



UNITED STATES

Disease Burden

Prevalence, Diagnosis, and Comorbidities

The 2019 Atopic Dermatitis in America (ADIA) study found a prevalence of AD of 7.3% in a cohort of 1,278 US adults.⁴ Of those with AD, 28.9% had moderate disease and 11% had severe disease.

Extrapolating to the entire US population, the authors estimated that 6.6 million US adults in the US met criteria for moderate-to-severe AD.⁴ US children have an estimated AD prevalence between 6% and 12.98%⁶⁴; a cross-sectional study of 10 primary care practices in 5 US states found a lifetime prevalence of AD of 24% of US children aged 0 to 5 years;⁶⁵ a different study estimated a lifetime prevalence of 15% among children under the age of 1 and 38% among children aged 4 to 5 years.⁴⁴

Several studies have suggested that the prevalence of AD may vary across several demographic dimensions. The ADIA study found that the odds of receiving an AD diagnosis were higher for female patients (vs. male patients), for those with an annual household income of less than \$15,000 (vs. higher income categories), and for multiracial non-Hispanic patients (vs. white non-Hispanic patients).⁴ Similarly, Silverberg et al. found that AD was more prevalent in multiracial patients (14.6%) than in white patients (10.5%) and Black patients (7.7%).⁸⁰

Black patients may be at higher risk for undiagnosed AD because the morphology differs from the erythematous patches that physicians are trained to recognize in white patients.⁶⁶ Despite the possibility of underdiagnosis, some studies have found that AD is more prevalent and persistent in non-Hispanic Black children than in non-Hispanic white children.^{67,68} Similarly, a prospective cohort study of 4,898 women and children residing in 20 urban environments found that Black children had increased odds of having persistent AD. Additionally, the prevalence of AD among urban children of all races in the US was estimated at 15%,⁶⁹ higher than overall national

⁶⁴Silverberg, J. I. Public Health Burden and Epidemiology of Atopic Dermatitis. *Dermatol Clin* 35, 283–289 (2017).

⁶⁵Al-Naqeeb, J. et al. The Burden of Childhood Atopic Dermatitis in the Primary Care Setting: A Report from the Meta-LARC Consortium. *J Am Board Fam Med* 32, 191–200 (2019).

⁶⁶Vachiramon, V., Tey, H. L., Thompson, A. E. & Yosipovitch, G. Atopic Dermatitis in African American Children: Addressing Unmet Needs of a Common Disease. *Pediatric Dermatology* 29, 395–402 (2012).

⁶⁷Abuabara, K. et al. Genetic ancestry does not explain increased atopic dermatitis susceptibility or worse disease control among African American subjects in 2 large US cohorts. *J Allergy Clin Immunol* 145, 192–198.e11 (2020).

⁶⁸Kim, Y. et al. Racial/ethnic differences in incidence and persistence of childhood atopic dermatitis. *J Invest Dermatol* 139, 827–834 (2019).

⁶⁹McKenzie, C. & Silverberg, J. I. The prevalence and persistence of atopic dermatitis in urban United States children. *Ann Allergy Asthma Immunol* 123, 173–178.e1 (2019).



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estimates.⁷⁰ In short, the evidence suggests multiracial patients, urban patients and Black patients experience the highest burden of disease and thus the highest concentration of unmet needs.

A wealth of US-based studies investigated comorbid conditions. Patients with AD have a heightened risk of autoimmune disorders,⁷¹ ocular disease,⁷² infections (including serious, extracutaneous, and systemic infections)⁷³, decreased physical activity,⁷⁴ headaches,⁷⁵ cardiovascular disease,⁷⁶ central obesity and high blood pressure (specifically in children with moderate-to-severe AD),⁷⁷ osteoporosis and osteopenia,⁷⁸ reduced bone mineral density (BMD) in children (particularly in malnourished children and Hispanic children),⁷⁹ and fractures and joint injury.⁸⁰ In general, disease severity is correlated with the likelihood of experiencing comorbidities.^{81,82}

Physical and Psychosocial Consequences

The burden inflicted directly by physical symptoms has been well described by several studies. The ADIA study found that AD patients were most bothered by itch, dryness and scaling, and red or inflamed skin.⁴ Skin pain has been identified as a separate, distinct symptom from itch and inflammation; skin pain was present in 61% of adults surveyed in the ADIA study and was reported to be caused most commonly by scratching, followed by fissures in the skin, skin inflammation, and to a lesser extent by burning/stinging from topicals.⁸³

