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To participate in polling and Q&A at today's meeting, please scan the QR code with your mobile phone

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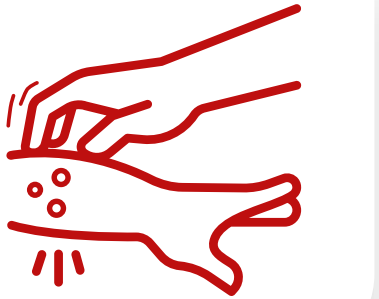
The faculty will answer as many questions as possible at the end of the symposium

The Benefits of Early Intervention in AD: More Than Skin Deep



ADVENT
dermatology • AD

Saturday, March 9, 2024
7:00PM–9:00PM PST
San Diego, California

AD, atopic dermatitis.

ADVENT is a medical education non-promotional program for healthcare professionals organized by Sanofi and Regeneron.

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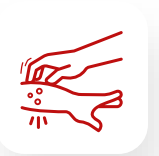

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- The content contained in this program was jointly developed by the speaker and medical teams from Sanofi and Regeneron and is not eligible for CME credits

CME, continuing medical education.

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- Lawrence F. Eichenfield, MD: Abbvie, Amgen, Arcutis, Castle Biosciences, Dermavant, Galderma, Lilly, Ortho Dermatologics, Regeneron, Sanofi-Genzyme
- Katrina Abuabara, MD, MA, MSCE: L'Oreal, Pfizer
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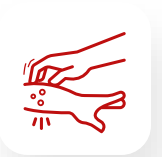
Agenda



Welcome, Introductions, and Objectives — 5 mins
Eric Simpson

New Data on the Systemic (Multi-Organ) Burden of AD in Children and the Need for Early Intervention — 23 mins
Lawrence F. Eichenfield

Importance of Achieving Disease Control in Adults With Moderate-to-Severe AD — 23 mins
Eric Simpson

Practical Considerations in Older Patients With AD — 23 mins
Katrina Abuabara

Perspectives on the Management of Patients With Moderate-to-Severe AD Across Age Groups — 15 mins
Eric Simpson, Katrina Abuabara, Lawrence F. Eichenfield

Conclusions, Panel Discussion, and Q&A — 20 mins
Eric Simpson, Katrina Abuabara, Lawrence F. Eichenfield

Objectives of the Symposium

Present new data on the systemic burden of underlying **type 2 inflammation** in AD **within** and **beyond the skin** across age groups

Discuss the cumulative **life impact** of uncontrolled AD and the importance of **early intervention** and **disease control** across age groups

Relate perspectives on **management** of moderate-to-severe AD and the **potential** for **disease modification**

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POLLS

Submit questions to the faculty throughout the symposium

Q&A

Submit feedback in the evaluation form

EVALUATION

The faculty will answer as many questions as possible at the end of the symposium

New Data on the Systemic (Multi-Organ) Burden of AD in Children and the Need for Early Intervention

Lawrence F. Eichenfield, MD

Polling Question

Which of these statements about the of prevalence atopic comorbidities in pediatric patients with AD is correct?

Select one response

A. Approximately 1/3 of patients have ≥1 atopic comorbidity, this number increases with age and asthma is the most frequent comorbidity

B. Approximately 2/3 of patients have ≥1 atopic comorbidity, this number decreases with age, with asthma and allergic rhinitis being the most frequent

C. Over 75% of patients have ≥1 atopic comorbidity, this number increases with severity and age, with food allergy, allergic rhinitis, and asthma being the most frequent

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Polling Question

Do you believe that by addressing dysregulated type 2 inflammation early in infants with severe AD we can impact the incidence or progression of the disease?

Select one response

A Yes

B No

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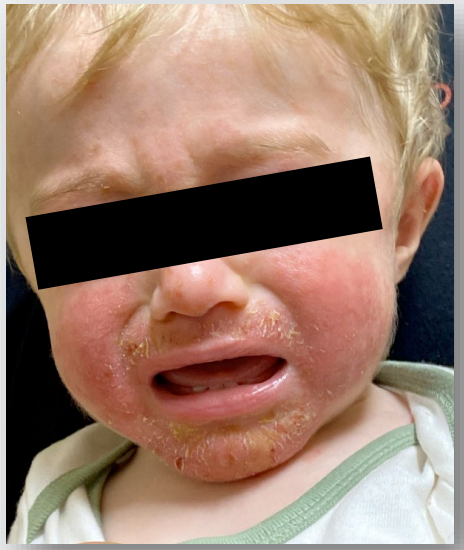
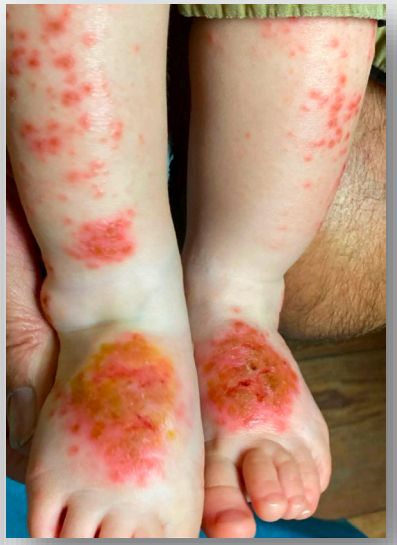
Case Study: AD in a Pediatric Patient

