Incyte Dermatology

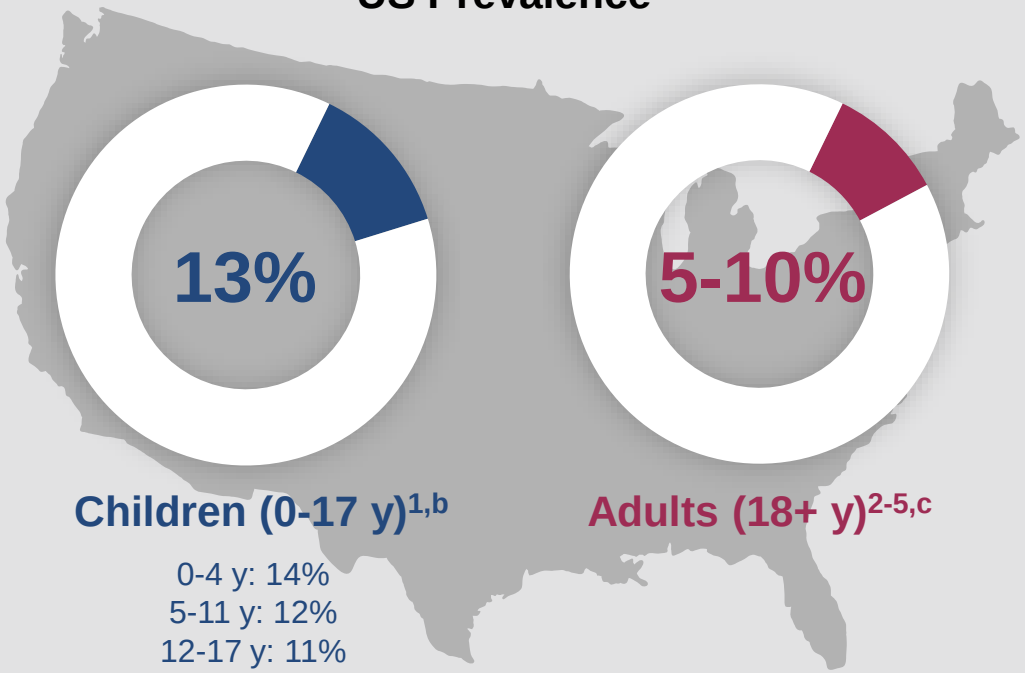
Atopic Dermatitis

Understanding the Pathophysiology and Burden of Disease

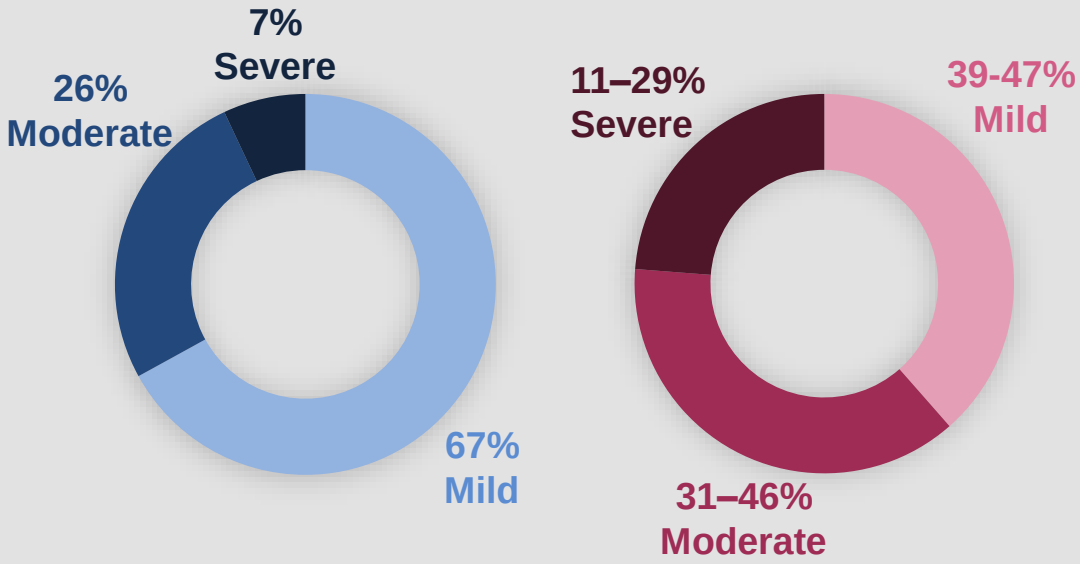
MSL-DIS-US-0023 09/22

Atopic Dermatitis Is One of the Most Common Inflammatory Skin Diseases That Affects Children and Adults

US Prevalence[a]



Disease Severity[a]