The severity and persistence of physical symptoms translates into poorer quality of life in many domains. In the ADIA study, patients with AD and especially those with severe disease involvement had higher scores (denoting poorer outcomes) on the DLQI than control patients;⁴ among those with severe AD, 68.8% of patients reported a moderate to large effect on their quality of life.⁴

The QoL burden of AD can be compared quantitatively with other disease burdens via health utility metrics; in the US, these studies have focused on adults. In a cross-sectional study of 3,495 US adults with AD, Silverberg et al. used the SF-6D to determine health utilities scores. US adults with AD averaged an SF-6D score of 0.69, significantly lower than the 0.79 averaged by adults without AD. An even lower score was associated with severe AD (0.59). Interestingly, when AD disease onset was within 2 years of the survey, lower SF-6D scores than other chronic conditions such as autoimmune disorders, diabetes, food allergy, and heart disease were observed.²⁸ The

⁷⁰Hua, T. & Silverberg, J. I. Atopic dermatitis is associated with increased hospitalization in US children. *Journal of the American Academy of Dermatology* 81, 862–865 (2019).

⁷¹Narla, S. & Silverberg, J. I. Association between atopic dermatitis and autoimmune disorders in US adults and children: A cross-sectional study. *J Am Acad Dermatol* 80, 382–389 (2019).

⁷²Govind, K., Whang, K., Khanna, R., Scott, A. W. & Kwatra, S. G. Atopic dermatitis is associated with increased prevalence of multiple ocular comorbidities. *J Allergy Clin Immunol Pract* 7, 298–299 (2019).

⁷³Narla, S. & Silverberg, J. I. Association between atopic dermatitis and serious cutaneous, multiorgan and systemic infections in US adults. *Ann Allergy Asthma Immunol* 120, 66–72.e11 (2018).

⁷⁴Silverberg, J. I. et al. Atopic Dermatitis Is Associated with Less Physical Activity in US Adults. *J Invest Dermatol* 136, 1714–1716 (2016).

⁷⁵Silverberg, J. I. Association between childhood eczema and headaches: An analysis of 19 US population-based studies. *J Allergy Clin Immunol* 137, 492–499.e5 (2016).

⁷⁶Silverberg, J. I. Association between adult atopic dermatitis, cardiovascular disease, and increased heart attacks in three population-based studies. *Allergy* 70, 1300–1308 (2015).

⁷⁷Silverberg, J. I. et al. Central obesity and high blood pressure in pediatric patients with atopic dermatitis. *JAMA Dermatol* 151, 144–152 (2015).

⁷⁸Shahen, M. S. & Silverberg, J. I. Atopic dermatitis is associated with osteoporosis and osteopenia in older adults. *Journal of the American Academy of Dermatology* 80, 550–551 (2019).

⁷⁹Silverberg, J. I. Association between childhood atopic dermatitis, malnutrition, and low bone mineral density: a US population-based study. *Pediatr Allergy Immunol* 26, 54–61 (2015).

⁸⁰Garg, N. & Silverberg, J. I. Association between eczema and increased fracture and bone or joint injury in adults: a US population-based study. *JAMA Dermatol* 151, 33–41 (2015).

⁸¹Eckert, L. et al. The burden of atopic dermatitis in US adults: Health care resource utilization data from the 2013 National Health and Wellness Survey. *J Am Acad Dermatol* 78, 54–61.e1 (2018).

⁸²Shrestha, S. et al. Burden of Atopic Dermatitis in the United States: Analysis of Healthcare Claims Data in the Commercial, Medicare, and Medi-Cal Databases. *Adv Ther* 34, 1989–2006 (2017).

⁸³Silverberg, J. I. et al. Pain Is a Common and Burdensome Symptom of Atopic Dermatitis in United States Adults. *J Allergy Clin Immunol Pract* 7, 2699–2706.e7 (2019).

