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Association between atopic dermatitis and hospitalization for mental health disorders in the United States

Derek Y. Hsu, MD[#1], **Ben Smith, BA**[#1], and **Jonathan I. Silverberg, MD, PhD, MPH**[#2]

[1]Department of Dermatology, Northwestern University Feinberg School of Medicine, Chicago, IL 60611

[2]Departments of Dermatology, Preventive Medicine and Medical Social Sciences, Northwestern University Feinberg School of Medicine, Chicago, IL, 60611

[#] These authors contributed equally to this work.

Abstract

Little is known about mental health (MH) emergencies in AD and their financial burden. We sought to determine hospitalization rates and costs of MH disorders in AD patients. We analyzed data from the Nationwide Inpatient Sample from 2002–2012, containing a representative 20% sample of US hospitalizations. Overall, 835 (1.36%) AD and 2,434,703 (0.75%) non-AD patients had a primary admission for a MH disorder. AD patients admitted for MH disorders were more likely to be younger, Asian and Black race, higher income-quartile, and have an increasing number of chronic conditions. In multivariable logistic regression models adjusting for demographics, AD was associated with a primary admission for mental health disorders in adults, including mood disorders, schizophrenia, and developmental disorders. AD was not associated with a primary admission for a MH disorder in children. There were an estimated $183,821,629 excess costs of care annually for MH disorders in inpatients with vs. without AD. In conclusion, AD was associated with higher odds of hospitalization for all MH disorders and substantial excess costs of inpatient care.

Corresponding author: Jonathan I Silverberg, MD, PhD, MPH, Department of Dermatology, Suite 1600, 676 N. St. Clair St., 312-503-4985, Northwestern University Feinberg School of Medicine, Chicago, IL 60611, JonathanISilverberg@Gmail.com.

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Study concept and design: JI Silverberg
Acquisition of Data: JI Silverberg, B Smith, DY Hsu
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atopic dermatitis (AD); eczema; burden; cost of care; mental health; depression; anxiety; suicidality; psychosis; schizophrenia; adjustment disorder; impulse disorder; hospitalization; inpatient; length of stay; morbidity; mortality; prognosis

Introduction

Atopic dermatitis (AD) is a chronic inflammatory skin disease affecting 13% of children[1] and 7–10% of adults in the United States[2, 3]. AD is associated with considerable morbidity, including the sequelae of itch, skin pain, sleep disturbance, difficulties with activities of daily living, relationships and performance at school and work[4-7]. In turn, these may lead to or exacerbate symptoms of depression, anxiety and/or inattentiveness in AD patients.

Previous studies demonstrated significantly higher rates of diagnosed depression, anxiety, and other mental health (MH) disorders in both children and adults with AD[8-11]. However, little is known about the financial burden of MH disorders in AD. In particular, MH emergencies often require hospitalization, which can be prolonged and costly[12]. We hypothesized that the AD patients have increased rates of hospitalization for psychiatric emergencies, prolonged length of stay and higher costs of care.

Previous studies found that the strongest associations with comorbid MH disorders in AD patients were disease severity and profound sleep disturbance[8, 10, 13]. This suggests that at least some MH comorbidity may be mitigated by improved control of AD. If so, then limited access to dermatologic and other specialty care for AD may be associated with poorer MH outcomes. We hypothesized that there are healthcare disparities of MH disorders in patients with AD. In the present study, we examined the associations of AD and MH hospitalizations in US children and adults.

Methods

We analyzed data from the 2002–2012 Nationwide Inpatient Sample (NIS) provided by the Healthcare Cost and Utilization Project (HCUP) from the Agency for Healthcare Research and Quality (AHRQ). Each year of NIS contains an approximately 20% stratified representative sample of all inpatient hospitalizations in the United States. Sample weights were created by NIS that factored the complex sampling design of US hospitals and allowed for representative estimates of discharges across the whole country. All data were de-identified and no attempts were made to identify any of the individuals in the database. All parties with access to the HCUP were compliant to HCUP's formal data use agreement. The study was approved by the institutional review board at Northwestern University.

Identification of AD and MH disorders

The NIS lists only one primary diagnosis and up to 24 secondary diagnoses. Per HCUP inpatient database standards, the first listed diagnosis is the principal diagnosis, i.e. the primary reason for hospitalization. The databases were searched for a primary and secondary diagnosis of AD using the *International Classification of Diseases, Ninth Revision, Clinical*

Modification (ICD-9-CM) codes 691.8. Primary and secondary diagnosis of AD were coded separately. We previously found the code 691.8 to be sufficiently valid to identify AD in the inpatient setting[14]. The control group included all patients without any diagnosis of AD, excluding live births and normal pregnancies, yielding a representative cohort of hospitalized patients in the US.

MH comorbidities were pre-coded according to Association for Healthcare Research and Quality (AHRQ) comorbidity measures and through the NIS Clinical Classification Software (CCS). Comorbidities pre-coded by the AHRQ also utilized Diagnosis-Related Groups (DRG) and thus would capture a higher frequency of the comorbidities in comparison to use of *ICD-9-CM* codes alone. Admission for a MH emergency was identified by a primary diagnosis of the disorder. A MH comorbidity was considered present with a secondary diagnosis of the disorder. The MH disorders, included mood disorders (including bipolar disorder and depression), anxiety, suicidality, substance abuse, cognitive, developmental, adjustment, impulse, personality, pediatric and other MH disorders and alcohol abuse. A variety of ICD-9-CM codes for mental health disorders, including those for alcohol abuse, depression[15], schizophrenia[16], suicide attempt, substance abuse[17], psychosis, bipolar disorder, and affective disorders[18], have been found to have strong positive predictive value for the use in epidemiological studies The codes used to create these variables are presented in Supplemental Table 1. A composite variable was created for any MH disorder.

Statistics

All data was processed using SAS 9.4 (SAS Institute, Cary, North Carolina). Baseline characteristics of patient subsets were determined. Complete case analysis was performed. A 2-sided P-value <0.05 was taken to indicate statistical significance for all estimates.

The prevalence of having a primary or secondary MH disorder was determined in children and/or adults with or without AD. Results were stratified by sex (male/female), race (white/black/Hispanic/other), insured (yes/no) and age (by decade). To examine the associations of AD with any MH comorbidities as well as with a primary admission for MH emergencies, multivariable logistic regression models adjusting for age, sex, and race/ethnicity were constructed with any diagnosis or a primary diagnosis of each of the MH comorbidities as the dependent variables, respectively. Adjusted odds ratios (aOR) and 95% confidence intervals (CI) were estimated. Post hoc correction for multiple dependent tests was performed by minimizing the false discovery rate with the approach of Benjamini and Hochberg and corrected P-values are presented [19]. aOR and 95% CI were presented in Forest plots using OpenMeta Analyst, an open-source software supported by Brown University and the AHRQ.