[a]Ranges are provided for prevalence and severity as variations exist in methodology, population evaluated, and PRO measure or definition of AD used. [b]US Health Interview survey of children aged 0 to 17 years. Based on the questions, "During the past 12 months, has [child's name] had any of the following conditions? Hay fever? Any kind of respiratory allergy? Any kind of food or digestive allergy? Eczema or any kind of skin allergy?" A child may be counted in more than one category. [c]Cross-sectional, population-based AD in America survey sampling the GfK Knowledge panel. AD was defined based on an adaptation of the UK working party criteria, which included having an itchy skin condition during the past 12 months. Respondents were asked, “Have you ever been diagnosed with a skin condition known as “eczema?” or “atopic dermatitis?” (yes/no/not sure). Self-assessments of AD severity included the PO-SCORAD index (range, 0-103), NRS-Itch (range, 0-10), and POEM (7 questions; range, 0-28). Limitations included all exposures and outcomes being assessed by self report and not verified by physical examination. [d]Cross-sectional, population-based, National Survey of Children’s Health from 2007-2008. AD prevalence was determined using the question, “During the past 12 months, have you been told by a doctor or other health professional that (child) had eczema or any kind of skin allergy?” Severity was determined using the question, “Would you describe (child’s name) eczema or skin allergy as mild, moderate, or severe?”

AD, atopic dermatitis; NRS, numeric rating scale; POEM, Patient-Oriented Eczema Measure; PO-SCORAD, Patient-Oriented SCORing Atopic Dermatitis; PRO, patient-reported outcome.

1. Summary Health Statistics: National Health Interview Survey, 2018. https://ftp.cdc.gov/pub/Health_Statistics/NCHS/NHIS/SHS/2018_SHS_Table_C-2.pdf [ftp.cdc.gov]. Accessed June 14, 2021. 2. Silverberg JI. *Dermatol Clin*. 2017; 35:283-289. 3. Chiesa Fuxench ZC, et al. *J Invest Dermatol*. 2019;139:583-590. 4. Silverberg JI, et al. *J Allergy Clin Immu*nol. 2013;132:1132-1138. 5. Silverberg JI, et al. *J Invest Dermatol*. 2015;135:56-66. 6. Silverberg JI,et al. *Dermatitis*. 2014;25:107-114. 7. Silverberg JI, et al. *J Allergy Clin Immunol Pract*. 2019;7:1524-1532.

The Clinical Phenotype of Atopic Dermatitis Differs by Age of Presentation

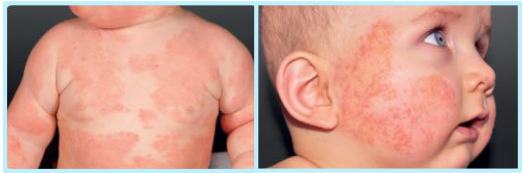
AD is a chronic, heterogeneous, highly pruritic, relapsing inflammatory skin disease characterized by pruritus, eczematous skin lesions, dry skin, lichenification, immune system dysregulation, and underlying skin barrier defects[1,2]

Signs and symptoms of AD often present in infancy and may persist into adulthood, although onset in adulthood may also occur[3-11]

Symptom Presentation by Age

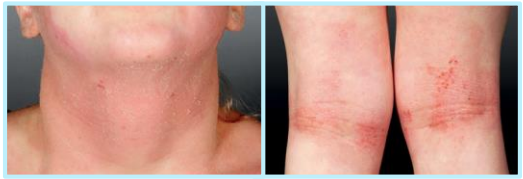
Infants[10,11]

- Acute, widely distributed lesions, often present on face, trunk (except the diaper area), and extensor surfaces of limbs
- Characterized by severe erythema, edema, excoriations, and serous exudate manifesting as oozing and crusting



Toddlers and children[10,11]

- Lesions are localized and chronic with milder erythema and xerosis, and commonly impact flexor surfaces

