839,775	82.0 [80.9, 83.1]	399,032	91.3 [81.6, 100.0]		1,905,851,617	81.9 [80.9, 83.0]	14,387,191	89.6 [87.3, 91.9]	
Black	256,673,443	11.0 [10.2, 11.8]	33,649	7.7 [0.0, 17.0]		256,008,535	11.0 [10.2, 11.8]	698,556	4.3 [2.9, 5.8]	
Multiracial/other	164,772,487	7.0 [6.3, 7.7]	4,238	1.0 [0.0, 3.0]		163,802,680	7.0 [6.3, 7.7]	974,045	6.1 [4.2, 7.9]	
Marital Status					0.13					0.003
Married	1,291,836,635	55.2 [54.5, 55.9]	130,785	29.9 [7.6, 52.2]		1,282,178,147	55.1 [54.4, 55.8]	9,789,273	61.0 [56.8, 65.1]	
Widowed/separated/divorced	501,903,627	21.4 [20.9, 21.9]	122,850	28.1 [4.7, 51.6]		498,576,637	21.4 [20.9, 21.9]	3,449,840	21.5 [18.1, 24.9]	
Never married	547,495,937	23.4 [22.9, 23.9]	183,284	41.9 [14.6, 69.3]		544,858,541	23.4 [23.0, 23.9]	2,820,680	17.6 [14.3, 20.8]	
Insurance coverage					0.98					<0.0001
Private	1,653,505,202	70.6 [69.9, 71.4]	309,378	70.8 [47.9, 93.7]		1,641,200,324	70.6 [69.8, 71.3]	12,614,256	78.5 [75.1, 82.0]	
Public	429,314,370	18.3 [17.7, 18.9]	86,131	19.7 [0.7, 38.7]		426,866,058	18.4 [17.7, 19.0]	2,534,443	15.8 [13.0, 18.6]	
None	258,466,132	11.0 [10.7, 11.4]	41,409	9.5 [0.0, 24.7]		257,596,449	11.1 [10.7, 11.5]	911,093	5.7 [3.8, 7.5]	

1 * Rao-Scott Chi square test
2 Bold face indicate statistically significant P-values.

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Table 2. Associations of AD or psoriasis with PHQ-2 and K-6 scores and items.

Variable	AD				Psoriasis			
	No	Yes			No	Yes		
	Wtd Freq (% Prev [95% CI])	Wtd Freq (% Prev [95% CI])	Adjusted OR [95% CI]	P	Wtd Freq (% Prev [95% CI])	Wtd Freq (% Prev [95% CI])	Adjusted OR [95% CI]	P
PHQ2								
<2	1,788,179,026 (78.1 [77.8, 78.5])	243,413 (55.7 [32.5, 78.9])	1.00 [ref]	–	1,775,904,530 (78.1 [77.7, 78.5])	12,517,909 (79.4 [76.4, 82.4])	1.00 [ref]	–
≥2	501,132,809 (21.9 [21.5, 22.2])	193,505 (44.3 [21.1, 67.5])	2.86 [1.14, 7.16]*	0.02	498,080,984 (21.9 [21.5, 22.3])	3,245,330 (20.6 [17.6, 23.6])	0.92 [0.76, 1.10]*	0.35
Depressed mood								
Not at all	1,682,637,283 (73.4 [73.0, 73.8])	208,344 (47.7 [21.3, 74.1])	1.00 [ref]	–	1,670,904,532 (73.4 [73.0, 73.7])	11,941,095 (75.7 [72.4, 78.9])	1.00 [ref]	–
Several/more than half the days/nearly every day	610,602,239 (26.6 [26.2, 27.0])	228,574 (52.3 [25.9, 78.7])	2.94 [1.05, 8.24]*	0.04	606,990,173 (26.6 [26.3, 27.0])	3,840,640 (24.3 [21.1, 27.6])	0.90 [0.75, 1.07]*	0.23
Anhedonia								
Not at all	1,681,897,819 (73.3 [72.9, 73.7])	232,585 (52.2 [30.2, 76.3])	1.00 [ref]	–	1,670,388,244 (73.3 [72.9, 73.7])	11,742,160 (74.3 [71.0, 77.6])	1.00 [ref]	–
Several/more than half the days/nearly every day	613,641,957 (26.7 [26.3, 27.1])	204,333 (46.8 [23.7, 69.8])	2.47 [1.00, 6.12]*	0.05	609,775,382 (26.7 [26.3, 27.1])	4,070,908 (25.7 [22.4, 29.0])	0.93 [0.78, 1.11]*	0.42
Kessler-6								
Severe distress: K6 ≥ 13								
No	2,146,813,989 (94.5 [94.3, 94.7])	323,643 (74.1 [55.2, 93.0])	1.00 [ref]	–	2,132,429,966 (94.5 [94.3, 94.7])	14,707,665 (94.2 [92.4, 96.0])	1.00 [ref]	–
Yes	124,971,397 (5.5 [5.3, 5.7])	113,276 (25.9 [7.0, 44.8])	6.04 [2.28, 16.00]*	0.0003	124,176,402 (5.5 [5.3, 5.7])	908,271 (5.8 [4.0, 7.6])	1.06 [0.77, 1.45]*	0.74
Nervousness								
None of the time	1,008,259,039 (43.9 [43.5, 44.3])	111,508 (25.5 [5.0, 46.0])			1,001,937,134 (43.9 [43.5, 44.3])	6,433,413 (40.8 [36.9, 44.8])		
Little/some of the time	1,162,435,353 (50.6 [50.2, 51.0])	289,068 (66.2 [43.2, 89.1])	1.89 [0.76, 4.73]**	0.17	1,154,360,156 (50.6 [50.2, 51.0])	8,364,265 (53.1 [49.2, 57.0])	1.17 [1.00, 1.36]**	0.05
Most/all of the time	126,335,656 (5.5 [5.3, 5.7])	36,342 (8.3 [0.0, 24.0])			125,418,993 (5.5 [5.3, 5.7])	953,004 (6.1 [4.4, 7.7])		
Hopeless								
None of the time	1,674,575,183 (73.0 [72.6, 73.4])	221,964 (50.8 [31.4, 70.2])	2.51 [1.10, 5.75]**	0.03	1,662,998,528 (73.0 [72.6, 73.4])	11,798,619 (74.8 [71.5, 78.2])	0.93 [0.79, 1.11]**	0.43
Little/some of the time	528,155,338	168,409			524,950,888	3,372,860		