Summary statistics were determined for length of stay (LOS) and cost of inpatient care, including total and geometric mean (95% CI). To determine the predictors of hospitalization, survey weighted multivariable logistic regression models were constructed with hospitalization for MH disorders as the dependent variable and AD as the independent variable. To determine the predictors of cost of care and LOS, multivariable linear regression models were constructed with log-transformed cost of care and LOS as the dependent

variables. Cost of care and LOS were log-transformed because they were not normally distributed. Other independent variables included age (0–4/5–10/11–17/18–39/40–59/60–79/≥80 yr), gender (male/female), race/ethnicity (white/black/Hispanic/Asian/Native American/other), mean annual income of the hospital zip-code (quartiles), health insurance coverage (yes/no; Medicare/Medicaid/private/self-pay/no charge/other) number of chronic conditions (0–1/2–5/≥6), season of admission (winter/spring/summer/autumn), and hospital location (metropolitan/fringe-metropolitan/micropolitan/not metropolitan or micropolitan; Northeast/Midwest/South/West) and admission year. Multivariable logistic regression models used stepwise selection from the abovementioned covariates (alpha<0.1).

Results

Overall, there were 68,490,364 (weighted 334,336,213) discharges captured in the NIS between the years 2002–2012 after exclusion of live births and normal pregnancies. Patients without AD were 54.1% female, 70.0% white, and a mean age of 57.2 years (Table 1). Among patients with AD, patients were 46.7% female, 46.2% white, and a mean age of 28.6 years.

Among patients with AD, 14,981 (16.36%) had a concomitant diagnosis of any MH disorder and 835 (1.36%) AD patients were primarily admitted for a MH disorder. In contrast, 51,709,075 (16.01%) patients without AD had a concomitant diagnosis of any MH disorder and 2,434,703 (0.75%) were primarily admitted for a MH disorder.

Association of demographics with AD patients

In multivariable logistic regression models adjusting for demographics, decreasing age (adjusted OR [95% CI] 5–10 yr: 0.64 [0.57–0.73]; 11–17 yr: 0.30 [0.27–0.33]; 18–39 yr: 0.068 [0.062–0.075]; 40–59 yr: 0.049 [0.045–0.054]; 60–79 yr: 0.034 [0.031–0.038]; 80+ yr: 0.035 [0.031–0.039]), Asian (3.01 [2.74–3.32]) and Black (1.44 [1.37–1.52]) race/ethnicity, higher income quartile (1^{st}: 0.85 [0.80–0.90]; 2^{nd}: 0.94 [0.89–1.00]; 3^{rd}: 0.99 [0.94–1.05]), increasing number of chronic conditions (2–5: 58.19 [30.83–109.81]; 6+: 118.21 [62.62–223.15]), and hospital in a metropolitan area (fringe/metro: 0.77 [0.74–0.81]; micropolitan: 0.70 [0.65–0.75]; not metropolitan or micropolitan: 0.78 [0.71–0.85]) were associated with hospitalization for MH disorders among patients with AD (Table II).

The prevalence of primary hospitalization for a MH disorder significantly decreased between 2002–2003 and 2006–2007, 2008–2009, and 2010–2012 among patients with and without AD (survey logistic regression; P<0.001).

Association of AD and primary admission for MH disorders

In multivariable logistic regression models adjusting for age, race/ethnicity and sex, AD was associated with admission for any MH disorder among adults (aOR [95% CI]: 1.78 [1.48–2.15]) but not children (0.68 [0.47–1.00]) (Figure 1). AD was associated with a primary admission for MH disorders, including mood disorders, schizophrenia, and developmental disorders. AD was not associated with primary admission for a MH disorder in children overall or for specific MH disorders.

Association of AD and any MH disorders

In multivariable logistic regression models, AD was associated with any (primary or secondary) diagnosis of MH disorders (130 [1.25–1.36]) (Figure 2). Among both adults and children, AD was associated with anxiety disorders and developmental disorders. However, AD was only associated with mood disorders, schizophrenia, cognitive disorders, suicide or self-inflicted injury, alcohol abuse, substance abuse, personality disorders, adjustment disorders, Attention deficit disorder / Attention deficit hyperactivity disorder (ADD/ADHD) or conduct disorders in adults but not children.

Cost of care and length of stay

The geometric-mean cost of inpatient care for any MH disorder was significantly higher in patients with vs. without AD ($12,112 vs. $4504, P<0.0001) (Table III). Geometric-mean cost of hospitalization was greater for patients with vs. without AD admitted for schizophrenia, mood disorders, personality disorders, substance-related disorders, disorders diagnosed in childhood, alcohol use disorder, cognitive disorders, impulse control disorders, ADD/ADHD, and miscellaneous mental health disorders. There were an estimated $183,821,629 excess costs of hospital care annually for MH disorders in patients with vs. without AD, with mood disorders, delirium/cognitive disorders, and anxiety disorders accounting for the most excess costs associated with MH disorders. For patients admitted primarily for a MH disorder with AD as a comorbidity, increased cost of care was associated with Asian and other race/ethnicity and hospital location in micropolitan area (linear regression; P<0.05 for all) (Table III).

The geometric mean LOS was significantly higher in patients with AD (15.51 days) vs. without AD (8.32; P<0.0001) for hospitalization for any MH disorder. The geometric mean LOS was greater for patients with AD vs. without AD for schizophrenia, mood disorders, personality disorders, alcohol use disorder, cognitive disorders, impulse control disorders, and other mental health disorders. There were an estimated 288,520 excess days of hospitalization annually for MH disorders in patients with vs. without AD, with mood disorders, delirium/cognitive disorders, and anxiety disorders accounting for the most excess LOS associated with MH disorders. For patients admitted primarily for a MH disorder with AD as a comorbidity, increased LOS was not associated with any demographic factors.

Impact of AD on inpatient mortality

Patients who were admitted primarily for a MH disorder had similar inpatient mortality in those with vs. without AD (Table IV). None of the MH disorders demonstrated higher rates of mortality in AD patients.