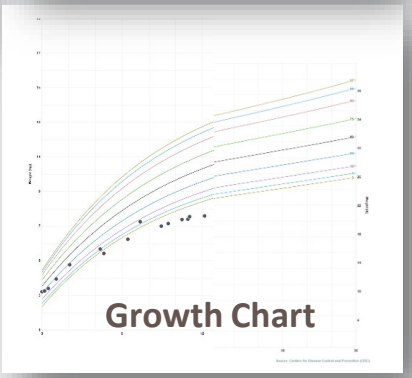
Matthew

Male, 18-months-old





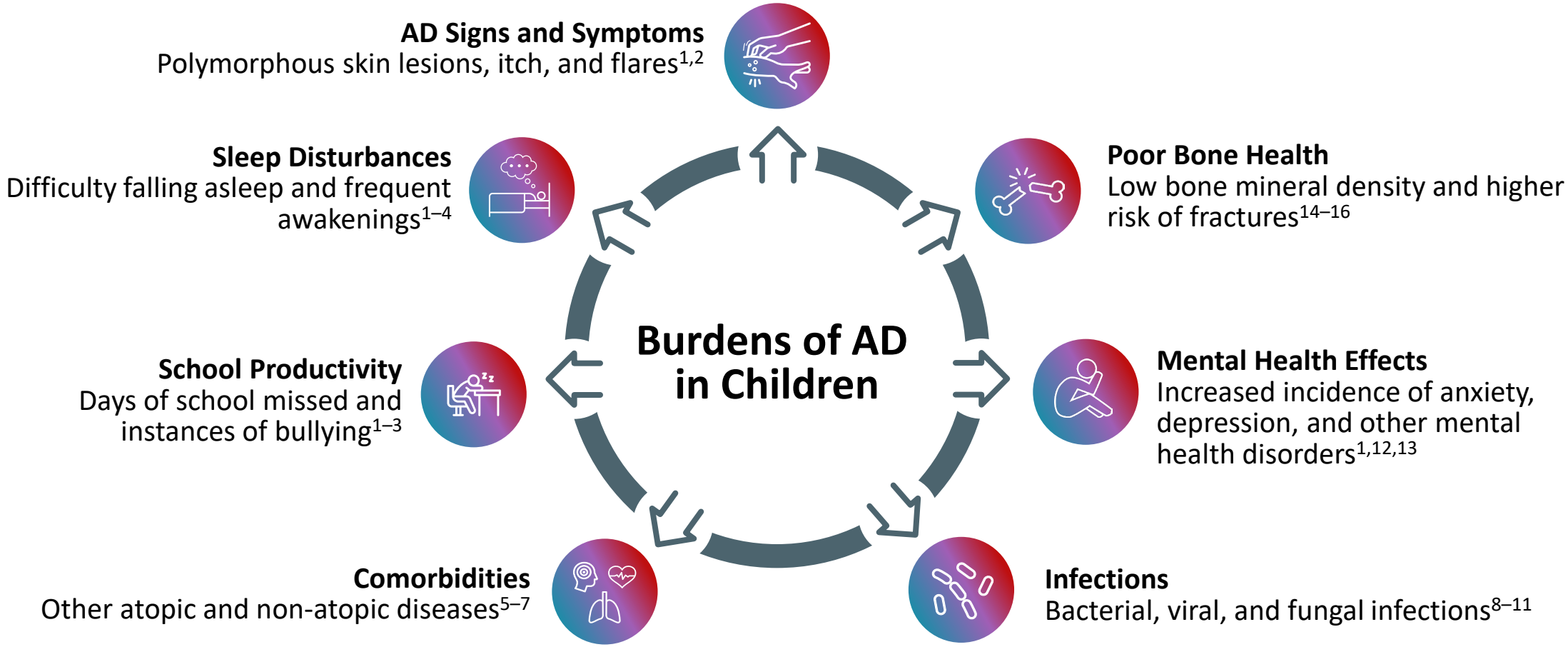
v-IGA: Severe (4)
EASI: 29
BSA: 41%



Clinical history	• Diagnosed with AD at 5 months of age • Inadequately controlled with TCS, bleach baths, tacrolimus, black tea soaks • Worsened significantly at 18 months of age • Multiple bouts of cutaneous infection treated with oral antibiotics • Food allergies to dairy, egg, peanut, tree nuts; environmental allergies; allergic rhinitis; dysphagia
Treatment history	• Triamcinolone 0.1% (neck to toe) • Hydrocortisone 2.5% (face) • Tacrolimus (0.03%) • Regular use of emollients; allergen avoidance
Burden	• Poor sleeping • Scratches “constantly” • Concerns with weight loss and “family living their whole lives around the eczema”

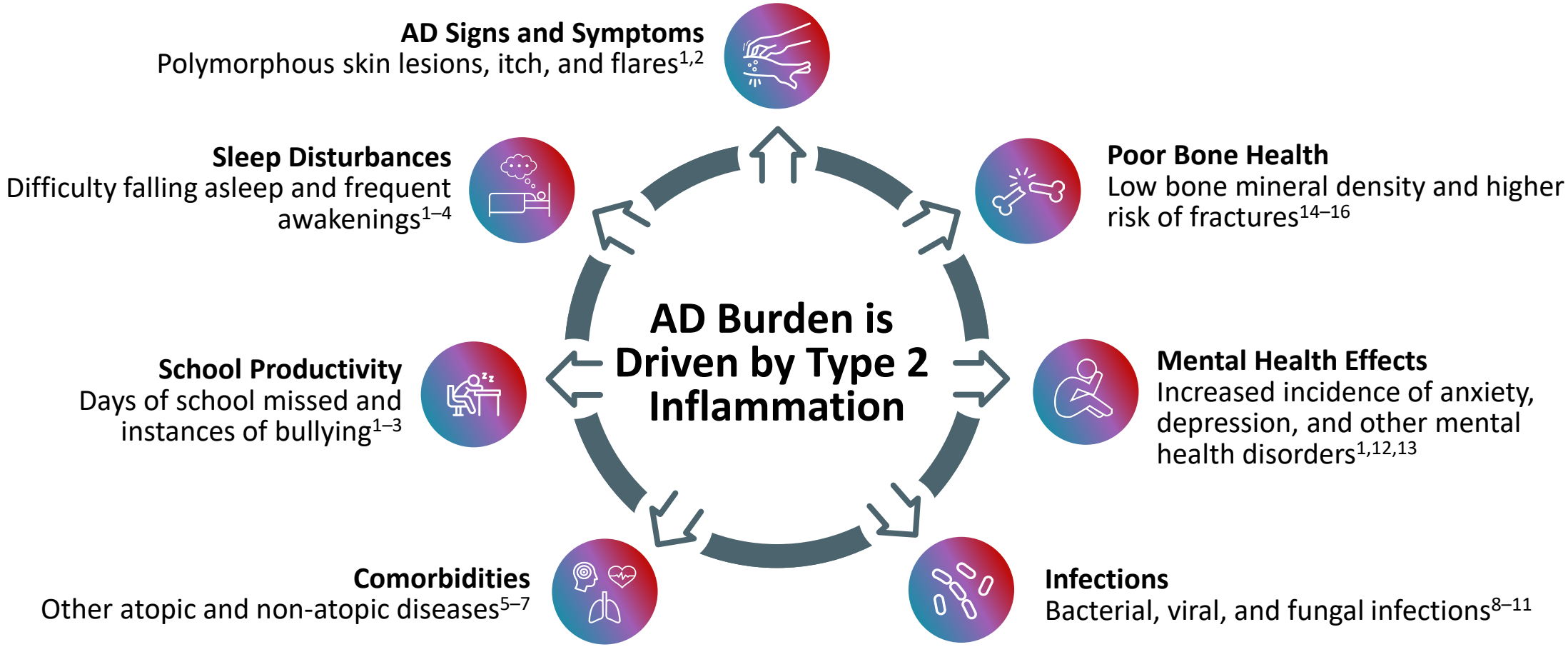
BSA, body surface area; EASI, Eczema Area and Severity Index; TCS, topical corticosteroid; v-IGA, validated Investigator’s Global Assessment.
Case study and photos reprinted with permission from Eichenfield LF.