	(23.0 [22.7, 23.3])	(38.5 [19.6, 57.5])			(23.0 [22.7, 23.4])	(21.4 [18.2, 24.5])		
Most/all of the time	91,027,586 (4.0 [3.8, 4.1])	46,545 (10.7 [0.0, 26.9])			90,475,839 (4.0 [3.8, 4.1])	598,292 (3.8 [2.4, 5.2])		
Restless								
None of the time	1,058,838,277 (46.2 [45.8, 46.6])	113,431 (26.0 [7.3, 44.6])	2.88 [1.03, 8.05]**	0.04	1,051,995,103 (46.2 [45.8, 46.6])	6,956,605 (44.3 [40.7, 47.8])	1.09 [0.95, 1.24]**	0.22
Little/some of the time	1,083,272,564 (47.3 [46.9, 47.6])	230,159 (52.7 [33.5, 71.9])			1,075,726,322 (47.2 [46.9, 47.6])	7,776,401 (49.5 [45.9, 53.0])		
Most/all of the time	150,105,672 (6.5 [6.4, 6.7])	93,329 (21.4 [2.3, 40.4])			149,218,622 (6.6 [6.4, 6.7])	980,379 (6.2 [4.6, 7.8])		
Depressed								
None of the time	1,761,475,351 (76.8 [76.4, 77.1])	253,569 (58.0 [36.4, 79.7])	2.42 [0.96, 6.06]**	0.06	1,749,434,496 (76.8 [76.4, 77.1])	12,294,424 (78.0 [74.8, 81.1])	0.96 [0.80, 1.15]**	0.63
Little/some of the time	460,525,721 (20.1 [19.8, 20.4])	132,970 (30.4 [10.0, 50.9])			457,726,729 (20.1 [19.8, 20.4])	2,931,961 (18.6 [15.6, 21.6])		
Most/all of the time	72,252,274 (3.1 [3.0, 3.3])	50,379 (11.5 [0.0, 27.8])			71,765,976 (3.1 [3.0, 3.3])	536,677 (3.4 [2.0, 4.8])		
Everything is an effort								
None of the time	1,296,873,159 (56.6 [56.1, 57.0])	139,061 (31.8 [13.3, 50.4])	3.20 [1.34, 7.64]**	0.009	1,288,221,300 (56.6 [56.1, 57.0])	8,790,920 (55.7 [51.8, 59.6])	1.00 [0.86, 1.17]**	0.98
Little/some of the time	806,574,862 (35.2 [34.9, 35.5])	193,840 (44.4 [25.8, 63.0])			801,011,228 (35.2 [34.8, 35.5])	5,757,473 (36.5 [32.9, 40.0])		
Most/all of the time	189,527,369 (8.3 [8.0, 8.5])	104,018 (23.8 [3.7, 43.9])			188,388,733 (8.3 [8.0, 8.5])	1,242,654 (7.9 [5.9, 9.9])		
Worthless								
None of the time	1,834,671,076 (80.1 [79.7, 80.4])	258,020 (59.1 [38.0, 80.1])	3.06 [1.20, 7.80]**	0.02	1,821,980,547 (80.0 [79.7, 80.4])	12,948,548 (82.2 [79.4, 85.1])	0.88 [0.72, 1.07]**	0.19
Little/some of the time	372,237,641 (16.2 [16.0, 16.5])	109,560 (25.1 [8.7, 41.4])			370,182,838 (16.3 [16.0, 16.5])	2,164,362 (13.7 [11.2, 16.2])		
Most/all of the time	84,552,776 (3.7 [3.6, 3.8])	69,339 (15.9 [0.0, 33.1])			83,991,117 (3.7 [3.6, 3.8])	630,998 (4.0 [2.5, 5.5])		

3 * Binary logistic regression
4 ** Ordinal logistic regression
5 All regression models includes age (continuous) and sex (male/female) as covariables.
6 Bold face indicate statistically significant P-values.