Medical Expenditure Survey (MEPS) also used the SF-6D and found significantly lower SF-6D scores in adults with versus without AD (0.69 vs. 0.76; $p = 0.04$). The SF-6D decreased further in AD patients with comorbid anxiety, depression, or lower SES.⁸⁴

Zimmerman et al. used a similar quality of life survey, the EQ-5D, as part of dermatology clinical trials of dupilumab. Among US adults who were unresponsive to topical therapy, those with moderate disease scored an average of 0.684, while those with severe AD scored 0.535 prior to treatment with dupilumab. Interestingly, these scores are lower than in European studies that used the EQ-5D; the European Tacrolimus Ointment Study found average scores of 0.770 and 0.665 among adults with moderate and severe AD, respectively.⁸⁵

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Other studies have examined the impact of AD on specific QoL dimensions—sleep, anxiety, and depression—and again, studies in the US context have focused predominantly on adults. Regarding sleep, the National Health and Nutrition Examination Survey (NHANES) found that patients with AD were more likely than controls to have sleep disturbances, a short sleep duration, difficulty falling asleep, early morning awakenings, feeling unrested, and feeling too fatigued to perform Instrumental Activities of Daily Living (IADLs).⁸⁶ Utilizing the 2012 National Health Interview Survey (NHIS), Silverberg et al. found that adults with AD were at higher odds of experiencing fatigue, daytime sleepiness, and insomnia after controlling for sleep duration, allergies, demographic factors, and body mass index (BMI). Adults with AD and either fatigue, sleepiness, or insomnia were at increased risk for poorer health status, absenteeism from work, and increased healthcare utilization.⁸⁷

Regarding psychiatric consequences, in an analysis of the 2013 US National Health and Wellness Survey, Eckert et al. compared patients with AD to non-AD controls and found significantly more anxiety (29.8% vs. 16.1%), depression (31.2% vs. 17.3%), and sleep disorders (33.2% vs. 9.2%).⁸¹ An analysis of the 2004–2015 Medical Expenditure Surveys (MEPS) found that adults with (vs. without) AD were more likely to screen positive for depression via the PHQ-2 assessment and severe psychologic distress via the Kessler-6 (K-6) index; patients with AD and low SES had even more severe K-6 scores.⁸⁸ An analysis of the 2005–2006 NHANES and 2012 NHIS databases found that adults with (vs. without) AD had a higher likelihood of depression as measured by the PHQ-9 survey; they also were more likely to have moderate or severe depression, to have had depression within the past year, and to have had depression ever in their lives.⁸⁹ Depression in AD has been associated with pruritus, sleep loss, unhappiness with the appearance of skin lesions, and personal financial costs.⁸⁹

The ADIA study also examined associations between AD and both anxiety and depression. 24.73% of adults with AD reported clinically significant anxiety and 13.98% met clinical criteria for depression;⁴ suggesting the presence of clinically significant, untreated mental health conditions in this population. Adults with (vs. without) AD also scored higher on the surveys for Hospital Anxiety and Depression Scale-Anxiety (HADS-A) and HADS-Depression (HADS-D).⁹⁰ Higher HADS-A and

⁸⁴ Cheng, B. T. & Silverberg, J. I. Association between atopic dermatitis and lower health utility scores in US adults. *Ann Allergy Asthma Immunol* 124, 88–89 (2020).

⁸⁵ Poole, C. D., Chambers, C., Allsopp, R. & Currie, C. J. Quality of life and health-related utility analysis of adults with moderate and severe atopic dermatitis treated with tacrolimus ointment vs. topical corticosteroids. *Journal of the European Academy of Dermatology and Venereology* 24, 674–678 (2010).

⁸⁶ Yu, S. H., Attarian, H., Zee, P. & Silverberg, J. I. Burden of Sleep and Fatigue in US Adults With Atopic Dermatitis. *Dermatitis* 27, 50–58 (2016).

⁸⁷ Silverberg, J. I., Garg, N. K., Paller, A. S., Fishbein, A. B. & Zee, P. C. Sleep disturbances in adults with eczema are associated with impaired overall health: a US population-based study. *J Invest Dermatol* 135, 56–66 (2015).

⁸⁸ Cheng, B. T. & Silverberg, J. I. Depression and psychological distress in US adults with atopic dermatitis. *Ann Allergy Asthma Immunol* 123, 179–185 (2019).

⁸⁹ Yu, S. H. & Silverberg, J. I. Association between Atopic Dermatitis and Depression in US Adults. *J Invest Dermatol* 135, 3183–3186 (2015).

⁹⁰ Silverberg, J. I. et al. Symptoms and diagnosis of anxiety and depression in atopic dermatitis in U.S. adults. *Br J Dermatol* 181, 554–565 (2019).

