

The Disease Burden of Atopic Dermatitis

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■ Abstract

Recent studies have shed light on the nature of the burden of atopic dermatitis. Analysis of observational data has revealed the effect of atopic dermatitis in diverse areas such as work productivity, physical activity, mood, and risk of comorbidities beyond other atopic conditions.

Studies on adults with moderate to severe disease show that the symptoms and consequences of atopic dermatitis affect many aspects of their lives. A clearer understanding of the burden for patients can inform open, sensitive discussions about goals of therapy.

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■ Keywords

Atopic dermatitis; comorbidities; disease burden; mood; quality of life; sleep; work productivity

The impact of atopic dermatitis on patients in terms of symptoms and quality of life has been well characterized in children and their families.¹⁻⁴ Until recently, less study has been devoted to the effects on the lives of adult patients. A growing body of data about the impact of atopic dermatitis on the daily life and functioning of adults has yielded some startling information. Some findings are specific to those with moderate to severe disease, but others relate to a broad range of adults with atopic dermatitis.

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Moderate to Severe Atopic Dermatitis: Symptoms Nearly Every Day

Some of the most recent information about symptom frequency, severity, and quality of life in atopic dermatitis comes from patient-reported data collected during screening for a clinical trial of dupilumab, the first targeted biologic therapy to receive US Food and Drug Administration approval for treatment of atopic dermatitis. All trial participants were adults with moderate to severe atopic dermatitis (N=380). The findings paint a picture of a disease that affects many patients nearly every day, often at a severe level.¹

- High proportions of patients with moderate to severe atopic dermatitis reported experiencing dry, rough skin (91%), flaking skin (77.6%), cracking skin (66.6%), and even bleeding (51.1%) 5 to 7 days per week.
- The average itch score was the same as the worst itch score (mean, 6.5 of a 0-10 scale [2.1], Pruritus Numerical Rating Scale [NRS]).
- More than 60% of patients characterized their itch as either severe (46.3%) or unbearable (14.2%; 5-D Pruritus Scale).
- Most (85.8%) reported experiencing itch every day (Patient-Oriented Eczema Measure [POEM]).
- More than half (62.8%) said they experienced itch at least 12 hours/day (5-D Pruritus Scale).

Quality of Life

The impact of atopic dermatitis on health-related quality of life (HRQoL) on adults with moderate to severe (N=380) disease was pervasive. More than half (61.6%) of trial participants reported feeling embarrassed or self-conscious a lot or very much within the prior week. Substantial proportions of patients reported that atopic dermatitis affected their relationships (26.6%), sexual activities (19.2%), social and leisure activities (43.9%), work or studying (41.8%), and even clothes worn (57.9%).¹ All of these findings come from the Dermatology Life Quality Index.¹

Results of the 2013 US National Health and Wellness Survey found that self-reported atopic dermatitis (n=428) was associated with significantly poorer HRQoL, compared with not having the disease (n=74,572; $P<0.0001$; SF-36v2 Health Survey). The National Health and Wellness Survey is an Internet-based general population survey. About 42% of survey respondents with self-reported atopic dermatitis characterized their disease as mild (n=182); these findings thus apply to the full range of disease severity.⁵

Sleep Disruption and Its Consequences

Atopic dermatitis has significant impact on sleep in young children and their families. The disease also is associated with substantial sleep impairment among adult patients. In adults with moderate to severe atopic dermatitis (N=380), sleep was disrupted an average of 4.4 nights—more than half the prior week (weighted average, POEM). More than two-thirds of

patients in this population (68.2%) reported that itch delayed falling asleep and occasionally or frequently awakened them at night (5-D Pruritus Scale). For more than one-third (36.1%), sleep was disturbed every night (POEM). Another 55.0% said that sleep was disrupted 5 to 7 nights per week.¹

Analyses of data from two US population studies in which disease severity was not specified document more frequent sleep disruption in patients with self-reported atopic dermatitis than in others.^{6,7} One-third of adults with atopic dermatitis (33.4%) reported sleep disturbances to clinicians, compared with 23.7% of those without the disease (odds ratio [OR] 1.62, 95% confidence interval [CI], 1.10-2.38; $P=0.04$).⁶ These findings come from the 2005-2006 National Health and Nutrition Examination Survey (NHANES; $N=5563$). After adjusting for sociodemographic and lifestyle factors, people with atopic dermatitis also were more likely to report feeling unrefreshed, being overly sleepy during the day, and feeling as if they did not get enough sleep.⁶