Discussion

The present study found strong associations between AD and numerous MH disorders in both children and adults. In particular, AD was associated higher odds of primary admission for multiple MH disorders, including mood disorders, schizophrenia, and developmental disorders. Associations of MH disorders among AD patients were younger age, non-white race/ethnicity, increasing number of chronic conditions, and higher household-income. AD

was associated with increased LOS and cost of hospitalization for any MH disorder and when examined individually. However, AD was not associated with increased inpatient mortality among those primarily admitted primarily for a MH disorder. Taken together, the results of this study indicate that AD is associated with substantially increased morbidity from MH disorders, but not inpatient mortality. Moreover, AD was associated with an excess $180 million cost of hospitalization for a MH comorbidity.

This study expands on previous studies that demonstrated significantly higher rates of MH disorders in persons with vs. without AD[7, 8, 20, 21]. A US-population based survey (National Survey of Children's Health) found that children with vs. without AD had significantly higher prevalences of depression, anxiety, oppositional defiant and conduct disorders[8]. Two US-population based surveys found that approximately 1 in 5 adults with AD met SIGECAPS criteria for major depressive disorder (National Health and Nutrition Examination Survey) or were diagnosed by a healthcare provider with depression (National Health Interview Survey); the odds of depression were significantly higher in those with vs. without AD even after controlling for multiple potential confounders[7]. Previous studies also found higher incidence of major depressive disorder in Taiwanese adolescents/adults (1.42 vs. 0.20 per 1000 person-years)[20] and higher prevalence of depression in Korean males with vs. without AD (10.4% vs. 5.3%)[21]. A previous study from the Danish national health registries found higher rates of depression, anxiety, and suicidal ideation in the general population, increased use of antidepressant and anxiolytic mediation particularly among patients with moderate-severe AD, but no increased risk of hospitalization for depression, anxiety, or suicidality[22]. In contrast, we found significantly higher odds of hospitalization primarily for all MH disorders among those with vs. without AD. The higher rates of hospitalization for MH disorders observed in the US, but not Denmark, may be related to racial/ethnic disparities. This is supported by the association of MH admissions among AD patients who were non-white. However, there are likely other factors that contribute to increased hospitalization for MH disorders in AD.

The finding that AD is associated with significantly higher rates of multiple MH disorders has several clinical ramifications. AD patients should be screened for MH symptoms in the primary care, allergy and/or dermatology setting and treated with or referred for appropriate psychiatric care. AD patients with comorbid MH symptoms may warrant pharmacologic and/or psychotherapeutic management of their MH disorders. The optimal management approaches for such patients have not been studied. They may also warrant earlier, more aggressive topical and/or systemic treatments for their AD. However, it is yet unknown if more aggressive management of AD can mitigate the higher rates of MH disorders or lower the associated morbidity of AD while being hospitalized for a MH disorder.

The relationship between AD and MH is likely bidirectional. AD may directly cause or exacerbate MH symptoms, e.g. depression, anxiety and inattentiveness, secondary to chronic and bothersome itch, pain, sleep deprivation, self-consciousness and social isolation[23-25]. Many of these MH symptoms may be reversible with optimized management of patients' cutaneous disease. Whereas, stress and MH comorbidity may trigger AD[26]. In fact, worsening of skin disease by emotional factors is one of minor diagnostic criterion of AD

from Hanifin and Rajka[27]. Given the cross-sectional nature of the study, we were unable to assess the direction of association between AD and MH disorders.

Previous studies speculated multiple mechanisms by which AD upregulate neuroimmune factors, e.g. brain-derived neurotrophic factor[28], neuropeptide-induced sensitivity[29] and inflammatory cytokines, resulting in heightened sensitivity to stimuli[30, 31], poor sleep and the subsequent development of MH disorders[32, 33]. Sleep disturbance in AD might be related to chronic itch, inflammation[34, 35] and degree of atopy[36]. In turn, these sleep disturbances may unmask other psychiatric symptoms. Another potential contributor to MH disorders in AD patients is use of systemic corticosteroids for moderate-severe disease, which have been shown to cause multiple MH symptoms[37-39]. Unfortunately, we were not able to assess use of systemic corticosteroids and other medication history, as these were not recorded in the NIS database. The mechanisms of relationship between AD, sleep disturbance and MH disorders warrant further study.

Strengths of this study include an analysis of a nationally representative sample of all-payer data over a period of 11 years with over 65 million records. Limitations of this study include the inability to perform temporal analysis of comorbidities, as date of diagnosis was not present. We were unable to assess the medications used before, during, or after admission. Identification of comorbid health conditions was performed using ICD-9-CM and DRG codes and not by review of the health record. Some MH disorders can lead to impaired self-care and nutritional disorders with associated cutaneous eruptions, which may be misclassified as AD. The NIS lacks the ability to classify patients by the severity of the AD. Lastly, as there was no patient identifiers, patient re-hospitalization could not be identified.

In conclusion, AD was associated with a considerable MH burden, especially among adults, with higher prevalence of MH disorders, overall, and primary admissions, in particular, as well as increased LOS and cost of hospitalization for MH disorders, although without any substantial mortality. Future studies are needed to determine the optimal management approaches for their AD and MH disease.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations used:

AD	atopic dermatitis
ICD-9-CM	International Classification of Disease 9th edition Clinical Modification

LOS	length of stay
NIS	National Inpatient Sample
OR	odds ratio
CI	confidence interval
MH	mental health