More Than Skin Deep: Moderate-to-Severe AD Has a Multidimensional Disease Burden With Potential Long-term Consequences in Children



1. Paller AS, et al. *Dermatol Ther*. 2023;13:961–980. 2. Neri I, et al. *J Asthma Allergy*. 2023;16:383–396. 3. Ramirez FD, et al. *Jama Pediatr.* 2019:173:e190025. 4. de Carvalho V, et al. Rad. 2022. Poster 211. 5. Weidinger S, et al. *BJD*. 2023;ljad449. 6. Wan J, et al. *J Allergy Clin Immunol Pract*. 2023:S2213-2198(23)00905-4. 7. Wan J, *et al. J Allergy Clin Immunol Pract.* 2023:S2213-2198(23)01251-5. 8. Huang AH, et al. *J Am Acad Dermatol.* 2021;85:893–900. 9. Ong PY, Leung DYM. *Clin Rev Allergy Immunol*. 2016;51:329–337. 10. Wang V, et al. *Ann Allergy Asthma Immunol*. 2021;126:3e1. 11. Cameron S, et al. *Allergy*. 2023;00:1–11. 12. Hou A, Silverberg JI. *Pediatr Dermatol*. 2021;38:606–612. 13. Kern C, et al. *JAMA Dermatol*. 2021;157:1200–1208. 14. Wu D, et al. *Ann Transl Med*. 2021;9:40. 15. Silverberg JI. *Pediatr Allergy Immunol*. 2015;26:54–61. 16. Lee AW, et al. *Allergy*. 2023;78:871–875.

More Than Skin Deep: Moderate-to-Severe AD Has a Multidimensional Disease Burden With Potential Long-term Consequences in Children



1. Paller AS, et al. *Dermatol Ther*. 2023;13:961–980. 2. Neri I, et al. *J Asthma Allergy*. 2023;16:383–396. 3. Ramirez FD, et al. *Jama Pediatr.* 2019:173:e190025. 4. de Carvalho V, et al. Rad. 2022. Poster 211. 5. Weidinger S, et al. *BJD*. 2023;ljad449. 6. Wan J, et al. *J Allergy Clin Immunol Pract*. 2023:S2213-2198(23)00905-4. 7. Wan J, *et al. J Allergy Clin Immunol Pract.* 2023:S2213-2198(23)01251-5. 8. Huang AH, et al. *J Am Acad Dermatol.* 2021;85:893–900. 9. Ong PY, Leung DYM. *Clin Rev Allergy Immunol*. 2016;51:329–337. 10. Wang V, et al. *Ann Allergy Asthma Immunol*. 2021;126:3e1. 11. Cameron S, et al. *Allergy*. 2023;00:1–11. 12. Hou A, Silverberg JI. *Pediatr Dermatol*. 2021;38:606–612. 13. Kern C, et al. *JAMA Dermatol*. 2021;157:1200–1208. 14. Wu D, et al. *Ann Transl Med*. 2021;9:40. 15. Silverberg JI. *Pediatr Allergy Immunol*. 2015;26:54–61. 16. Lee AW, et al. *Allergy*. 2023;78:871–875.

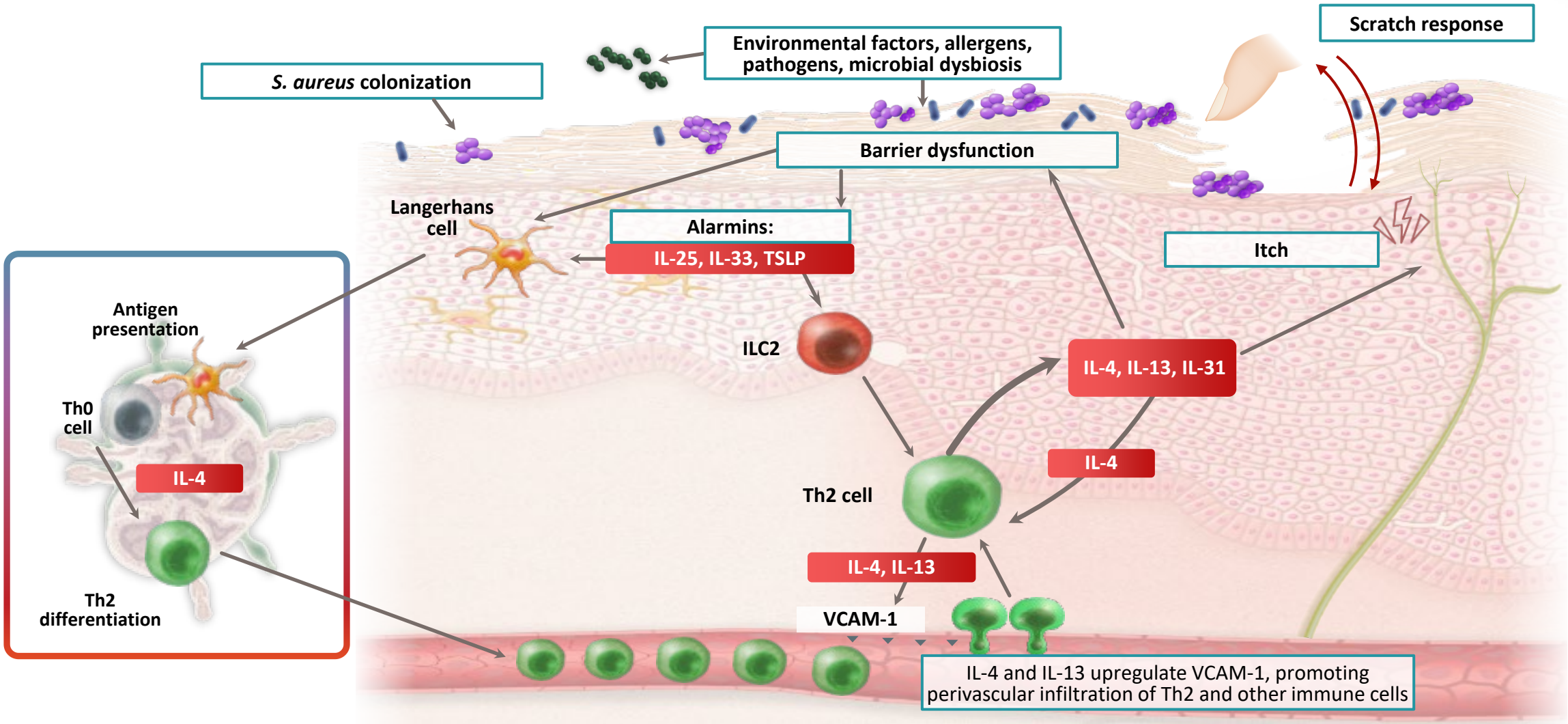
Type 2 Immunity Is Upregulated in AD and Contributes to Both Systemic and Local Inflammatory Processes