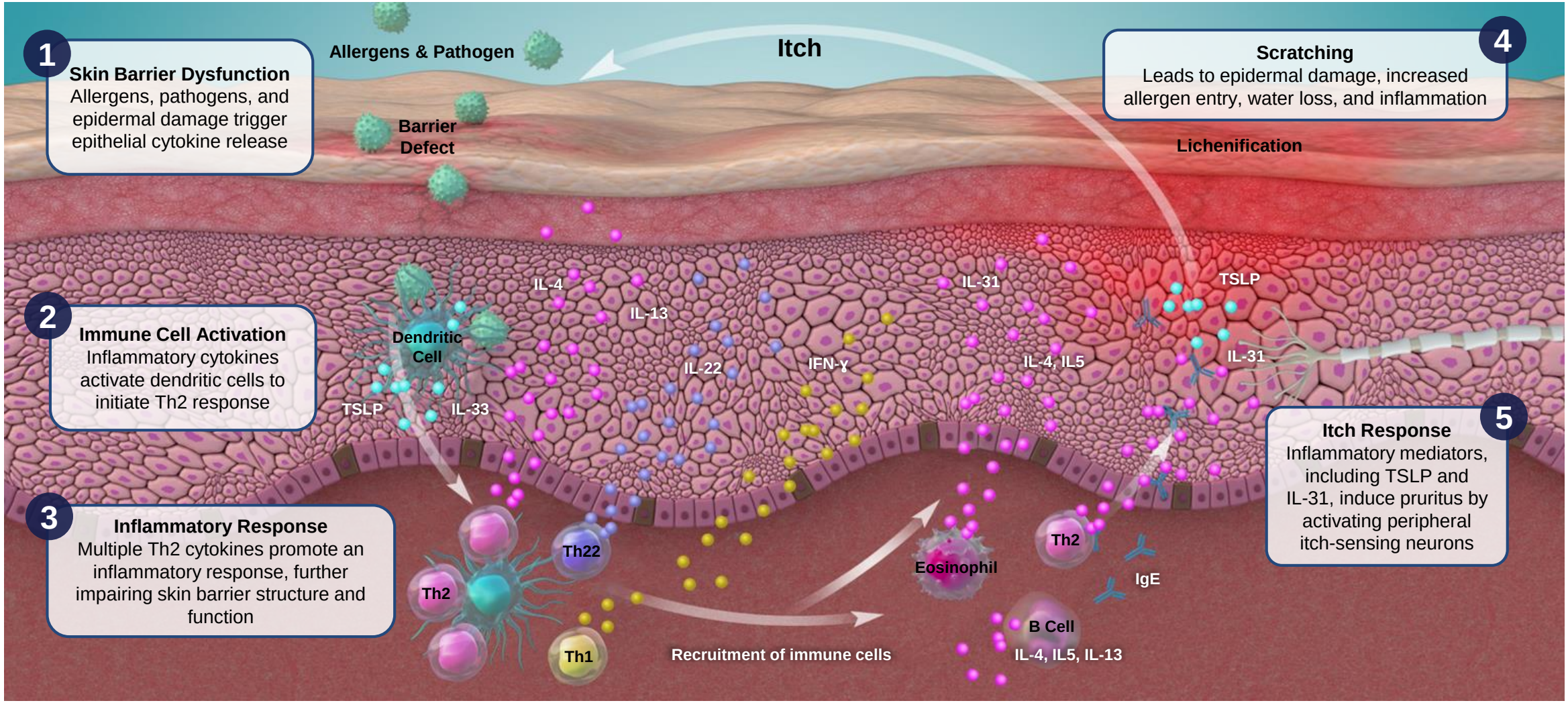


Adolescents and adults[10,11]

- Lesions present with a diffuse pattern but may be localized, particularly impacting the hands, wrists, ankles, eyelids, and flexor surfaces
- Xerosis and lichenification may be present
- Adults may have chronic hand or head and neck AD (often involves the upper trunk, shoulders, and scalp)

1. Eichenfield LF, et al. *J Am Acad Dermatol*. 2014;70:116-132. 2. Boguniewicz M, et al. *Ann Allergy Asthma Immunol*. 2018;120:10-22. 3. Silverberg JI. *Dermatol Clin*. 2017;35:283-289. 4. Lyons JJ, et al. *Immunol Allergy Clin North Am*. 2015;35:161-183. 5. Silverberg JI, et al. *Dermatitis*. 2014;25:107-114. 6. Shaw TE, et al. *J Invest Dermatol*. 2011;131:67-73. 7. Silverberg JI, et al. *Pediatr Allergy Immunol*. 2013:24:476-486. 8. Chiesa Fuxench ZC, et al. *J Invest Dermatol*. 2019;139:583-590. 9. Silverberg JI, et al. *J Allergy Clin Immunol*. 2013;1321132-1138. 10. Weidinger S, et al. *Nat Rev Dis Primers*. 2018;4:1. 11. Langan SM, et al. *Lancet*. 2020;396:345-360.

The Pathophysiology of Atopic Dermatitis Is Mediated by Inflammatory Cytokines That Perpetuate and Exacerbate the Itch-Scratch Cycle[1-3]