HADS-D scores reflected higher odds of self-reporting moderate, severe, or very severe disease (based on PO-SCORAD, PO-SCORAD itch, and POEM scores). Hsu et al.'s analysis of the National Inpatient Survey (NIS) revealed that a diagnosis of AD was associated with increased rates of hospitalization for all mental health disorders.⁹¹

Only a couple of studies have focused on mental health outcomes in children, specifically. An analysis of the 2007 National Survey of Children's Health found that children with vs. without AD were at higher risk for also having comorbid ADHD, depression, anxiety, conduct disorder, and autism; the association between each of these comorbidities increased in a dose-dependent fashion with the severity of AD.⁹² An analysis of the 2012 NHIS found that children with AD raised in family structures that differed from two married biological parents were more likely to have only good, fair or poor health (vs. very good or excellent overall health) and had a higher odds of depression, anxiety, or stress.⁹³



Caregiver Burden

A social media survey developed by Capozza et al. and posted on social media platforms measured the severity of the child's disease via POEM and asked caregivers about 8 domains of the impact of pediatric AD on caregivers: sleep, social isolation, time requirements, life decisions, family relationship dynamics, energy/fatigue, mental health impacts, and unmet treatment needs. Capozza et al. found that the child's disease severity correlated with increased sleep disturbances, low energy/fatigue, and an increased time burden among the caregivers. Further, caregivers reported significant mental health burden associated with caring for a child with AD, including anxiety, isolation, and depression.¹³

Balkrishnan et al. surveyed the parents/caregivers of children with AD before and after physician intervention. The parent/caregiver's perception of AD disease severity had the strongest correlation with the impact of the child's AD on the family.⁹⁴ An additional survey-based study by Balkrishnan et al. identified three factors that most strongly predicted an increased family impact score: the perception that the child's AD was severe (as in the previous study), the frequent use of nonmedical services for the care of AD, and the personal financial burden associated with the child's AD.⁹⁵

A study analyzing the impact of childhood disease on caregiver sleep patterns found that the caregivers of children with AD (vs. healthy children) were more likely to experience poor sleep quality, clinically significant insomnia, an average total sleep time of less than 6 hours, and waking at least once per week to care for their child's AD.⁹⁶

Financial Burden

US patients with AD face a heftier personal financial burden than in any other COI. The National Eczema Association (NEA)⁶ surveyed 1,118 US respondents with a median income between \$50,000-\$74,999; disease severity was minimal in 23.2%, somewhat controlled in 40.1%, moderate in 47.5%, and severe in 26.5%. The median annual OOP cost was \$600; 42% of respondents paid more than \$1000 annually, and 8.5% paid more than \$5000 annually. Another study compared the OOP costs in adult patients with AD versus adult patients without AD. Those with AD paid \$371-\$489 more OOP per person-year.⁶³ Also, individuals with both AD and an allergic condition (a common comorbidity) had a financial burden 1.5 times greater than individuals with AD alone.⁹⁷

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⁹¹Hsu, D. Y., Smith, B. & Silverberg, J. I. Association between atopic dermatitis and hospitalization for mental health disorders in the United States. *Dermatitis* 30, 54–61 (2019).

⁹²Yaghmaie, P., Koudelka, C. W. & Simpson, E. L. Mental Health Comorbidity in Atopic Dermatitis. *J Allergy Clin Immunol* 131, 428–433 (2013).

⁹³McKenzie, C. & Silverberg, J. I. Association of family structure with atopic dermatitis in US children. *J Am Acad Dermatol* 79, 638–644.e4 (2018).

⁹⁴Balkrishnan, R., Housman, T., Carroll, C., Feldman, S. & Fleischer, A. Disease severity and associated family impact in childhood atopic dermatitis. *Arch Dis Child* 88, 423–427 (2003).

⁹⁵Balkrishnan, R. et al. The family impact of atopic dermatitis in children: the role of the parent caregiver. *Pediatr Dermatol* 20, 5–10 (2003).

⁹⁶Meltzer, L. J. & Booster, G. D. Sleep Disturbance in Caregivers of Children With Respiratory and Atopic Disease. *J Pediatr Psychol* 41, 643–650 (2016).

⁹⁷Suh, D.-C. et al. Economic burden of atopic manifestations in patients with atopic dermatitis--analysis of administrative claims. *J Manag Care Pharm* 13, 778–789 (2007).