References

1. Silverberg JI, Simpson EL. Association between severe eczema in children and multiple comorbid conditions and increased healthcare utilization. Pediatr Allergy Immunol. 2013;24(5):476–86. [PubMed: 23773154]
2. Silverberg JI, Garg NK, Paller AS, Fishbein AB, Zee PC. Sleep disturbances in adults with eczema are associated with impaired overall health: a US population-based study. J Invest Dermatol. 2015;135(1):56–66. [PubMed: 25078665]
3. Silverberg JI, Hanifin JM. Adult eczema prevalence and associations with asthma and other health and demographic factors: a US population-based study. The Journal of allergy and clinical immunology. 2013;132(5):1132–8. [PubMed: 24094544]
4. Vakharia P, Chopra R, Sacotte R, Patel K, Singam V, Patel N, et al. Burden of skin pain in atopic dermatitis. Annals of Allergy, Asthma and Immunology. 2018;In Press.
5. Mitchell AE, Fraser JA, Ramsbotham J, Morawska A, Yates P. Childhood atopic dermatitis: a cross-sectional study of relationships between child and parent factors, atopic dermatitis management, and disease severity. Int J Nurs Stud. 2015;52(1):216–28. [PubMed: 25441758]
6. Carroll CL, Balkrishnan R, Feldman SR, Fleischer AB, Jr., Manuel JC. The burden of atopic dermatitis: impact on the patient, family, and society. Pediatr Dermatol. 2005;22(3):192–9. [PubMed: 15916563]
7. Yu SH, Attarian H, Zee P, Silverberg JI. Burden of Sleep and Fatigue in US Adults With Atopic Dermatitis. Dermatitis. 2016;27(2):50–8. [PubMed: 26983091]
8. Yaghmaie P, Koudelka CW, Simpson EL. Mental health comorbidity in patients with atopic dermatitis. The Journal of allergy and clinical immunology. 2013;131(2):428–33. [PubMed: 23245818]
9. Yu SH, Silverberg JI. Association between Atopic Dermatitis and Depression in US Adults. J Invest Dermatol. 2015;135(12):3183–6. [PubMed: 26316069]
10. Strom MA, Fishbein AB, Paller AS, Silverberg JI. Association between atopic dermatitis and attention deficit hyperactivity disorder in U.S. children and adults. Br J Dermatol. 2016;175(5): 920–9. [PubMed: 27105659]
11. Whiteley J, Emir B, Seitzman R, Makinson G. The burden of atopic dermatitis in US adults: results from the 2013 National Health and Wellness Survey. Curr Med Res Opin. 2016:1–7.
12. Fulop G, Strain JJ, Vita J, Lyons JS, Hammer JS. Impact of psychiatric comorbidity on length of hospital stay for medical/surgical patients: a preliminary report. Am J Psychiatry. 1987;144(7): 878–82. [PubMed: 3111277]
13. Schmitt J, Chen CM, Apfelbacher C, Romanos M, Lehmann I, Herbarth O, et al. Infant eczema, infant sleeping problems, and mental health at 10 years of age: the prospective birth cohort study LISAplus. Allergy. 2011;66(3):404–11. [PubMed: 21029113]
14. Hsu D, Dalal P, Sable K, Voruganti N, Nardone B, West D, et al. Validation of international classification of disease ninth revision codes for atopic dermatitis. Allergy. 2017;72(7):1091–5. [PubMed: 27997983]
15. Fiest KM, Jette N, Quan H, St. Germaine-Smith C, Metcalfe A, Patten SB, et al. Systematic review and assessment of validated case definitions for depression in administrative data. BMC Psychiatry. 2014;14:289. [PubMed: 25322690]

16. Tonelli M, Wiebe N, Fortin M, Guthrie B, Hemmelgarn BR, James MT, et al. Methods for identifying 30 chronic conditions: application to administrative data. BMC Medical Informatics and Decision Making. 2015;15:31. [PubMed: 25886580]
17. Kim HM, Smith EG, Stano CM, Ganoczy D, Zivin K, Walters H, et al. Validation of key behaviourally based mental health diagnoses in administrative data: suicide attempt, alcohol abuse, illicit drug abuse and tobacco use. BMC Health Services Research. 2012;12(1):18. [PubMed: 22270080]
18. Davis KAS, Sudlow CLM, Hotopf M. Can mental health diagnoses in administrative data be used for research? A systematic review of the accuracy of routinely collected diagnoses. BMC Psychiatry. 2016;16:263. [PubMed: 27455845]
19. Benjamini Y, Hochberg Y. Controlling the False Discovery Rate: A Practical and Powerful Approach to Multiple Testing. Journal of the Royal Statistical Society Series B (Methodological). 1995;57(1):289–300.
20. Cheng CM, Hsu JW, Huang KL, Bai YM, Su TP, Li CT, et al. Risk of developing major depressive disorder and anxiety disorders among adolescents and adults with atopic dermatitis: a nationwide longitudinal study. Journal of affective disorders. 2015;178:60–5. [PubMed: 25795537]
21. Kim SH, Hur J, Jang JY, Park HS, Hong CH, Son SJ, et al. Psychological Distress in Young Adult Males with Atopic Dermatitis: A Cross-Sectional Study. Medicine. 2015;94(23):e949. [PubMed: 26061325]
22. Thyssen JP, Hamann CR, Linneberg A, Dantoft TM, Skov L, Gislason GH, et al. Atopic dermatitis is associated with anxiety, depression, and suicidal ideation, but not with psychiatric hospitalization or suicide. Allergy. 2018;73(1):214–20. [PubMed: 28632893]
23. Kantor R, Dalal P, Cella D, Silverberg JI. Research letter: Impact of pruritus on quality of life-A systematic review. J Am Acad Dermatol. 2016;75(5):885–6 e4. [PubMed: 27576705]
24. Lewis-Jones S Quality of life and childhood atopic dermatitis: the misery of living with childhood eczema. Int J Clin Pract. 2006;60(8):984–92. [PubMed: 16893440]
25. Chamlin SL, Frieden IJ, Williams ML, Chren MM. Effects of atopic dermatitis on young American children and their families. Pediatrics. 2004;114(3):607–11. [PubMed: 15342828]
26. Oh SH, Bae BG, Park CO, Noh JY, Park IH, Wu WH, et al. Association of stress with symptoms of atopic dermatitis. Acta dermato-venereologica. 2010;90(6):582–8. [PubMed: 21057740]
27. Hanifin J, Rajka G. Diagnostic features of atopic eczema. Acta dermato-venereologica. 1980;92:44–7.
28. Vinnik T, Kirby M, Bairachnaya M, Koman I, Tarkina T, Sadykova G, et al. Seasonality and BDNF polymorphism influences depression outcome in patients with atopic dermatitis and psoriasis. World J Biol Psychiatry. 2016:1–11.
29. Labrecque G, Vanier MC. Biological rhythms in pain and in the effects of opioid analgesics. Pharmacology & therapeutics. 1995;68(1):129–47. [PubMed: 8604435]
30. Shani-Adir A, Rozenman D, Kessel A, Engel-Yeger B. The relationship between sensory hypersensitivity and sleep quality of children with atopic dermatitis. Pediatr Dermatol. 2009;26(2): 143–9. [PubMed: 19419459]
31. Engel-Yeger B, Mimouni D, Rozenman D, Shani-Adir A. Sensory processing patterns of adults with atopic dermatitis. Journal of the European Academy of Dermatology and Venereology : JEADV. 2011;25(2):152–6. [PubMed: 20561126]
32. Buske-Kirschbaum A, Schmitt J, Plessow F, Romanos M, Weidinger S, Roessner V. Psychoendocrine and psychoneuroimmunological mechanisms in the comorbidity of atopic eczema and attention deficit/hyperactivity disorder. Psychoneuroendocrinology. 2013;38(1):12–23. [PubMed: 23141851]
33. Suarez AL, Feramisco JD, Koo J, Steinhoff M. Psychoneuroimmunology of psychological stress and atopic dermatitis: pathophysiologic and therapeutic updates. Acta dermato-venereologica. 2012;92(1):7–15. [PubMed: 22101513]
34. 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):415–20. [PubMed: 18280338]