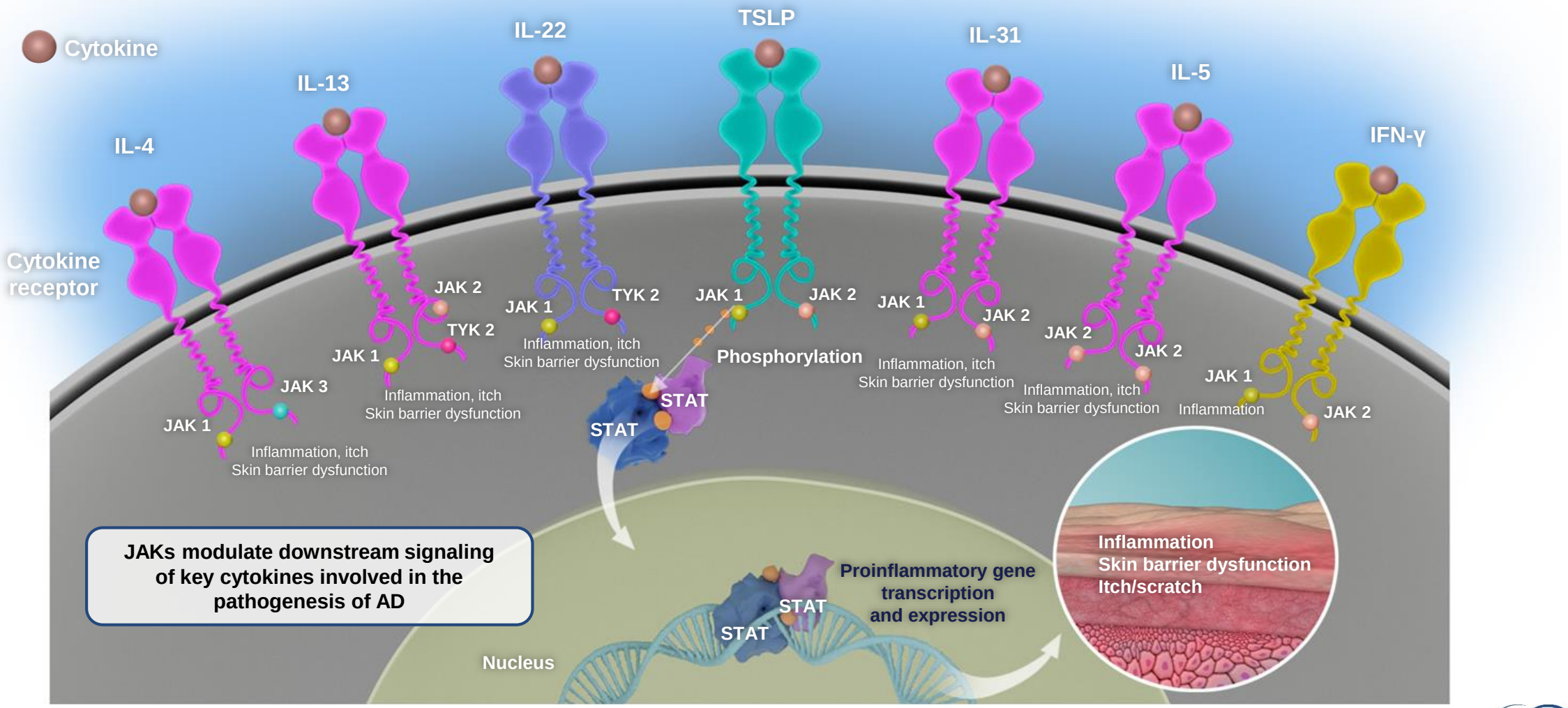


IFN, interferon; IgE, immunoglobulin E; IL interleukin; Th, T helper; TSLP, thymic stromal lymphopoietin.

1. Howell M, et al. Front Immunol. 2019;10:2342. 2. Howell M, et al. *Ann Allergy Asthma Immunol*. 2018;120:367-375. 3. Langan SM, et al. *Lancet*. 2020;396:345-360.

4

Multiple Cytokines Involved in Atopic Dermatitis Require the JAK-STAT Pathway to Mediate Inflammation and Transmit Itch Signals[1-7]

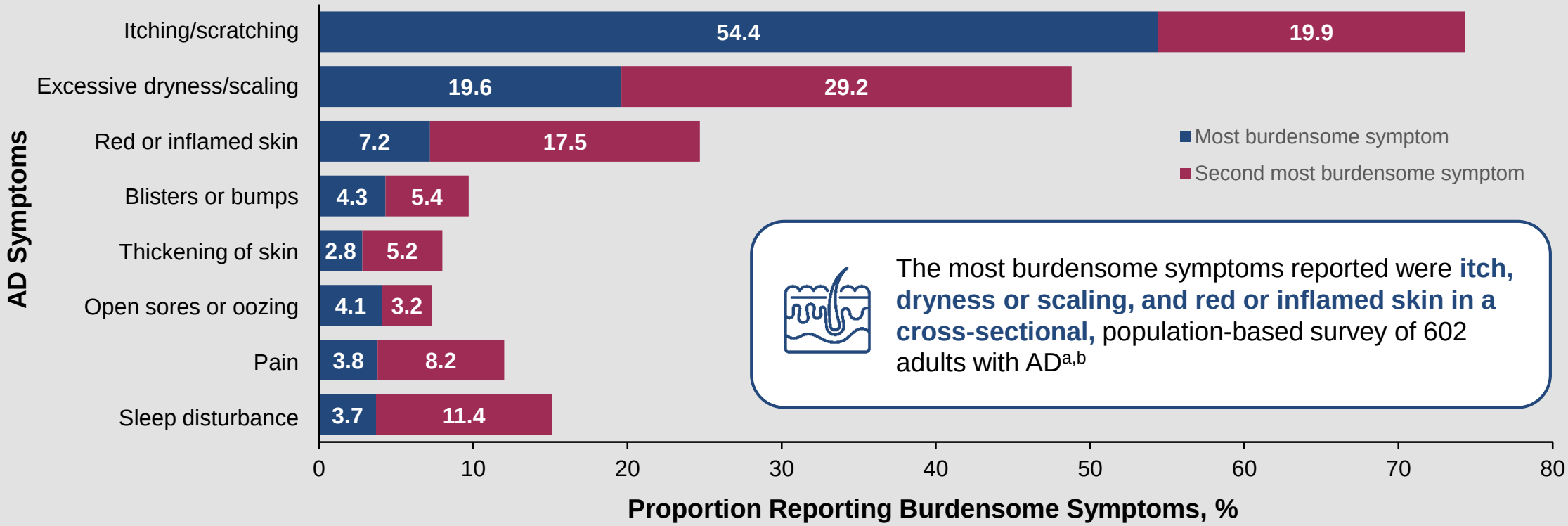


IFN-γ; interferon-gamma; JAK, Janus kinase; STAT, signal transducer and activator of transcription; TYK, tyrosine kinase.