Data from the 2012 US National Health Interview Survey ($N=34,613$ adults) reported similar findings. After adjustment for factors including sleep duration and other atopic disorders, adults with atopic dermatitis were roughly twice as likely as other respondents to report regular fatigue (OR 2.23; 95% CI 1.93-2.58), daytime sleepiness (OR 2.04; 95% CI 1.75-2.38), and insomnia (OR 1.83; 95% CI 1.59-2.12).⁷

Lack of sleep and feeling tired can result in functional consequences. People with atopic dermatitis were significantly more likely than others to report difficulty concentrating, remembering, eating, engaging in hobbies, handling finances, driving, and navigating public transportation due to fatigue in the 2005-2006 NHANES ($N=5563$).⁶

Reduced Physical Activity

On the postulation that disrupted sleep and eczematous lesions on the hands and feet may affect physical activity, researchers analyzed objective data from the 2005-2006 NHANES addressing this point. More than 3,000 adult participants in NHANES wore an actigraph for 7 days to measure physical activity. Self-reported atopic dermatitis (reported in 189/3,061) was associated with significantly less daily activity (average total daily counts; $P=0.03$) and moderate-vigorous physical activity ($P=0.02$). This association remained after controlling for sleep disturbance, depression, and comorbid asthma.⁸

Reduced Work Productivity

Analysis of data from the 2013 US National Health and Wellness Survey also found that atopic dermatitis was associated with substantial impact on work performance, as measured on the Work Productivity and Activity Impairment (WPAI) questionnaire (Figure 1). This instrument asks about work absenteeism (percentage of work time missed due to health), presenteeism (percentage of impairment while at work due to health), and overall work impairment (total percentage of work time missed due to absenteeism or presenteeism). Among the 428 survey respondents with self-reported atopic dermatitis, 182 reported mild disease and 184 characterized their disease as moderate to severe.⁵ Rates of absenteeism and overall work impairment were significantly higher among those with self-characterized moderate to severe atopic dermatitis.⁵ Consistent with these findings, nearly half (46.0%; $n=379$) of patients with moderate to severe atopic dermatitis indicated that itch frequently or always disrupted work or study (5-D Pruritus Scale).¹

Risk of Comorbidities in Atopic Dermatitis

Atopic Comorbidities

Multiple studies indicate that patients with atopic dermatitis are likely to have other atopic conditions. The rates of asthma and nasal allergies/hay fever were significantly higher among adults with self-reported atopic dermatitis ($n=349$) compared with non-atopic-dermatitis-affected controls ($n=698$) (24.1% vs 8.9% for asthma; 48.4% vs 24.4% for nasal allergies; atopic dermatitis patients and controls, respectively; $P<0.001$ for both comparisons). These data come from the 2013 US National Health and Wellness Survey. Participants with atopic dermatitis included those with mild ($n=146$) and moderate to severe ($n=160$) disease.⁹

In children, multiple datasets show high rates of atopic comorbidities. In a prospective study of more than 1,000 infants with atopic dermatitis over almost 3 years, approximately 11% developed asthma and 37% had one or more atopic comorbidities. Development of allergic rhinitis and food allergy correlated with baseline severity of atopic dermatitis.¹⁰ Data from a random sample of 10,000 adults in Leipzig, Germany, also reported significantly higher rates of allergic rhinitis (33.6% vs 13.1%) and asthma (19.9% and 7.6%) among those with atopic dermatitis compared with controls ($P<0.0001$).¹¹

A retrospective analysis of claims data found that patients with atopic dermatitis were significantly more likely than those without the disease to develop at least one of the following atopic conditions: asthma, allergic rhinitis, allergic conjunctivitis, or food allergy. Most of the data come from adults patients; roughly three-quarters of the patients included in this analysis were 20 years of age or older.¹²

Among a cohort of adults with moderate to severe atopic dermatitis ($N=380$), atopic comorbidities were common: 51.3% had allergic rhinitis, 40.3% had asthma, 24.2% had allergic conjunctivitis, and 60.5% had other allergies.¹