All ages

Immune Pathway[1–3]	Type 1	Type 2	Type 3
Primary immune cells	Innate: ILC1, Macrophage, NK Adaptive: Th1	Innate: ILC2, Mast cell, Basophil, Eosinophil Adaptive: Th2, Tfh2	Innate: ILC3, Neutrophil Adaptive: Th17
Key cytokines	IL-2, IFNγ, TNFβ, IL-12, IL-18, IL-6	IL-4, IL-5, IL-13, IL-31, IL-25, TSLP, IL-33	IL-17, IL-6, IL-22, IL-23
Physiologic targets	Viruses, Intracellular bacteria	Helminth parasites	Extracellular bacteria, Fungi

Figure adapted with permission from Haddad EB, et al. *Dermatol Ther (Heidelb)*. 2022;12:1501–1533. Copyright 2022 Springer Nature.
Simplified depiction based on key published information, not meant to be exhaustive in nature. IL-25 is also known as IL-17E.
IFN-γ, interferon gamma; IL, interleukin; ILC, innate lymphoid cell; NK, natural killer cell; Tfh, T follicular helper; Th, T helper; TNF, tumor necrosis factor; TSLP, thymic stromal lymphopoietin.
1. Haddad EB, et al. *Dermatol Ther (Heidelb).* 2022;12:1501–1533. 2. Beck LA, et al. *JID Innov*. 2022;2:100131. 3. Annunziato F, et al. *J Allergy Clin Immunol*. 2015;135:626–635.

Type 2 Inflammation Contributes to Epidermal Barrier Dysfunction and AD Signs and Symptoms[1–11]



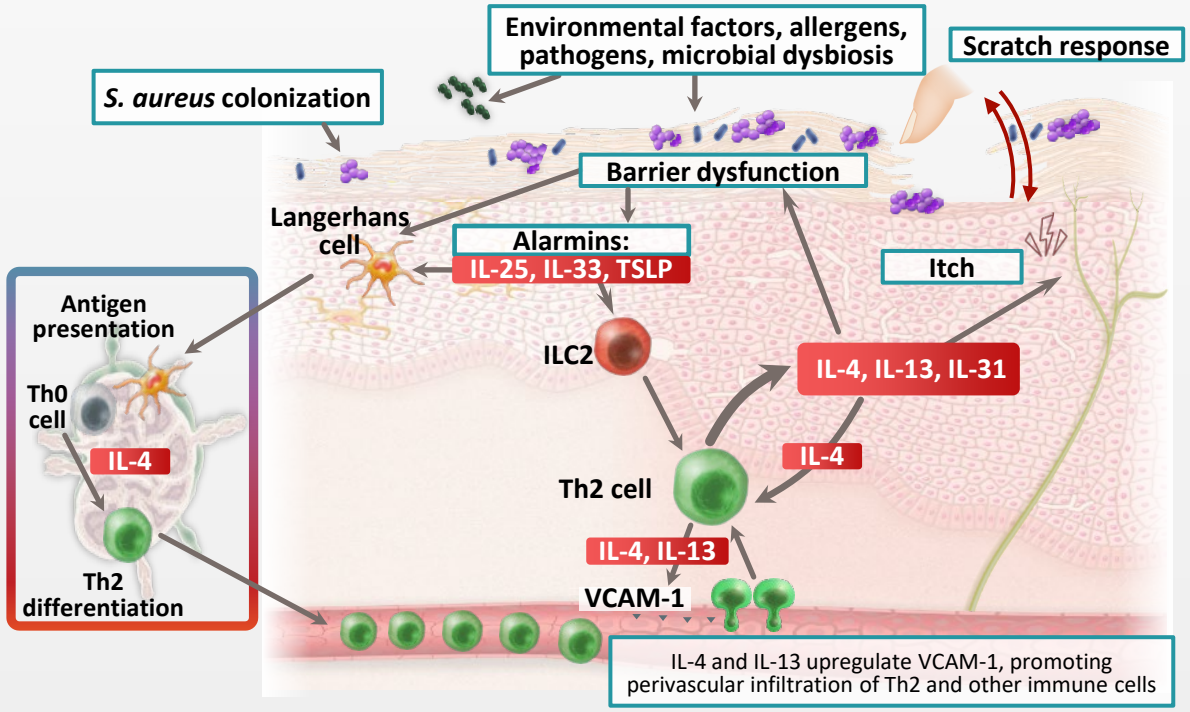
IL, interleukin; ILC, innate lymphoid cell; *S. aureus*, *Staphylococcus aureus*; Th, T helper cell; VCAM-1, vascular cell adhesion molecule 1.

1. Haddad EB, et al. *Dermatol Ther (Heidelb)*. 2022;12:1501–1533. 2. Weidinger S, Novak N. *Lancet*. 2016;387:1109–1122. 3. Moniaga CS, et al. *Diagnostics (Basel)*. 2021;11:2090. 4. Jin J, et al. *J Int Med Res*. 2022;50:1–14. 5. Toyama S, et al. *Int J Mol Sci*. 2021;22:12365. 6. Kong DH, et al. *Int J Mol Sci*. 2018;19:1057. 7. Beck LA, et al. *JID Innovations*. 2022:doi:100131. 8. Yosipovitch G, et al. *J Eur Acad Dermatol Venereol.* 2020;34:239–250.
9. Cevikbas F, Lerner EA. *Physiol Rev*. 2020;100:945–982. 10. Garcovich S, et al. *Vaccines (Basel)*. 2021;9:303. 11. Bochner BS, et al. *J Immunol.* 1995;154:799–803.