1. Howell M, et al. *Front Immunol*. 2019;10:2342. 2. Howell M, et al. *Ann Allergy Asthma Immunol*. 2018;120:367-375. 3. Lee H, et al. *J Invest Dermatol*. 2016;136:2427-2435. 4. Bao L, et al. *Mol Immunol*. 2012;50:91-97. 5. Borriello F, et al. *Eur J Immunol*. 2015;45:2042-2051. 6. Howell MD, et al. *Allergy*. 2015;70:887-896. 7. Solimani F, et al. *Front Immunol*. 2019;10:2847.

Most Patients Report Itch as the Most Burdensome Symptom of Atopic Dermatitis

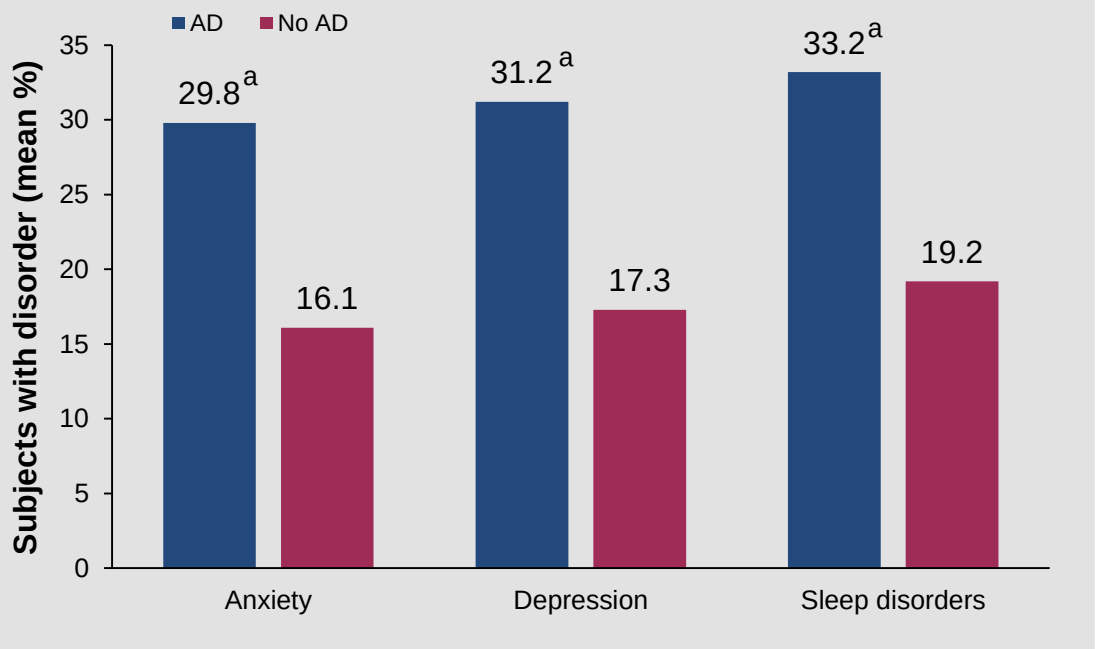
Most Burdensome Symptoms Among Adult Patients With AD[a,b]