Several studies have identified the primary sources of OOP expenses. As a chronic condition, AD requires ongoing healthcare utilization, so patients with AD have more copays than patients without AD.⁶⁴ In the NEA survey, the three most common domains of OOP expenses were medical appointments, deductibles, and prescriptions (including some not covered by insurance); nonprescription healthcare products; and complementary, alternative, and cleaning products.⁶ Another study of OTC treatment costs found that US AD patients paid an average of \$9.94 monthly for moisturizers and \$7.88 monthly for OTC medications, resulting in an annual average of \$213 for non-prescription topical maintenance therapy.⁹⁸

Other studies have focused on expenses paid by the caregivers. In a study of caregivers of children with moderate-to-severe AD, Filanovsky et al. found that caregivers incurred an average of \$274 in monthly direct costs (e.g., healthcare, treatment) and \$199 in monthly indirect costs (e.g., absenteeism, childcare).⁹⁹ On average, 34.8% of the caregivers' monthly budget was spent on costs related to AD management, and this resulted in an additional emotional burden in lower income families.⁹⁹

Indirect costs affect adults with AD as well. Silverberg et al. found that AD was associated with lifestyle limitations, social interaction avoidance, and activity impairment.¹⁰⁰ An analysis of the 2013 US National Health and Wellness Survey found that adults with (vs. without) AD had higher rates of work absenteeism (9.9% vs. 3.6%) and activity impairment (33.6% vs. 25.2%).⁸¹ Whiteley et al. analyzed the same data and found that 30% of employed AD patients reported lost work productivity (vs. 16.3% of non-AD patients); furthermore, AD severity had a negative relationship with work productivity and a positive relationship with difficulty with daily activities.¹⁰¹ In a separate study, adult patients with (vs. without) AD were more likely to have lost workdays because of illness and to have paid for urgent care, emergency care, and hospitalizations.¹⁰²

Treatment

The high cost of medical care in the US heightens the need for effective therapies that reduce healthcare utilization, improve QoL, and minimize the side-effect profiles associated with current systemic therapies. In a study about the adequacy of existing systemic treatments for adults with moderate-to-severe AD, 38.3% reported no relief from oral corticosteroids, systemic immunosuppressant therapy (e.g., cyclosporine, azathioprine, mycophenolate mofetil, methotrexate, cyclophosphamide), or phototherapy in the preceding 12 months.¹⁰³ Armstrong et al. found that patients treated (vs. not treated) with immunosuppressant therapy required additional monitoring and were more likely to require systemic corticosteroids.¹⁰⁴ Dupilumab is a promising new therapy that has been estimated to add 1.9 Quality-Adjusted Life Years (QALYs), but it is currently expensive. At willingness-to-pay (WTP) thresholds of \$50,000, \$100,000, and \$150,000, the probability of dupilumab being cost-effective compared to usual therapy was determined to be 2%, 59%, and 88%, respectively.¹⁰⁵ At the other end of the severity spectrum, it is possible that improved emollient adherence may reduce the cost of AD treatment; a study has investigated this possibility in the UK⁵⁹ but not yet in the US.

There is much variation in the type of systemic therapy used to treat severe AD in US and Canadian children, suggesting an unmet need for optimal management in this patient population. Among children in the US and Canada, cyclosporine (CSA; 45.2%) and methotrexate (MTX; 29.6%) were the most common first-line systemic agents; MTX (31.3%) and mycophenolate mofetil (MMF; 30.4%) were the most common second-line agents; and azathioprine (AZA; 33.0%) and MMF (24.3%) were the most common third-line agents. The fact that no single agent comprises a majority of prescriptions at any level of treatment indicates substantial heterogeneity in prescribing practices. A larger issue may be parent and caregiver concern with such



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⁹⁸Anderson, R. T. & Rajagopalan, R. Effects of allergic dermatitis on health-related quality of life. *Curr Allergy Asthma Rep* 1, 309–315 (2001).

⁹⁹Filanovsky, M. G. et al. The Financial and Emotional Impact of Atopic Dermatitis on Children and Their Families. *J Pediatr* 169, 284–290.e5 (2016).

¹⁰⁰Silverberg, J. I. et al. Patient burden and quality of life in atopic dermatitis in US adults: A population-based cross-sectional study. *Ann Allergy Asthma Immunol* 121, 340–347 (2018).

¹⁰¹Whiteley, J., Emir, B., Seitzman, R. & Makinson, G. The burden of atopic dermatitis in US adults: results from the 2013 National Health and Wellness Survey. *Current Medical Research and Opinion* 32, 1645–1651 (2016).