35. Leo HL, Bender BG, Leung SB, Tran ZV, Leung DY. Effect of pimecrolimus cream 1% on skin condition and sleep disturbance in children with atopic dermatitis. The Journal of allergy and clinical immunology. 2004;114(3):691–3. [PubMed: 15446293]

36. Chang YS, Chou YT, Lee JH, Lee PL, Dai YS, Sun C, et al. Atopic dermatitis, melatonin, and sleep disturbance. Pediatrics. 2014;134(2):e397–405. [PubMed: 25022734]

37. Yu SH, Drucker AM, Lebwohl M, Silverberg JI. A systematic review of the safety and efficacy of systemic corticosteroids in atopic dermatitis. Journal of the American Academy of Dermatology. 2018;78(4):733–40 e11. [PubMed: 29032119]

38. Ciriaco M, Ventrice P, Russo G, Scicchitano M, Mazzitello G, Scicchitano F, et al. Corticosteroid-related central nervous system side effects. J Pharmacol Pharmacother. 2013;4(Suppl 1):S94–8. [PubMed: 24347992]

39. Brown ES, Chandler PA. Mood and Cognitive Changes During Systemic Corticosteroid Therapy. Prim Care Companion J Clin Psychiatry. 2001;3(1):17–21. [PubMed: 15014624]

Primary reason for admission	Age (yr)	AD: No Freq (%)	AD: Yes Freq (%)	aOR (95%CI)	P
Any mental health disorder	All	2,434,703 (0.75%)	835 (11.38%)	1.08 [0.91-1.28]	0.7
	≤18	177,132 (0.78%)	165 (3.62%)	0.68 [0.47-1.00]	0.1
	≥18	2,256,571 (0.75%)	666 (24.25%)	1.78 [1.48-2.15]	0.001
Mood disorders	All	4,573,147 (1.41%)	443 (6.04%)	0.93 [0.82-1.05]	0.4
	≤18	521,762 (2.29%)	58 (1.28%)	1.01 [0.81-1.27]	0.9
	≥18	4,051,385 (1.35%)	380 (13.85%)	1.55 [1.33-1.81]	0.001
Anxiety disorders	All	200,304 (0.062%)	191 (2.61%)	0.79 [0.43-1.47]	0.7
	≤18	27,335 (0.12%)	35 (0.75%)	1.41 [0.67-2.98]	0.7
	≥18	172,969 (0.058%)	157 (5.71%)	0.68 [0.22-2.11]	0.75
Schizophrenia	All	2,062,985 (0.64%)	47 (0.64%)	1.40 [1.16-1.69]	0.03
	≤18	37,488 (0.16%)	≤10	NE	-
	≥18	2,025,497 (0.67%)	47 (1.71%)	1.76 [1.45-2.14]	0.001
Delirium, dementia, or other cognitive disorder	All	303,920 (0.094%)	53 (0.72%)	0.97 [0.46-2.04]	0.9
	≤18	3,950 (0.017%)	≤10	NE	-
	≥18	299,970 (0.10%)	53 (1.93%)	1.20 [0.57-2.52]	0.8
Suicide or self-inflicted injury	All	9,549 (0.003%)	33 (0.45%)	NE	-
	≤18	1,072 (0.0047%)	≤10	NE	-
	≥18	8,477 (0.0028%)	24 (0.85%)	NE	-
Alcohol abuse	All	556,635 (0.17%)	105 (1.42%)	1.25 [0.84-1.87]	0.8
	≤18	10,432 (0.046%)	≤10	NE	-
	≥18	546,203 (0.18%)	99 (3.62%)	1.51 [1.01-2.26]	0.1
Substance Abuse	All	447,910 (0.14%)	125 (1.70%)	0.93 [0.58-1.51]	0.9
	≤18	19,818 (0.087%)	≤10	0.77 [0.29-2.08]	0.8
	≥18	428,093 (0.14%)	120 (4.37%)	1.07 [0.62-1.84]	0.9
Personality disorders	All	25,316 (0.0078%)	≤10	0.65 [0.09-4.59]	0.9
	≤18	2,335 (0.010%)	≤10	2.11 [0.29-15.19]	0.8
	≥18	22,981 (0.0076%)	≤10	NE	-
Developmental Disorder	All	12,796 (0.004%)	52 (0.71%)	2.80 [0.69-11.27]	0.4
	≤18	1,340 (0.0059%)	15 (0.33%)	NE	-
	≥18	11,456 (0.0038%)	37 (1.35%)	7.16 [1.79-28.59]	0.03
Adjustment Disorder	All	239,863 (0.074%)	34 (0.46%)	0.43 [0.20-0.96]	0.1
	≤18	39,401 (0.17%)	18 (0.40%)	NE	-
	≥18	200,462 (0.067%)	16 (0.58%)	1.05 [0.41-2.72]	0.9
Impulse Disorder	All	61,210 (0.019%)	NE	0.52 [0.33-0.84[]	0.04
	≤18	24,288 (0.11%)	≤10	NE	-
	≥18	36,923 (0.012%)	≤10	2.80 [0.91-8.58]	0.2
ADD/ADHD	All	54,840 (0.017%)	86 (1.17%)	0.06 [0.00-0.43]	0.03
	≤18	42,785 (0.19%)	31 (0.69%)	0.09 [0.01-0.64]	0.08
	≥18	12,055 (0.0040%)	55 (2.01%)	NE	-
Disorders diagnosed in childhood	All	22,054 (0.0068%)	14 (0.31%)	0.89 [0.37-2.15]	0.9
	≤18	16,041 (0.071%)	14 (0.31%)	0.72 [0.23-2.23]	0.8
	≥18	6,013 (0.0020%)	≤10	NE	-
Other psychiatric disorder	All	178,094 (0.055%)	28 (0.40%)	0.53 [0.24-1.19]	0.2
	≤18	22,751 (0.10%)	19 (0.41%)	2.37 [0.76-7.43]	0.2
	≥18	155,343 (0.052%)	≤10	0.86 [0.32-2.31]	0.9