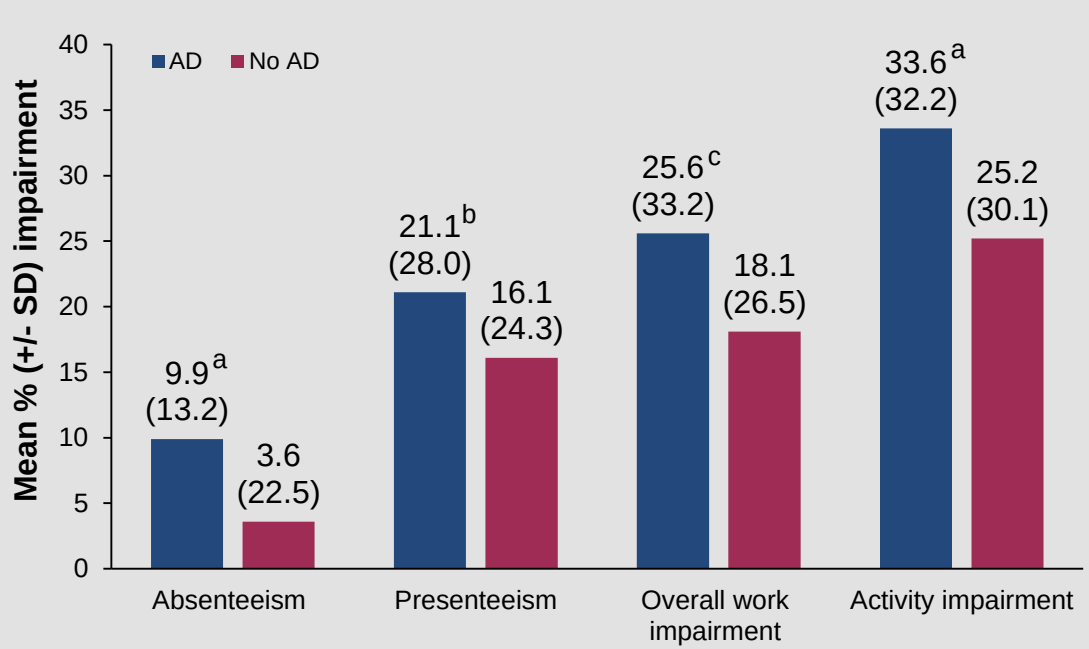


[a]Cross-sectional, population-based AD in America survey sampling the GfK Knowledge panel. This cohort included adults with AD based on an adaptation of the UK working party criteria for AD which included having an itchy skin condition during the past 12 months and 3 or more of the following: [1] history of skin crease involvement; [2] personal history of asthma or hay fever; [3] history of general dry skin during the past year; [4] visible flexural eczema; or [5] onset before the age of 2 years. Limitations included all exposures and outcomes being assessed by self report and not verified by physical examination and may be subject to misclassifications. [b]The most and second most burdensome self-reported symptoms and signs of AD were examined. QOL, quality of life.

Silverberg JI, et al. *Ann Allergy Asthma Immunol*. 2018;121:340-347.

Atopic Dermatitis Can Significantly Impact Patients' Mood, Sleep, and Daily Activities





A significantly highly proportion of individuals with AD reported mood and sleep disorders, as well as reduced work productivity and activity impairment compared to individuals without AD

Cross-sectional study using the 2013 US National Health and Wellness Survey (NHWS), assessing the burden of AD in adults. Respondents were defined as having AD if they responded yes to the question, "Which of the following conditions (dermatitis/eczema/AD) have you experienced in the past 12 months?'' If ''yes'' was chosen for AD, the following question was asked: ''Has your AD been diagnosed by a physician?'' The burden of AD on mental health was established using self-reported diagnoses of anxiety, depression, and/or sleep disorders based on a patient's response to separate questions for each disorder "Have you experienced anxiety/depression/sleep disorders in the past 12 months?" The WPAI was used to assess work productivity and activity impairment.

[a] $P<0.001$ vs No AD. [b] $P=0.027$ vs No AD. [c] $P=0.004$ vs No AD.

SD, standard deviation; WPAI Work Productivity and Activity Impairment questionnaire.

Eckert L, et al. *J Am Acad Dermatol*. 2017;77:274-279.

Diagnosis and Management of Atopic Dermatitis

Diagnosis of Atopic Dermatitis is Based on Essential, Important, and Associated Features

Essential Features
Required for AD diagnosis

Pruritus

Eczema (acute, subacute, chronic)

Typical morphology and age-specific patterns[a]