Type 2 Inflammation Contributes to Epidermal Barrier Dysfunction and AD Signs and Symptoms

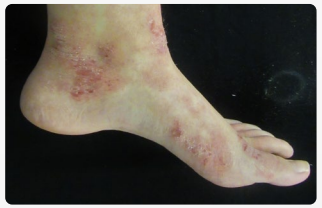
All ages

Dysregulated type 2 immunity links barrier disruption and itch[1–11]

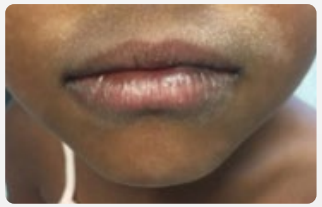


- Altered lipid components and metabolism
- Altered structural protein expression
- Stimulation of itch neurons; neuron density changes and neurite outgrowth
- Recruitment of inflammatory cells
- *S. aureus* colonization

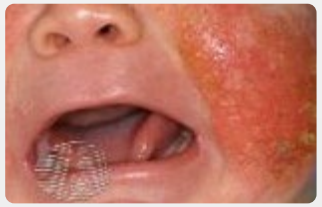
Clinical presentation



Polymorphous lesions



Postinflammatory pigment alteration



Impetiginized AD

Clinical features[2]

- Intense itch
- Skin lesions
- Increased risk of skin infections

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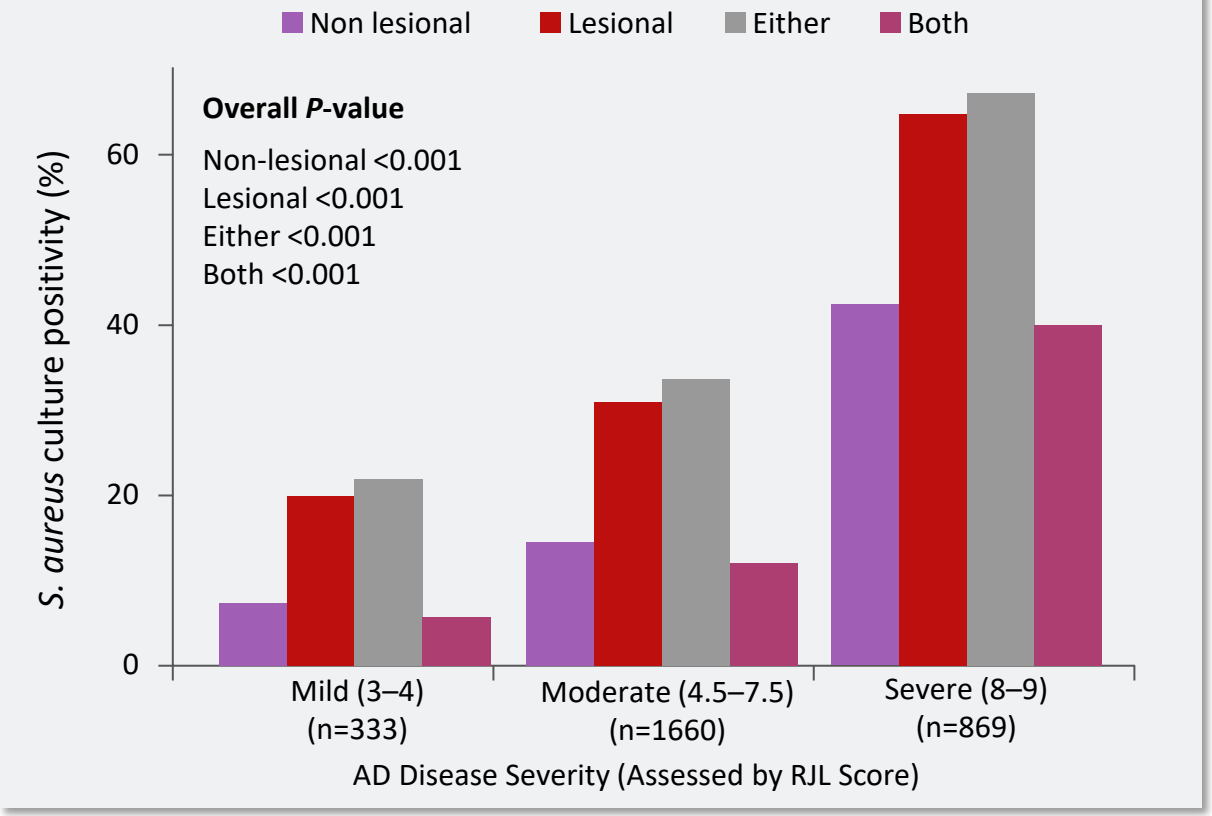
IL, interleukin; ILC, innate lymphoid cell; Th, T helper cell; VCAM-1, vascular cell adhesion molecule 1.

1. Haddad EB, et al. *Dermatol Ther (Heidelb)*. 2022;12:1501–1533. 2. Weidinger S, Novak N. *Lancet*. 2016;387:1109–1122. 3. Moniaga CS, et al. *Diagnostics (Basel)*. 2021;11:2090. 4. Jin J, et al. *J Int Med Res*. 2022;50:1–14. 5. Toyama S, et al. *Int J Mol Sci*. 2021;22:12365. 6. Kong DH, et al. *Int J Mol Sci*. 2018;19:1057. 7. Beck LA, et al. *JID Innovations*. 2022:doi:100131. 8. Yosipovitch G, et al. *J Eur Acad Dermatol Venereol.* 2020;34:239–250. 9. Cevikbas F, Lerner EA. *Physiol Rev*. 2020;100: 945–982. 10. Garcovich S, et al. *Vaccines (Basel)*. 2021;9:303. 11. Bochner BS, et al. *J Immunol.* 1995;154:799–803.