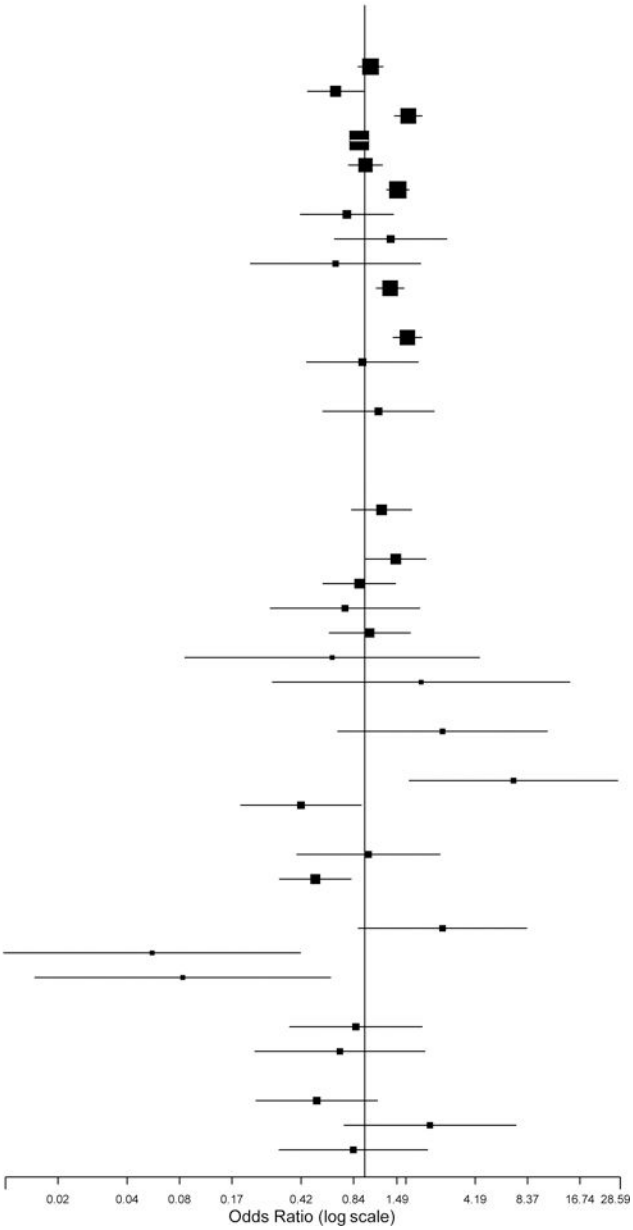

Figure 1.

Association between primary admission for MH disorders and atopic dermatitis. Survey logistic regression models were constructed with MH disorders as the independent variable and atopic dermatitis as the dependent variable. Odds ratios and 95% confidence intervals were estimated. Multivariate models included race/ethnicity, age and sex as covariates. Adjusted odds ratios and 95% confidence intervals were estimated. Forest-plots of the adjusted odds ratios and 95% confidence intervals are presented.

Mental health comorbidity	Age (yr)	AD: No Freq (%)	AD: Yes Freq (%)	aOR (95%CI)	P
Any mental health disorder	All	57,946,483 (17.93%)	14,981 (16.36%)	1.30 [1.25-1.36]	0.0002
	<18	1,753,062 (7.71%)	2,762 (5.74%)	1.13 [1.03-1.25]	0.02
	≥18	56,193,421 (18.70%)	12,097 (28.15%)	1.64 [1.56-1.73]	0.0002
Mood disorders	All	27,664,869 (8.56%)	6,940 (7.58%)	1.24 [1.17-1.32]	0.0002
	<18	858,576 (3.77%)	830 (1.73%)	0.93 [0.78-1.10]	0.5
	≥18	26,806,293 (8.92%)	6,028 (14.03%)	1.57 [1.47-1.68]	0.0002
Anxiety disorders	All	11,721,898 (3.63%)	3,255 (3.56%)	1.53 [1.41-1.66]	0.0002
	<18	329,232 (1.45%)	499 (1.04%)	1.46 [1.17-1.82]	0.002
	≥18	11,392,665 (3.79%)	2,735 (6.36%)	1.73 [1.58-1.90]	0.0002
Schizophrenia	All	5,148,204 (1.59%)	1,439 (1.57%)	1.31 [1.16-1.49]	0.0002
	<18	68,403 (0.30%)	89 (0.19%)	1.35 [0.84-1.90]	0.6
	≥18	5,079,801 (1.69%)	1,339 (3.11%)	1.56 [1.37-1.78]	0.0002
Delirium, dementia, or other cognitive disorder	All	12,565,460 (3.89%)	2010 (2.20%)	1.35 [1.21-1.50]	0.0002
	<18	27,372 (0.12%)	28 (0.058%)	0.88 [0.40-1.97]	0.8
	≥18	12,538,087 (4.17%)	1,982 (4.61%)	1.41 [1.26-1.57]	0.0002
Suicide or self-inflicted injury	All	2,458,914 (0.76%)	813 (0.89%)	0.89 [0.75-1.07]	0.3
	<18	204,190 (0.90%)	200 (0.42%)	1.08 [0.77-1.51]	0.7
	≥18	2,254,724 (0.75%)	579 (1.35%)	1.27 [1.03-1.57]	0.0002
Alcohol abuse	All	9,844,918 (3.05%)	2,253 (2.46%)	1.21 [1.09-1.34]	0.006
	<18	93,562 (0.41%)	63 (0.13%)	0.78 [0.42-1.46]	0.5
	≥18	9,751,356 (3.25%)	2,190 (5.10%)	1.34 [1.20-1.48]	0.0002
Substance Abuse	All	9,103,009 (2.82%)	2,122 (2.31%)	0.92 [0.82-1.02]	0.2
	<18	247,899 (1.09%)	162 (0.34%)	0.51 [0.35-0.76]	0.0002
	≥18	8,855,110 (2.95%)	1,915 (4.46%)	1.37 [1.21-1.56]	0.0002
Personality disorders	All	1,534,352 (0.47%)	484 (0.53%)	1.31 [1.05-1.63]	0.03
	<18	54,462 (0.24%)	42 (0.087%)	1.02 [0.53-1.96]	0.9
	≥18	1,479,890 (0.49%)	423 (0.98%)	1.62 [1.28-2.05]	0.0002
Developmental Disorder	All	1,720,933 (0.53%)	1,474 (1.61%)	1.42 [1.26-1.61]	0.0002
	<18	354,201 (1.56%)	898 (1.87%)	1.23 [1.06-1.44]	0.02
	≥18	1,366,732 (0.45%)	572 (1.33%)	2.36 [1.92-2.90]	0.0002
Adjustment Disorder	All	903,220 (0.28%)	382 (0.42%)	1.09 [0.84-1.41]	0.6
	<18	90,370 (0.40%)	106 (0.22%)	0.87 [0.52-1.44]	0.7
	≥18	812,850 (0.27%)	271 (0.63%)	1.96 [1.44-2.65]	0.0002
Impulse Disorder	All	237,861 (0.074%)	112 (0.12%)	0.52 [0.33-0.84]	0.02
	<18	71,618 (0.31%)	59 (0.12%)	1.15 [0.45-1.53]	0.7
	≥18	166,242 (0.055%)	54 (0.13%)	1.34 [0.64-2.83]	0.5
ADD/ADHD	All	1,310,009 (0.41%)	1,348 (1.47%)	0.90 [0.79-1.04]	0.2
	<18	602,012 (2.65%)	992 (2.06%)	1.14 [0.97-1.39]	0.2
	≥18	707,996 (0.24%)	342 (0.79%)	2.68 [2.06-3.49]	0.0002
Disorders diagnosed in childhood	All	298,309 (0.092%)	346 (0.38%)	0.87 [0.68-1.13]	0.4
	<18	165,392 (0.73%)	291 (0.62%)	1.09 [0.83-1.44]	0.6
	≥18	132,917 (0.044%)	55 (0.13%)	1.42 [0.64-3.17]	0.5
Other psychiatric disorder	All	1,110,919 (0.34%)	483 (0.53%)	1.40 [1.12-1.75]	0.05
	<18	83,156 (0.37%)	115 (0.24%)	1.11 [0.69-1.79]	0.7
	≥18	1,027,763 (0.34%)	46 (0.84%)	2.07 [1.61-2.68]	0.0002