Chronic or relapsing history

Important Features
Support AD diagnosis

Early age of onset

Atopy

Personal and/or family history

Immunoglobulin E reactivity

Xerosis

Associated Features
Suggest AD diagnosis but are nonspecific

Atypical vascular responses

Keratosis pilaris/ pityriasis alba/ hyperlinear palms/ ichthyosis

Ocular/periorbital changes

Other regional findings

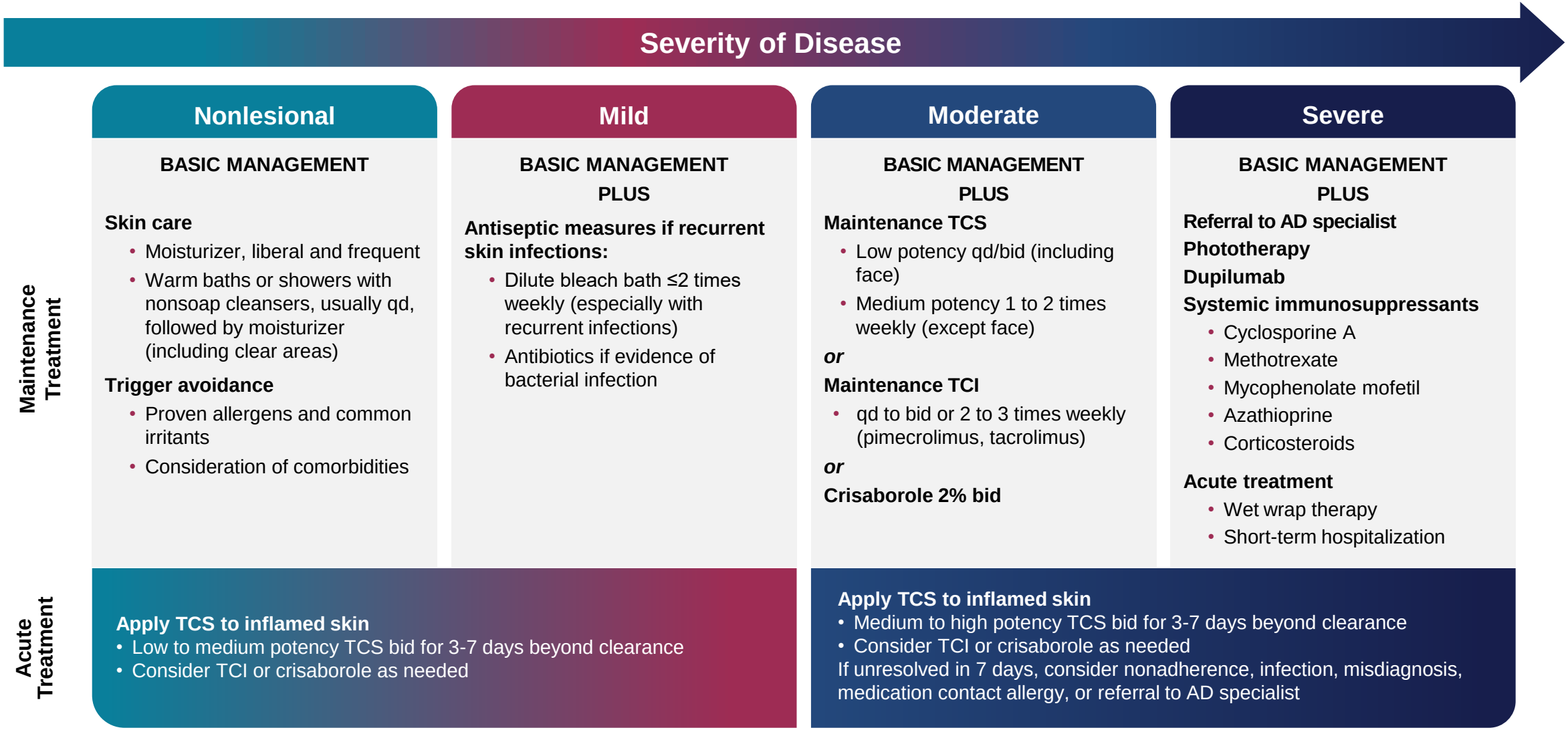
Perifollicular accentuation/lichenification/prurigo lesions

Exclusionary Conditions
It should be noted that a diagnosis depends upon excluding conditions, such as:

- Scabies
- Seborrheic dermatitis
- Contact dermatitis (irritant or allergic)
- Ichthyoses
- Cutaneous T-cell lymphoma
- Psoriasis
- Photosensitivity dermatoses
- Immune deficiency diseases
- Erythroderma of other causes

[a]Patterns include facial, neck, and extensor involvement in infants and children; current or previous flexural lesions in any age group; sparing of the groin and axillary regions.
Eichenfield LF, et al. *J Am Acad Dermatol*. 2014;70:338-351.

Treatment Algorithm for the Management of Atopic Dermatitis[a]



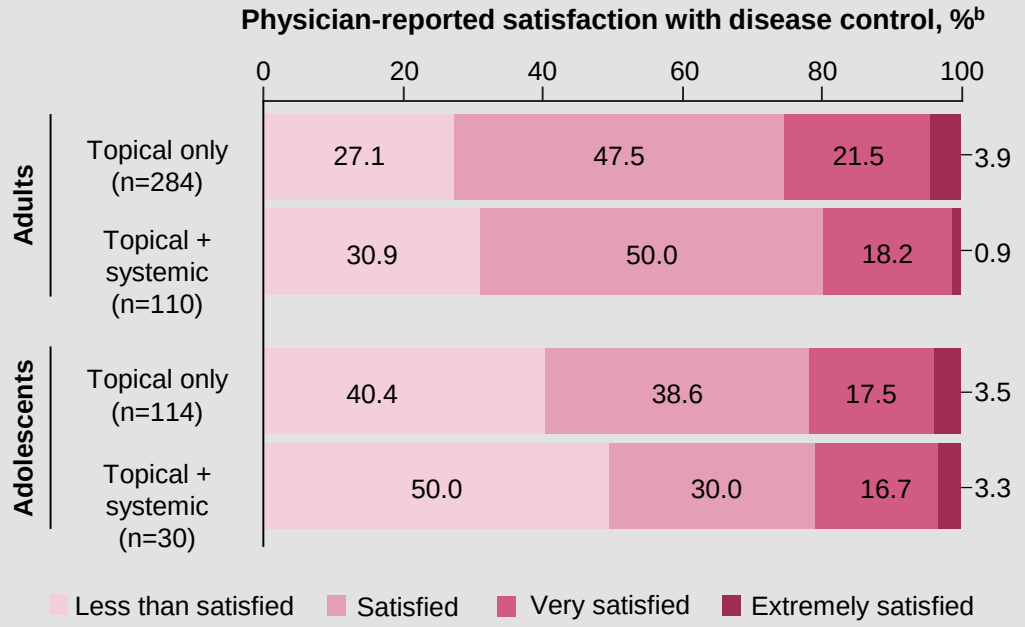
qd, once daily.