Type 2 Inflammation is Exacerbated by *S. aureus*, Which Promotes Flares and Skin Infections in AD[1–3]

All ages

Proportion of *S. aureus* positive skin swabs increased with AD severity[2]



S. aureus contributes to the release of type 2 inflammatory mediators and pruritogens[1]

Type 2 cytokine production[1]

Stimulates itch[1]

Increased risk of flares[3]

Skin and extra-cutaneous infection risk increases with AD severity[2]

Graph adapted with permission from Simpson EL, et al. *J Allergy Clin Immunol Pract*. 2023;11:2504–2515. Copyright 2023 Elsevier.
S. aureus, Staphylococcus aureus.
ADRN is a US registry of extensively phenotyped participants with AD (aged 0.73–80 years) enrolled at nine academic centers. Patients with AD (N=2862) whose disease was categorized as mild (11.6%), moderate (58%), or severe (30.4%) based on RJL scoring were enrolled. Information on family and medical history, examination, skin swabs (culture), and serum biomarkers were collected to evaluate their association with AD disease severity.
ADRN, Atopic Dermatitis Research Network; RJL, Rajka-Langeland score; *S. aureus*, *Staphylococcus aureus*.
1. Wan P, Chen J. *Dermatol Ther (Heidelb).* 2020;10:53–61. 2. Simpson EL, et al. *J Allergy Clin Immunol Pract.* 2023;11:2504–2515. 3. Kong HH, et al. *Genome Res*. 2012;22:850–859.

S. aureus Colonization and Skin Infections Increase With AD Disease Severity

All ages

AD severity is directly correlated with *S. aureus* colonization, and a history and/or presence of bacterial or viral skin infections[1–3]

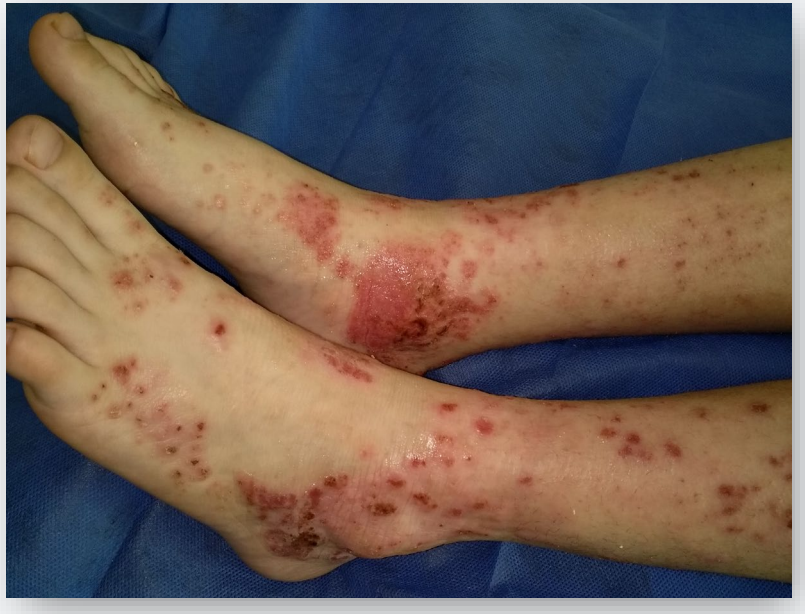


Photo provided courtesy of Dr. Vania Carvalho.

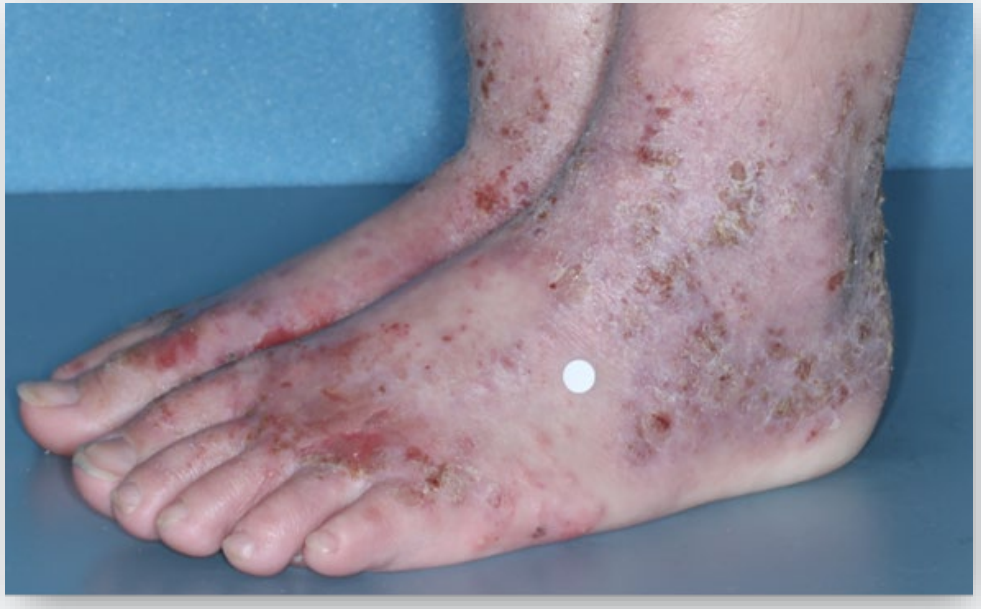
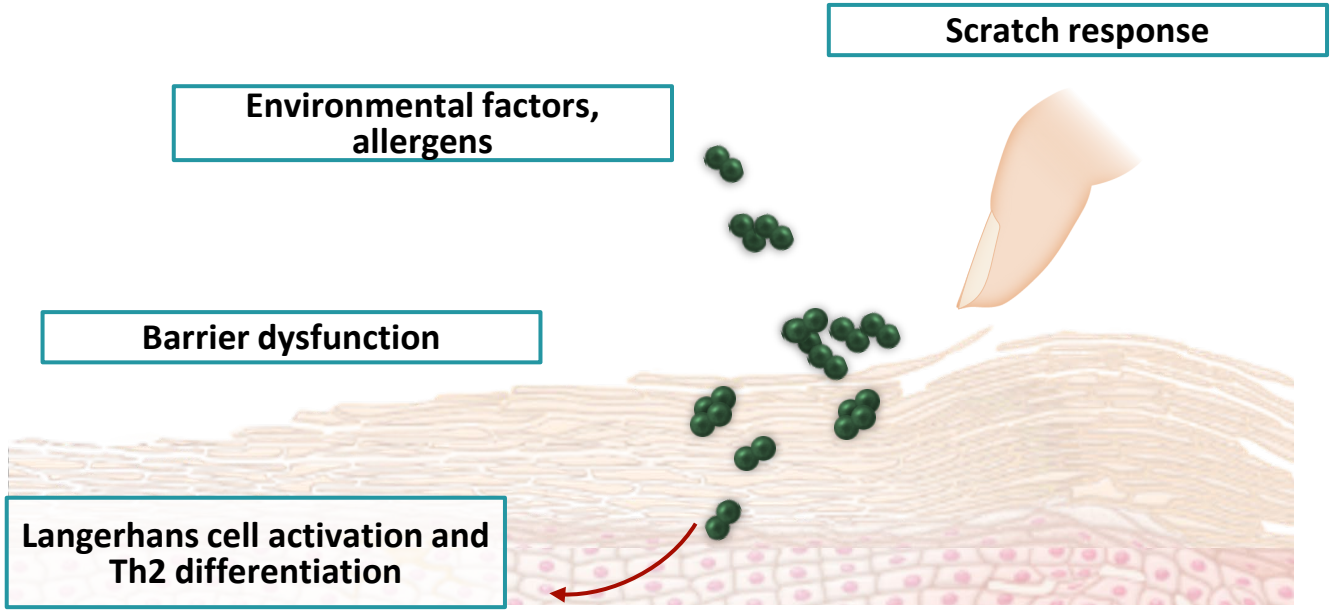


Photo provided courtesy of Dr. Ana B. Rossi.