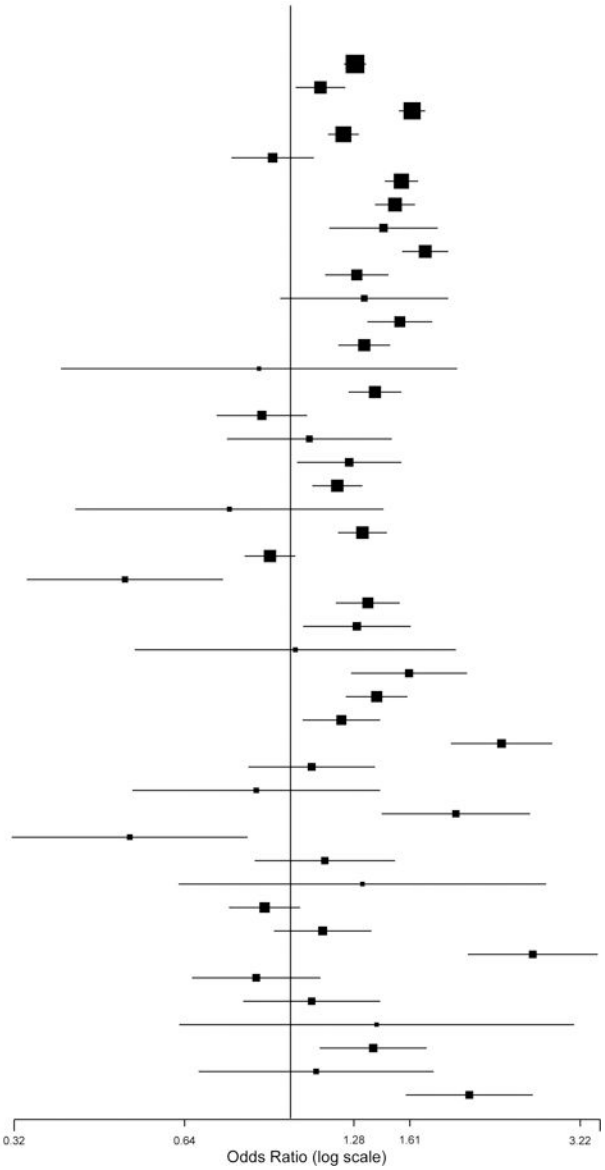

Figure 2.

Association between any diagnosis of a MH disorder and atopic dermatitis. Survey logistic regression models were constructed with MH disorders as the independent variable and atopic dermatitis as the dependent variable. Odds ratios and 95% confidence intervals were estimated. Multivariate models included race/ethnicity, age and sex as covariates. Adjusted odds ratios and 95% confidence intervals were estimated. Forest-plots of the adjusted odds ratios and 95% confidence intervals are presented.

Table 1.

Subject Demographics.

Variable	No AD	AD
Age (SD)	57.2 (0.003)	28.6 (0.21)
Female	36,787,940 (54.1%)	42,596 (46.7%)
Race/ethnicity		
White	37,890,139 (70.0%)	34,667 (46.2%)
Black	7,744,730 (14.3%)	21,313 (28.4%)
Hispanic	5,403,818 (9.9%)	10,290 (13.7%)
Asian	1,066,765 (2.0%)	4,129 (5.5%)
Native American	310,146 (0.6%)	662 (0.8%)
Multiracial/Other	7,471,109 (2.9%)	3,931 (5.2%)

Table II.

Associations of demographics with AD patients with psychiatric comorbidities

Variable	Adjusted OR [95% CI]	P-value
Age		
0–4	1.00 [ref]	-
5–10	0.64 [0.57–0.73]	<.0001
11–17	0.30 [0.27–0.33]	<.0001
18–39	0.068 [0.062–0.075]	<.0001
40–59	0.049 [0.045–0.054]	<.0001
60–79	0.034 [0.031–0.038]	<.0001
80+	0.035 [0.031–0.039]	<.0001
Season		
Winter	1.06 [1.007–1.19]	0.03
Spring	1.00 [ref]	-
Summer	0.98 [0.93–1.03]	0.4
Fall	0.96 [0.91–1.01]	0.1
Gender		
Female	1.02 [0.98–1.06]	0.4
Male	1.00 [ref]	-
Race		
White	1.00 [ref]	-
Black	1.44 [1.37–1.52]	<.0001
Hispanic	0.96 [0.89–1.03]	0.3
Asian	3.01 [2.74–3.32]	<.0001
Native American	1.09 [0.87–1.37]	0.4
Other	1.20 [1.08–1.34]	0.001
Income Quartile		
1	0.85 [0.80–0.90]	<.0001
2	0.94 [0.89–1.00]	0.051
3	0.99 [0.94–1.05]	0.9
4	1.00 [ref]	-
Insurance		
Medicare	0.93 [0.88–0.99]	0.02
Medicaid	0.88 [0.83–0.93]	<.0001
Private insurance	1.00 [ref]	-
Self-pay	0.78 [0.71–0.85]	<.0001
No charge	1.47 [1.18–1.82]	0.005
Other	0.99 [0.90–1.11]	0.9
Number of Chronic Conditions		
0–1	1.00 [ref]	-
2–5	58.19 [30.83–109.81]	<.0001
6+	118.21 [62.62-.223.15]	<.0001

Variable	Adjusted OR [95% CI]	P-value
Hospital Location		
Metropolitan ≥1million	1.00 [ref]	-
Fringe/Metro <1 million	0.77 [0.74–0.81]	<.0001
Micropolitan	0.70 [0.65–0.75]	<.0001
Not metropolitan or micropolitan	0.78 [0.71–0.85]	<.0001

Table III.