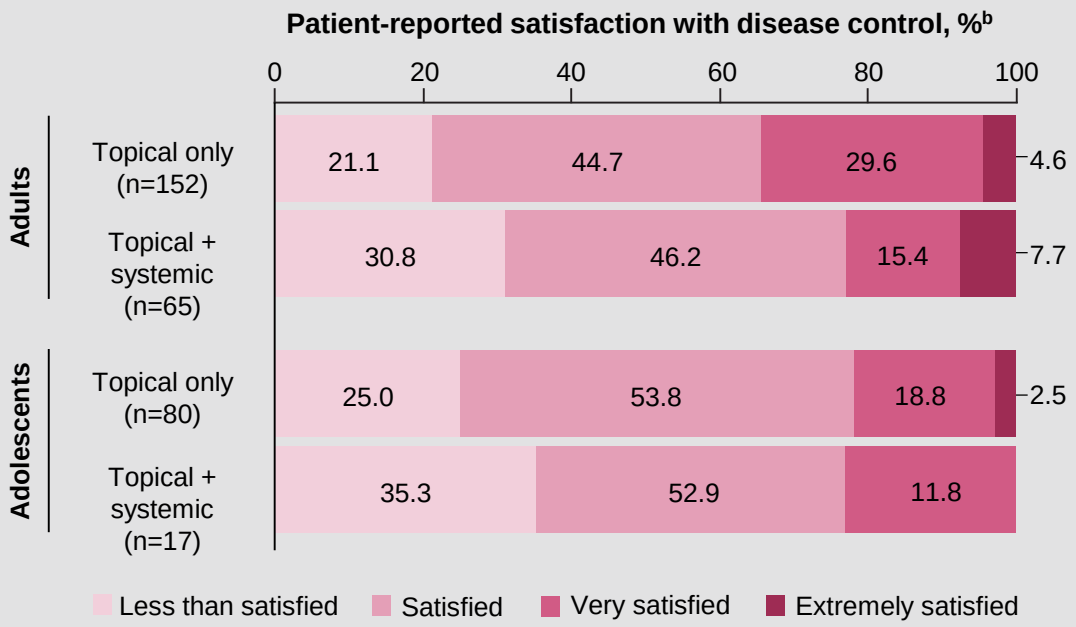
Boguniewicz M, et al. *Ann Allergy Asthma Immunol*. 2018;120:10-22.

High Rates of Uncontrolled Atopic Dermatitis Have Been Reported[a]

Analyses assessing disease control and treatment satisfaction in adults and adolescents with moderate to severe AD showed:[b]

- **Approximately 20 to 50%** of patients had *uncontrolled*[b] AD as assessed by their physician while using TCS, TCI, or crisaborole
- Up to **50% of physicians and 35% of patients** reported to be "less than satisfied" with the current level of disease control





[a]Analyses of disease control, physician and patient satisfaction, and patient-reported outcomes were conducted in the subpopulation of patients who were currently receiving topical therapy (TCS, TCI, or crisaborole) alone or in addition to systemic therapy (systemic corticosteroids, systemic immunosuppressants, or biologics); patients receiving systemic therapy alone were excluded. This was a retrospective, point-in-time, observational study of physician-completed records and matched patient surveys drawn from 2 Adelphi AD Disease Specific Programmes (DSPs) in the US in 2018 and 2019. Patients included in this analysis were adults (≥18 years) and adolescents (12-17 years) currently experiencing or with a history of moderate or severe AD who had been receiving current AD therapy for ≥1 month. [b]Controlled disease was defined as improving/stable; uncontrolled disease was defined as deteriorating/changing.

Anderson P, et al. *Dermatol Ther (Heidelb)*. 2021;11:1571-1585.

Summary

AD is a chronic, heterogeneous, highly pruritic, relapsing inflammatory skin disease that is associated with significant impact on QOL[1-4]

The pathophysiology of AD is mediated by inflammatory cytokines that perpetuate and exacerbate the itch-scratch cycle[5]

- Multiple cytokines involved in atopic dermatitis require the JAK-STAT pathway to mediate inflammation and transmit itch signals[6]

Itch is the most prominent, burdensome, and distressing symptom of AD, and is associated with significant impacts on mood, sleep, and daily activites[3,7]

Treatment for AD focuses on skin hygiene, trigger avoidance, and pharmacologic management of inflammation and itch, however many patients are inadequately controlled[2,4]

1. Eichenfield LF, et al. *J Am Acad Dermatol*. 2014;70(2):338-351. 2. Boguniewicz M, et al. *Ann Allergy Asthma Immunol*. 2018;120(1):10-22. 3. Silverberg JI, et al. *Ann Allergy Asthma Immunol.* 2018;12(3)1:340-347. 4. Silverberg JI, et al. *J Dermatol Treat*. 2016;27(6):568-586. 5. Langan SM, et al. *Lancet*. 2020;396(10247):345-360. 6. Howell MD, et al. *Front Immunol.* 2019;10:2342. 7. Eckert L, et al. *J Am Acad Dermatol.* 2017;77:274-279.