Other Immune-Mediated Inflammatory Diseases

Genetics studies have identified loci shared by atopic dermatitis and other immune-mediated inflammatory diseases. Analysis of data from German National Health Insurance beneficiaries up to age 40 found that patients with atopic dermatitis in 2005/2006

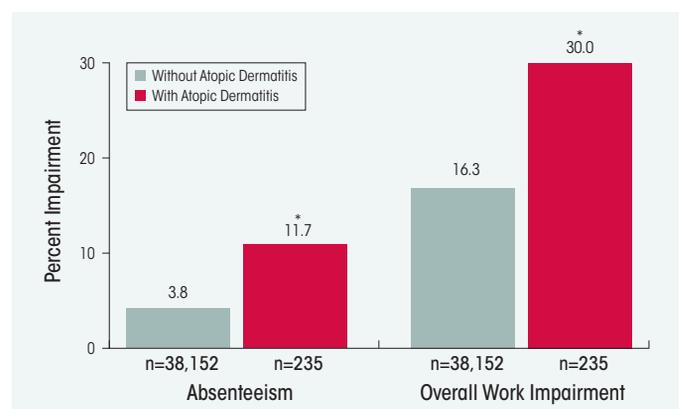


FIGURE 1 Atopic Dermatitis Work Performance.

Work Impaired in Patients With Atopic Dermatitis.

Percent lost productivity and activity impairment in the past week (WPAI). * $P=0.0001$ patients with atopic dermatitis versus patients without atopic dermatitis.

Source: Whitney J, et al.⁵

were at increased risk of incident rheumatoid arthritis (RA, risk ratio [RR], 1.72, 95% CI, 1.25-2.37), Crohn's disease (RR, 1.34; 95% CI, 1.11-1.61), and ulcerative colitis (RR, 1.25, 95% CI, 1.03-1.53) in 2007-2011.¹³ The presence of genetic loci associated with RA and inflammatory bowel disease did not explain the excess risk for these diseases among those with atopic dermatitis.¹³

Mood Disorders

In the 2013 US National Health and Wellness Survey, self-reported anxiety and depression were significantly more common in those with atopic dermatitis than in controls matched for demographic characteristics. Rates of anxiety were 29.8% and 16.1%; rates of depression, 31.2% and 17.3% (patients with atopic dermatitis and controls, respectively; $P < 0.001$). The rate of mood disorder did not differ significantly by severity of atopic dermatitis.¹⁴

Rates of anxiety and depression were high among a cohort of 380 patients with moderate to severe atopic dermatitis screened for a clinical trial. The Hospital Anxiety and Depression Scale (HADS) subscales for anxiety and depression (HADS-A and HADS-D, respectively) were used to assess mood symptoms. Nearly a quarter (24.2%) of those with moderate to severe atopic dermatitis had borderline abnormal levels of anxiety and 17.6% qualified for a diagnosis of clinical anxiety (score of ≥ 11). More than one-third (38.4%) had borderline-abnormal levels of depression (score of ≥ 8), and 10% would meet the criteria for a diagnosis of clinical depression (score of ≥ 11).¹

Rates of experience with bullying because of atopic dermatitis are high in children (39%) and with severe disease (33%).¹⁵ Psychological stresses may worsen itch and skin flares in those affected by AD, exacerbating the condition and contributing to the cycle of physical and mental distress.

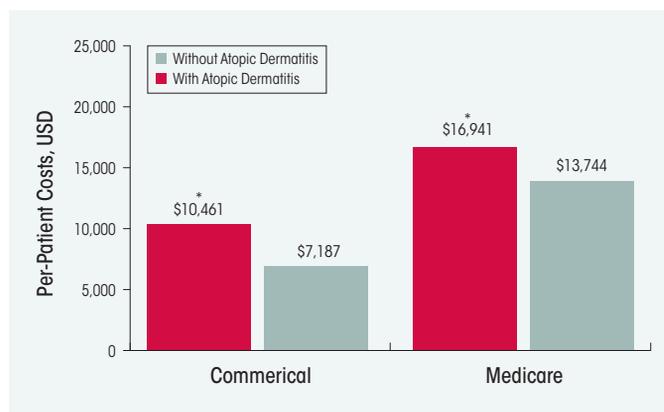
Higher Health Care Utilization and Costs