Survey weighted linear regression models of length of stay (LOS) and costs of care for hospitalization for mental health disorders among patients with atopic dermatitis.

Variable	LOS			Cost of care		
	LSM	Adjusted Beta [95% CI]	P-value	LSM	Adjusted Beta [95% CI]	P-value
Age						
0–17	2.10	Ref	-	8.81	Ref	-
18–39	2.08	−0.022 [−0.93–088]	0.9	8.59	−0.22 [−1.08–0.64]	0.6
40–59	2.03	−0.068 [−1.00–0.87]	0.9	8.92	0.11 [−0.75–0.97]	0.8
60–79	1.87	−0.23 [−1.15–0.68]	0.6	9.07	0.26 [−0.56–1.07]	0.5
80+	0.63	−1.46 [−3.46–0.53]	0.1	7.98	−0.83 [−2.91–1.24]	0.4
Gender						
Female	1.82	0.16 [−0.38–0.71]	0.6	8.61	−1.07 [−0.58–0.37]	0.7
Male	1.65	Ref	−	8.72	Ref	−
Race						
White	1.54	Ref	−	8.45	Ref	−
Black	1.60	0.061 [−0.62–0.75]	0.9	8.66	0.21 [−0.36–0.79]	0.5
Hispanic	1.38	−0.16 [−0.89–0.58]	0.7	7.62	−0.83 [−1.56- −0.095]	0.03
Asian	2.44	0.91 [−0.064–1.88]	0.1	9.36	0.91 [0.18–1.64]	0.01
Other	1.75	0.21 [−0.57–0.99]	0.9	9.30	0.085 [0.065–1.64]	0.03
Income Quartile						
1st to 25th percentile	1.76	−0.28 [−1.06–0.49]	0.5	8.49	−0.50 [−1.27–0.28]	0.2
26th to 50th percentile	1.71	−0.34 [−1.11–0.44]	0.4	8.62	−0.36 [−1.11–0.39]	0.3
51st to 75th percentile	1.45	−0.59 [−1.19–0.0067]	0.053	8.60	−0.38 [−0.97–0.21]	0.2
76th to 99th percentile	2.04	Ref	−	9.00	Ref	−
Insurance						
Medicaid	1.58	−0.11 [−0.77–0.54]	0.7	8.86	0.010 [−0.53–0.55]	0.9
Medicare	2.25	0.55 [−0.16–1.27]	0.1	8.74	−0.10 [−0.79–0.58]	0.8
Private insurance	1.70	Ref	−	8.85	Ref	−
Self-pay/Other	1.30	0.17 [−0.71–1.06]	0.7	8.20	−0.64 [−1.36–0.070]	0.08
Number of Chronic Conditions						
2–5	1.85	Ref	−	8.20	Ref	−
6+	1.80	−0.007 [−0.72–0.70]	0.9	8.53	0.30 [−0.43–1.04]	0.4
Hospital Location						
Metropolitan >1million	2.28	Ref	−	9.18	Ref	−
Fringe/Metro <1 million	1.72	−0.56 [−1.18–0.061]	0.08	8.57	−0.62 [−1.24–0.0037]	0.051
Micropolitan	2.35	0.074 [−1.02–1.17]	0.9	9.56	0.38 [−3.04- −0.54]	0.005
Not metropolitan or micropolitan	0.60	−1.67 [−2.79- −0.56]	0.004	7.39	−.179 [−3.04- −0.55]	0.005

LSM = Least squares means

Table IV.

Costs of care, length of stay and inpatient mortality for AD patients admitted for MH disorders.

Psychiatric comorbidity	No AD			AD		
	Mean Cost (SD)	Mean LOS (SD)	Inpatient mortality	Mean Cost (SD)	Mean LOS (SD)	Inpatient mortality
Any mental health disorder (without AD)	4,504 (6)	8.32 (0.018)	0.33%	12,112 (1298)	15.51 (1.83)	0%
Anxiety	3,625 (14)	6.80 (0.009)	0.05%	3,172 (661)	5.45 (0.70)	0%
Schizophrenia or other psychotic disorders	5,496 (8)	10.78 (0.023)	0.06%	9,642 (872)	20.37 (2.38)	0%
Mood disorders	3,882 (3)	6.80 (0.0084)	0.02%	8,976 (697)	11.57 (0.97)	0%
Personality disorders	3,494 (43)	6.00 (0.14)	0.02%	18,575 (10)	17.74 (2.48)	0%
Substance-related disorders	4,461 (13)	4.99 (0.011)	0.94%	6,763 (2038)	5.23 (0.025)	0%
Suicide or self-inflicted injury	2,649 (47)	2.82 (0.097)	0.05%	N/A	N/A	0%
Disorders diagnosed in childhood	4,961 (67)	9.09 (0.25)	0%	6,916 (2168)	8.00 (2.89)	0%
Alcohol use disorder	3,555 (8)	4.97 (0.021)	0.11%	5,186 (695)	6.85 (1.62)	0%
Miscellaneous mental health disorders	4,712 (22)	5.96 (0.052)	0.01%	7,836 (2959)	9.62 (3.44)	0%
Adjustment disorder	2,315 (9)	3.61 (0.023)	0.01%	2,316 (887)	4.16 (1.57)	0%
Delirium, dementia, other cognitive disorders	5,976 (19)	8.40 (0.055)	1.75%	8,454 (2660)	15.42 (6.16)	0%
Developmental disorders	4755 (83)	7.05 (0.41)	1.61%	4,200 (630)	5.36 (1.49)	0%
Impulse control disorders	3,993 (33)	8.88 (0.15)	0.04%	9,927 (3880)	22.81 (5.90)	0%
ADD/ADHD	4,334 (37)	9.15 (0.17)	0.03%	6,521 (1492)	8.54 (3.66)	0%