All patients/caregivers provided authorization for use of photos.
S. aureus, Staphylococcus aureus.
1. Simpson EL, et al. *J Allergy Clin Immunol Pract.* 2023;11:2504–2515. 2. Kim J, et al. *Allergy Asthma Immunol Res*. 2019;11:593–603. 3. Brauweiler AM, et al. *J Invest Dermatol.* 2014;134:2114–2121.

Skin Barrier Dysfunction Increases Exposure to Allergens, Increasing the Risk of Potential Sensitization

The dysfunctional skin barrier may allow transcutaneous entry of allergens and subsequent potential sensitization[1,2]



Can trigger AD flares[3]

May increase propensity for the development of other allergic diseases[4]

Th, T helper.

1. Sweeney A, et al. *Allergy Asthma Clin Immunol*. 2021;17:1–12. 2. Wang F, et al. *Cell*. 2021;184:422–440.e17.
3. Werfel T, et al. *J Allergy Clin Immunol*. 2015;136:96–103.e9. 4. Bieber T. *Nat Rev Drug Discov*. 2023. https://doi.org/10.1038/s41573-023-00735-0.

The AD Clinical Burden is Substantial for Children, Who Are at Increased Risk of Developing Other Atopic Diseases

PEDISTAD (N=1329)

61% of children aged <12 years with moderate-to-severe AD have **≥1 coexisting type 2 inflammatory disease** at baseline[1,a]

- **Food allergies** 58.7%
- **Allergic rhinitis** 33.7%
- **Asthma** 22.8%
- **Eosinophilic esophagitis** 0.6%
- **Allergic conjunctivitis** 11.2%
- **Nasal polyposis** 0.5%

EPI-CARE (N=1489)

Percentage of infants/preschoolers **aged 6 months to <6 years with AD** reporting **at least one coexisting type 2 inflammatory disease**[2,b]

- **76.5%–94.9%** with **mild AD**
- **80.2%–99.9%** with **moderate AD**
- **88.5%–100%** with **severe AD**

In patients with AD and coexisting atopic disease, AD is the most common initiating atopic condition[3]

[a]PEDISTAD (NCT03687359) is an ongoing, international, multicenter, 10-year, observational registry in 21 countries in children aged <12 years with moderate-to-severe AD receiving systemic therapy. Patients were either not controlled with topicals or topicals were not advisable. The aim is to assess real-world disease course, comorbidities, treatment and disease burden.[4,5] [b]EPI-CARE is a cross-sectional, web-based survey of pediatric patients with AD aged 6 months to <18 years conducted in 18 countries representing 5 geographic regions.

1. de Carvalho V, et al. *RAD.* 2022; 9–11 April 2022; Baltimore, MD, USA. 2. Weidinger S, et al. *Br J Dermatol.* 2023;ljad449. 3. Gabryszewski SJ, et al. *Ann Allergy Asthma Immunol.* 2021;127:293–300. 4. Paller AS, et al. *BMJ Open*. 2020;10:e033507. 5. ClinicalTrials.gov. NCT03687359. https://clinicaltrials.gov/study/NCT03687359. Accessed February 2024.

Coexisting Atopic Diseases in AD

How can we assess and manage coexisting atopic disease in pediatric patients?

Questions to assess coexisting atopic disease in pediatric patients[1,a]

- Have you ever been diagnosed with asthma or used a puffer? Does your child **wheeze**?
- Do you/does your child have **trouble breathing** through your/their nose?
- Does your child **refuse food**?
  Does your child vomit often?
- Have you/has your child ever had an immediate reaction within 1 to 2 hours after eating something specific?
- Do you/does your child have problems with a **runny nose, congestion, and itchy, red eyes**?

The prevalence of atopic comorbidities increases with age and AD severity[2,3]

[a]Questions based on Hong CH, et al.[1]

1. Hong CH, et al. *J Cutan Med Surg*. 2019;23(suppl):12S–18S. 2. Kapoor R, et al. *J Am Acad Dermatol*. 2008;58:68–73. 3. Weidinger S, et al. *Br J Dermatol.* 2023;ljad449.

Food Sensitization and Food Allergy Are Common in Children With AD

Studies in children with AD report prevalences of food sensitization between 39% and 66% and food allergy between 15% and 44%[1]

Infants who develop AD within the first year of life **are at greater risk of food allergy (20%)**, and **~50% of infants with AD** requiring use of TCS within the first 3 months of life developed food allergy[2]

An **IL-4Rα** variant was associated with increased risk of **severe food allergy**, and this association was mediated by the **presence of AD[3]**

It is hypothesized that by **preventing or treating AD** in early infancy or childhood, it may be possible to **prevent its progression to food allergy[2]**

IL-4Rα, interleukin 4 receptor alpha; TCS, topical corticosteroid.

1. Tsakok T, et al. *J Allergy Clin Immunol.* 2016;137:1071–1078. 2. Sweeney A, Sampath V, Nadeau KC. *Allergy Asthma Clin Immunol*. 2021;17:1–12.
3. Banzon TM, et al. *J Allergy Clin Immunol Pract*. 2022;10:2117–2124.