Analysis of data from adults in a commercial insurance database indicated that health care utilization over a 12-month period was significantly higher among those with atopic dermatitis ($n=83,106$) than in matched controls ($n=83,106$).¹⁶ Health care costs also were significantly higher for adults with atopic dermatitis (Figure 2).¹⁶

Self-reported data from the 2013 US National Health and Wellness Survey are consistent with these findings. The mean number of health care provider visits, emergency room visits, and hospitalizations over 6 months were significantly higher among those with atopic dermatitis than in matched controls.⁹ This survey did not collect medical expense data but the authors estimated the cost of visits using data stratified by age from the Medical Expenditure Panel Survey 2012. Mean annual total direct cost per patient was significantly higher for those with atopic dermatitis ($P < 0.001$).⁹

Summary

The effect of atopic dermatitis on adults in daily life is pervasive and invasive. Sleep disruption, daytime fatigue, reduced quality of life, less physical activity, missed time at work and impaired productivity when on the job, effect on mood, and increased risk of other, non-atopic comorbidities are among the burdens of this disease. A clearer picture of what patients face in daily life may build empathy and inform conversations with patients, as well as facilitate a more detailed discussion of desired treatment goals.



■ FIGURE 2 Medical Costs are Higher for Patients With Atopic Dermatitis.

Adjusted mean annual total per-patient costs.

Source: Shrestha S, et al.¹⁶

References

- Simpson EL, Bieber T, Eckert L, et al. Patient burden of moderate to severe atopic dermatitis (AD): insights from a phase 2b clinical trial of dupilumab in adults. *J Am Acad Dermatol*. 2016;74(3):491-498.
- Chamlin SL. The psychosocial burden of childhood atopic dermatitis. *Dermatol Ther*. 2006;19:104-107.
- 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;22:192-199.
- McKenna SP, Doward LC. Quality of life of children with atopic dermatitis and their families. *Curr Opin Allergy Clin Immunol*. 2008;8:228-231.
- 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;32(10):1645-1651.
- Yu SH, Attarian H, Zee P, Silverberg JI. Burden of sleep and fatigue in US adults with atopic dermatitis. *Dermatitis*. 2016;27(2):50-58.
- 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.
- Silverberg JI, Song J, Pinto D, et al. Atopic dermatitis is associated with less physical activity in US adults. *J Invest Dermatol*. 2016;136(8):1714-1716.
- Eckert L, Gupta S, Amand C, Gadkari A, Mahajan P, Gelfand JM. 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*. 2017. [Epub ahead of print]
- Schneider L, Hanifin J, Boguniewicz M, et al. Study of the atopic march: development of atopic comorbidities. *Pediatr Dermatol*. 2016;33(4):388-398.
- Treudler R, Zeynalova S, Walther F, Engel C, Simon JC. Atopic dermatitis is associated with autoimmune but not with cardiovascular comorbidities in a random sample of the general population in Leipzig, Germany. *J Eur Acad Dermatol Venereol*. 2017 Jul 31. [Epub ahead of print]
- Suh DC, Sung J, Gause D, Raut M, Huang J, Choi IS. Economic burden of atopic manifestations in patients with atopic dermatitis—analysis of administrative claims. *J Manag Care Pharm*. 2007;13(9):778-789.
- Schmitt J, Schwarz K, Baurecht H, et al. Atopic dermatitis is associated with an increased risk for rheumatoid arthritis and inflammatory bowel disease, and a decreased risk for type 1 diabetes. *J Allergy Clin Immunol*. 2016;137(1):130-136.
- Eckert L, Gupta S, Amand C, Gadkari A, Mahajan P, Gelfand JM. Impact of atopic dermatitis on health-related quality of life and productivity in adults in the United States: an analysis using the National Health and Wellness Survey. *J Am Acad Dermatol*. 2017;77(2):274-279.e273.
- Zuberbier T, Orlov SJ, Paller AS, et al. Patient perspectives on the management of atopic dermatitis. *J Allergy Clin Immunol*. 2006;118(1):226-232.
- Shrestha S, Miao R, Wang L, Chao J, Yuce H, Wei W. Burden of atopic dermatitis in the United States: analysis of healthcare claims data in the commercial, Medicare, and Medi-Cal databases. *Adv Ther*. 2017 Jul 13. [Epub ahead of print]