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7										
Table 3. Socio-demographic associations of increased Kessler-6 index among adults with AD or psoriasis.										
Characteristic	AD					Psoriasis				
	Mean [95% CI]	Crude Beta [95% CI]	P	Adj. Beta [95% CI]	P	Mean [95% CI]	Crude Beta [95% CI]	P	Adj. Beta [95% CI]	P
Sex										
Male	7.5 [-21.9, 37.0]	1.00 [ref]	-			3.1 [2.7, 3.6]	1.00 [ref]	-	1.00 [ref]	-
Female	5.8 [4.7, 7.0]	-1.72 [-8.45, 5.02]	0.0008			4.0 [3.5, 4.5]	0.86 [0.22, 1.51]	0.009	0.57 [-0.10, 1.24]	0.09
Age (years)										
18-39	5.2 [5.2, 5.2]	1.00 [ref]	-	1.00 [ref]	-	3.4 [3.0, 3.8]	1.00 [ref]	-	1.00 [ref]	-
40-59	4.8 [1.3-8.3]	-0.41 [-6.62, 5.80]	0.89	-1.52 [-5.29, 2.25]	0.41	3.8 [3.3, 4.4]	0.42 [-0.15, 1.00]	0.15	0.47 [-0.08, 1.03]	0.09
60+	14.3 [-12.6, 41.2]	9.07 [2.85, 15.29]	0.007	5.34 [-0.83, 11.50]	0.09	3.4 [2.7, 4.1]	-0.02 [-0.74, 0.69]	0.95	-0.23 [-0.93, 0.48]	0.53
Income										
Poor, near poor, low	11.9 [-15.9, 39.8]	7.73 [1.46, 13.99]	0.02	6.22 [0.88, 11.56]	0.02	5.8 [5.1, 6.5]	3.30 [2.57, 4.04]	<0.0001	2.48 [1.76, 3.20]	<0.0001
Middle income	7.1 [7.1, 7.1]	2.87 [-1.48, 7.23]	0.18	4.49 [0.39, 8.59]	0.03	4.0 [3.4, 4.6]	1.45 [0.76, 2.13]	<0.0001	1.27 [0.56, 1.98]	0.0005
High income	4.2 [3.4, 5.1]	1.00 [ref]	-	1.00 [ref]	-	2.5 [2.1, 3.0]	1.00 [ref]	-	1.00 [ref]	-
Race										
White	6.8 [-6.2, 19.8]	1.00 [ref]	-	1.00 [ref]	-	3.6 [3.2, 3.9]	1.00 [ref]	-	1.00 [ref]	-
Black	3.7 [3.7, 3.7]	-3.11 [-7.65, 1.43]	0.17	-7.36 [-11.70, -3.03]	0.002	3.2 [2.1, 4.2]	-0.44 [-1.46, 0.58]	0.40	-1.26 [-2.18, -0.33]	0.008
Multiracial/other	0.0 [0.0, 0.0]	-6.76 [-9.83, -3.70]	0.0002	-2.85 [-5.67, -0.03]	0.05	3.5 [2.5, 4.5]	-0.08 [-0.76, 0.61]	0.83	-0.12 [-0.72, 0.48]	0.69
Marital Status										
Married	4.8 [2.8, 6.7]	1.00 [ref]	-			3.1 [2.7, 3.6]	1.00 [ref]	-		
Widowed/separated /divorced	9.0 [-25.1, 43.0]	4.20 [-4.19, 12.58]	0.31			4.3 [3.6, 5.0]	1.14 [0.34, 1.95]	0.005		
Never married	6.0 [6.0, 6.0]	1.25 [-2.98, 5.47]	0.54			4.2 [3.6, 4.7]	1.04 [0.42, 1.66]	0.001		
Insurance coverage										
Private	4.4 [3.6, 5.1]	1.00 [ref]	-			3.0 [2.6, 3.4]	1.00 [ref]	-	1.00 [ref]	-
Public	13.0 [-13.5, 39.6]	8.66 [2.49, 14.84]	0.008			5.9 [4.9, 7.0]	2.94 [1.93-3.94]	<0.0001	2.01 [0.94, 3.08]	0.0003
None	8.3 [8.3, 8.3]	3.89	0.05			5.0 [3.9, 6.1]	1.97	0.0001	1.24	0.007

[0.98-2.96]

[0.35, 2.14]

8 Gray cells indicate that the variable was not included in the final selection models.

9 Bold face indicate statistically significant P-values.