¹⁰²Silverberg, J. I. Health Care Utilization, Patient Costs, and Access to Care in US Adults With Eczema: A Population-Based Study. *JAMA Dermatol* 151, 743–752 (2015).

¹⁰³Wei, W. et al. A real-world study evaluating adequacy of Existing Systemic Treatments for patients with moderate-to-severe Atopic Dermatitis (QUEST-AD): Baseline treatment patterns and unmet needs assessment. *Ann Allergy Asthma Immunol* 123, 381–388.e2 (2019).

¹⁰⁴Armstrong, A. W. et al. Real-world utilization patterns of systemic immunosuppressants among US adult patients with atopic dermatitis. *PLoS One* 14, (2019).

¹⁰⁵Zimmermann, M. et al. Economic Evaluation of Dupilumab for Moderate-to-Severe Atopic Dermatitis: A Cost-Utility Analysis. *J Drugs Dermatol* 17, 750–756 (2018).

treatments: 65.2% of pediatric dermatologists who responded to the survey said they did not prescribe systemic agents at all due to concerns held by parents and caregivers.¹⁰⁶

A systematic review found a lack of studies that examine the efficacy of systemic AD therapies in racial and ethnic minorities.¹⁰⁷ Unfortunately, the lack of research in this area may be contributing to poorer outcomes—Black children with AD tend to have worse disease control than non-Hispanic white children.⁶⁷ After investigating poorer treatment outcomes in minority patient populations, Vachiramon et al. recommended that providers emphasize emollient use and make dose adjustments for cyclosporine and phototherapy relative to the standard treatment courses for white patients.⁶⁶

The inadequacy of existing therapies translates into poor satisfaction among patients and caregivers. Paller et al.'s study of caregivers of children with AD found that 69% were “not at all satisfied” and 82% were at most “fairly satisfied” with current treatment options. Reasons for dissatisfaction included the messiness of topicals, ineffectiveness, cost, and side effects.¹⁰⁸ Patient and caregiver dissatisfaction with current treatments may drive the use of complementary and alternative medicine (CAM); an analysis of the 2007 NHIS found that 46.9% of children in the US used at least one CAM.¹⁰⁹ Unfortunately, certain common home-care practices may be detrimental to AD, suggesting a need for education on proper treatment guidelines in patients with AD and their caregivers.⁶⁵

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Interestingly, physicians view the existing prescription treatment options more favorably than patients—in a national survey, 91% responded that prescription treatment options for AD were “moderately” or “very” effective, while only 46% of patients reported the same.¹¹⁰ This overall satisfaction does not mean, however, that all physicians follow the same treatment strategies. A review of the NAMCS and National Hospital Ambulatory Care Survey (NHAMCS) databases revealed that dermatologists were more likely than non-dermatologists to prescribe higher potency TCS in accordance with evidence-based guidelines.¹¹¹

As in other countries, the effectiveness of existing topical regimens is often limited by patient and caregiver fears regarding TCS. In an interview-based study conducted with mothers of children with AD, treatment use was most affected by the ease of use, concerns about adverse effects of TCS, the physician-patient relationship, and education efforts.¹¹² Another study evaluated different education strategies and found, disappointingly, that patients' willingness to apply TCS was not affected by the type of explanation provided (namely, an explanation of the risks of not applying treatment versus the benefits of applying treatment).¹¹³ Among caregivers of children with AD, Curry et al. found that anchoring methods (e.g., proposing four-times-daily TCS therapy with the goal of improving adherence to a once-daily regimen) increased caregivers' willingness to treat children at least once daily with TCS.¹¹⁴

Finally, treatment effectiveness may be limited by the ability of patients and caregivers to understand the instructions for complicated regimens. Stringer et al. conducted a readability, suitability, and content analysis of eczema action plans (EAPs) submitted by the Society for Pediatric Dermatology and found that only one in five EAPs were written at or below the recommended 6th grade reading level.¹¹⁵ This shortcoming may be especially detrimental given that AD may be more prevalent among patients of lower SES,⁴ as discussed in the section on prevalence.

¹⁰⁶Totri, C. R. et al. Prescribing practices for systemic agents in the treatment of severe pediatric atopic dermatitis in the US and Canada: The PeDRA TREAT survey. *J Am Acad Dermatol* 76, 281–285 (2017).

¹⁰⁷Bhattacharya, T. & Silverberg, J. I. Efficacy of systemic treatments for atopic dermatitis in racial and ethnic minorities in the United States. *JAMA Dermatol* 150, 1232–1234 (2014).

¹⁰⁸Paller, A. S., McAlister, R. O., Doyle, J. J. & Jackson, A. Perceptions of physicians and pediatric patients about atopic dermatitis, its impact, and its treatment. *Clin Pediatr (Phila)* 41, 323–332 (2002).

¹⁰⁹Silverberg, J. I., Lee-Wong, M. & Silverberg, N. B. Complementary and alternative medicines and childhood eczema: a US population-based study. *Dermatitis* 25, 246–254 (2014).

¹¹⁰McAlister, R. O., Tofte, S. J., Doyle, J. J., Jackson, A. & Hanifin, J. M. Patient and physician perspectives vary on atopic dermatitis. *Cutis* 69, 461–466 (2002).

¹¹¹McGregor, S. P., Farhangian, M. E., Huang, K. E. & Feldman, S. R. Treatment of Atopic Dermatitis in the United States: Analysis of Data from the National Ambulatory Medical Care Survey. *J Drugs Dermatol* 16, 250–255 (2017).

¹¹²Fenerty, S. D., O'Neill, J. L., Gustafson, C. J. & Feldman, S. R. Maternal adherence factors in the treatment of pediatric atopic dermatitis. *JAMA Dermatol* 149, 229–231 (2013).

¹¹³Maghen, P. et al. Regardless of how risks are framed, patients seem hesitant to use topical steroids for atopic dermatitis. *British Journal of Dermatology* 181, 842–844 (2019).

¹¹⁴Curry, Z. A., Johnson, M. C., Unrue, E. L. & Feldman, S. R. Caregiver willingness to treat atopic dermatitis is not much improved by anchoring. *J Dermatol Treat* 30, 471–474 (2019).

¹¹⁵Stringer, T. et al. The readability, suitability, and content features of eczema action plans in the United States. *Pediatr Dermatol* 35, 800–807 (2018).

Healthcare

Utilization

A survey by Silverberg et al. found that one in ten adults with AD required an urgent care, ED, or hospital visit during the preceding year. Other risk factors for increased ED and urgent care visits included Black or Hispanic race, lower SES, and the insurance denial of AD prescriptions.¹¹⁶

Other studies have confirmed racial discrepancies in healthcare utilization for AD. Children with AD who indicated that their race was Black or “other” had higher odds of overnight hospitalization.⁷⁰ Black (vs. white) children with poorly controlled AD were less likely to be seen by a dermatologist.¹¹⁷ An analysis of 1990–1998 NAMCS data found that Black patients and Asian/Pacific islander patients were more likely than white patients to seek care for AD; the authors posit that unmet needs for treatment education and guidance may have driven this observation.¹¹⁸ A study by Fischer et al. found that after having at least one ambulatory care visit, non-Hispanic Black (vs. white) patients had higher healthcare utilization.¹¹⁹



Satisfaction with Care

An analysis of the Consumer Assessment of Healthcare Providers and Systems (CAHPS) data within the 2000–2015 MEPS survey data found that patients with (vs. without) AD were generally less satisfied with their healthcare; patients with AD also had lower odds of reporting the highest satisfaction in every category of CAHPS (listened carefully, explained in a way that was easy to understand, spent enough time, and showed respect). Other associations with lower patient satisfaction scores included low/middle income, non-white race/ethnicity, public/no insurance, and multimorbidity.¹²⁰ The suboptimal satisfaction of patients with AD has been replicated by other studies; Paller et al. found that only 44% of respondents were “a lot” or “very much” satisfied with the care provided by their physician; 50% were “somewhat” satisfied, and 6% were “not at all” satisfied.¹⁰⁸

Dissatisfaction may be rooted in different perceptions of disease severity and treatment options. Nearly one-third of patients with moderate-to-severe AD (based on DLQI scores) rated their disease as more severe than their physicians did.¹²¹ A survey study of parent-caregiver perceptions of pediatric AD found that although caregivers generally agreed with the physician’s assessment, those who disagreed tended to perceive their child’s AD as more severe than the physician.¹⁰⁸ Paller et al. found that patients preferred cream-based treatments while physicians preferred ointment-based treatments. Parents also expressed a desire for more educational content, including videos and access to support groups.¹⁰⁸

Patient-Centered Interventions

The literature search did not yield any additional intervention studies beyond those mentioned briefly in the Treatment section regarding TCS adherence.

Dissatisfaction may be rooted in different perceptions of disease severity and treatment options. Nearly one-third of patients with moderate-to-severe AD (based on DLQI scores) rated their disease as more severe than their physicians did.¹²¹

¹¹⁶Silverberg, J. I. et al. Atopic Dermatitis in US Adults: From Population to Health Care Utilization. *J Allergy Clin Immunol Pract* 7, 1524–1532.e2 (2019).

¹¹⁷Wan, J. et al. Racial/Ethnic Variation in Use of Ambulatory and Emergency Care for Atopic Dermatitis among US Children. *J Invest Dermatol* 139, 1906–1913.e1 (2019).

¹¹⁸Janumpally, S. R., Feldman, S. R., Gupta, A. K. & Fleischer, A. B. In the United States, blacks and Asian/Pacific Islanders are more likely than whites to seek medical care for atopic dermatitis. *Arch Dermatol* 138, 634–637 (2002).

¹¹⁹Fischer, A. H., Shin, D. B., Margolis, D. J. & Takeshita, J. Racial and ethnic differences in healthcare utilization for childhood eczema: an analysis of the 2001–2013 Medical Expenditure Panel Surveys. *J Am Acad Dermatol* 77, 1060–1067 (2017).

¹²⁰Cheng, B. T. & Silverberg, J. I. Atopic Dermatitis Is Associated With Lower Patient Satisfaction in US Adults. *Dermatitis* (2021) doi:10.1097/DER.0000000000000733.

¹²¹Wei, W. et al. Discordance Between Physician- and Patient-Reported Disease Severity in Adults with Atopic Dermatitis: A US Cross-Sectional Survey. *Am J Clin Dermatol* 18, 825–835 (2017).

KEY FINDINGS

A review in 2001 by Lapidus outlined three key areas for improvement: an accurate evaluation of the prevalence of AD; national programs to increase awareness of AD in healthcare systems, families, and schools with concurrent psychosocial intervention; and further research into treatment delivery methods, particularly for low-income patients.¹²² Much progress has been made toward the first goal—the factors associated with a higher odds of AD diagnosis, disease severity, QoL burden, and comorbidities are now so well described that the US appears to set a global standard in this regard. However, few studies have developed and tested patient-centered interventions (e.g., nurse-led education programs) that might alleviate the physical, psychosocial, and financial burdens of AD. Such studies exist in many other COI in this report, and US-specific studies should be conducted in light of important differences between the US and western European countries (namely, the diversity of the patient population and cost of healthcare).

An AD diagnosis confers a much greater financial burden on US patients than on patients in other COI. It is worth repeating that 42.6% of patients with moderate-to-severe disease paid \$1000 or more in annual OOP expenses, and 8.5% paid \$5000 or more.⁶ After considering indirect expenses such as work absenteeism, Filanovsky et al. found that the families of children with moderate-to-severe AD spent 34.8% of their monthly budget on expenses related to their child's AD.⁹⁹ Unsurprisingly, the personal financial burden is one of the main determinants of family impact. Especially in light of the cost of US healthcare and treatment, it may be worth investigating the possibility of reducing costs through interventions that promote regular moisturization even in the absence of a flare, as has been investigated in the UK and Denmark.

The physical and psychosocial consequences of AD are well characterized among US adults but not well studied in the pediatric population and only moderately well understood in caregivers. The existing evidence regarding caregivers' financial and sleep burdens suggest that pediatric dermatology clinical trials should include caregiver burden metrics as secondary endpoints. Otherwise, future US-based research should prioritize understanding the individual burden experienced across a diverse pediatric patient population, perhaps using the type of interview-based studies that have been insightful in Germany and the UK.

Finally, as in other COI, the current dissatisfaction of US patients and caregivers with both the available treatments and medical care lead to decreased adherence, and sometimes an increase in (costly) healthcare utilization. Studies in Germany and the UK show that educational interventions can be effective at increasing adherence to treatment regimens and improving QoL for patients and caregivers; perhaps similar initiatives should be pursued in the US as initially recommended by Lapidus.



¹²²Lapidus, C. S. Role of social factors in atopic dermatitis: The US perspective. *Journal of the American Academy of Dermatology* 45, S41–S43 (2001).