In a Randomized, Multicenter Study, Food Allergy was Reduced in Infants With AD Who Received Early Skin Management

Evaluation of efficacy of early proactive vs. reactive management with TCS[a] in reducing food allergy in infants with AD[b]

Randomization

Infants with AD lasting at least 28 days (N=650)[c]

Reactive therapy
TCS[a] on lesional skin only
(n=322[b])

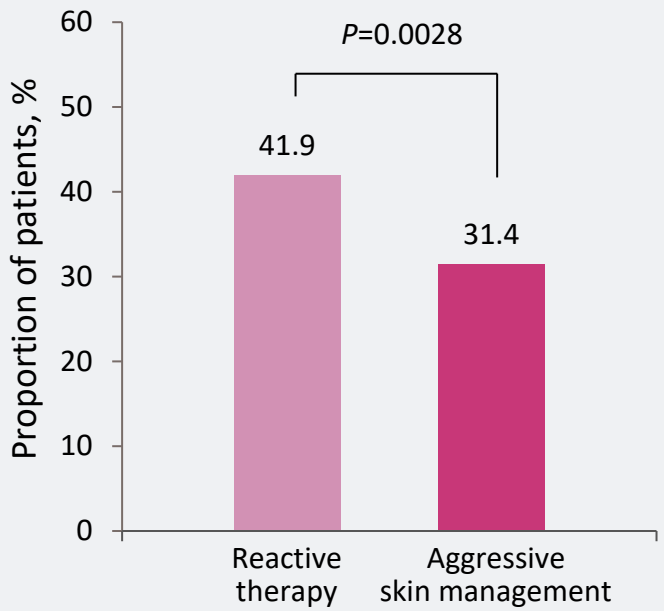
Early aggressive skin management
TCS on lesional and non-lesional skin
(n=318[b])

Age at entry: 7–13 weeks

28 weeks

Primary outcome: Oral food challenge-proven hen's egg allergy

Proportion of patients with hen's egg allergy at age 28 weeks



Safety Finding

Aggressive TCS management lowered body weight and height at 28 weeks of age

Mean difference:

- **Weight**: –422 g, 95% CI: –553 to –292
- **Height**: –0.8 cm, 95% CI: –1.22 to –0.33

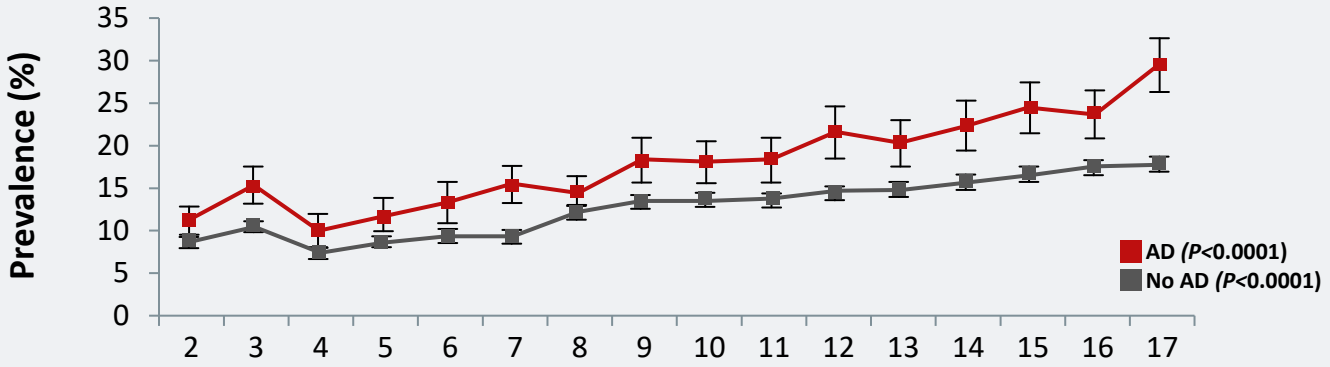
Adapted with permission from Yamamoto-Hanada K, et al. *J Allergy Clin Immunol*. 2023;152:126-135. Copyright 2023 Elsevier.
[a]Alclometasone dipropionate 0.1% [low potency in the US standard pharmacopoeia] for the whole face and betamethasone valerate 0.12% [medium potency in the US standard pharmacopeia] for the whole body except scalp and face twice a day for 14 days from the registration day (day 0) to day 14. [b]Multicenter, parallel-group, open-label, assessor-blind, randomized controlled trial (PACI study). The objective of this study was to determine the efficacy of early aggressive management with TCS applied to both clinically affected and unaffected skin, compared with reactive management (TCS on lesional skin only) to prevent food allergy in infants with AD. [c]Of 650 infants enrolled, data from 640 were analyzed.
PACI, Prevention of Allergy via Cutaneous Intervention; TCS, topical corticosteroids.
Yamamoto-Hanada K, et al. *J Allergy Clin Immunol.* 2023;152:126–135.

Pediatric Patients With AD Have a Higher Prevalence of Mental Health Disorders at All Ages Compared to Control

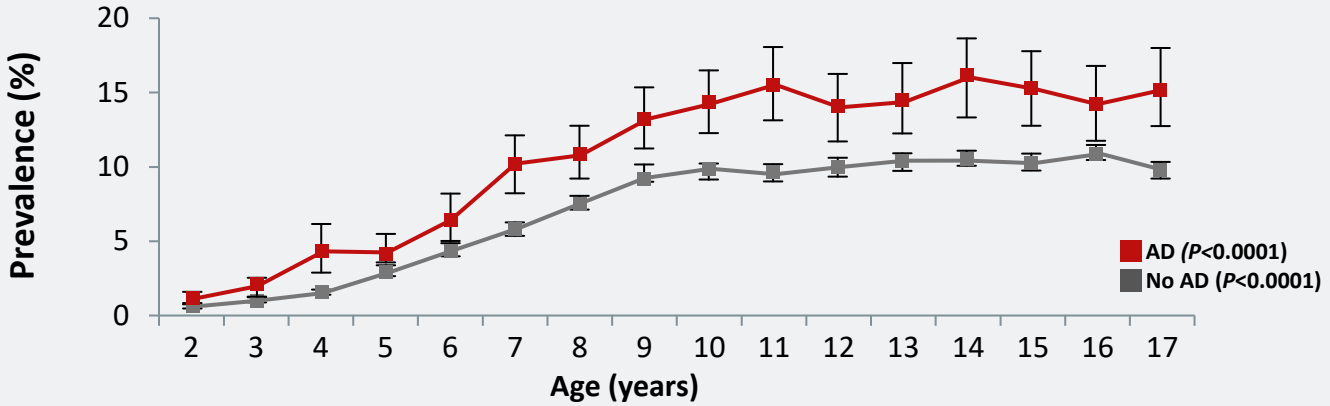
National Health Interview Survey (US data)

Age-dependent differences in prevalence of mental health comorbidities in children with AD

Depression/sadness



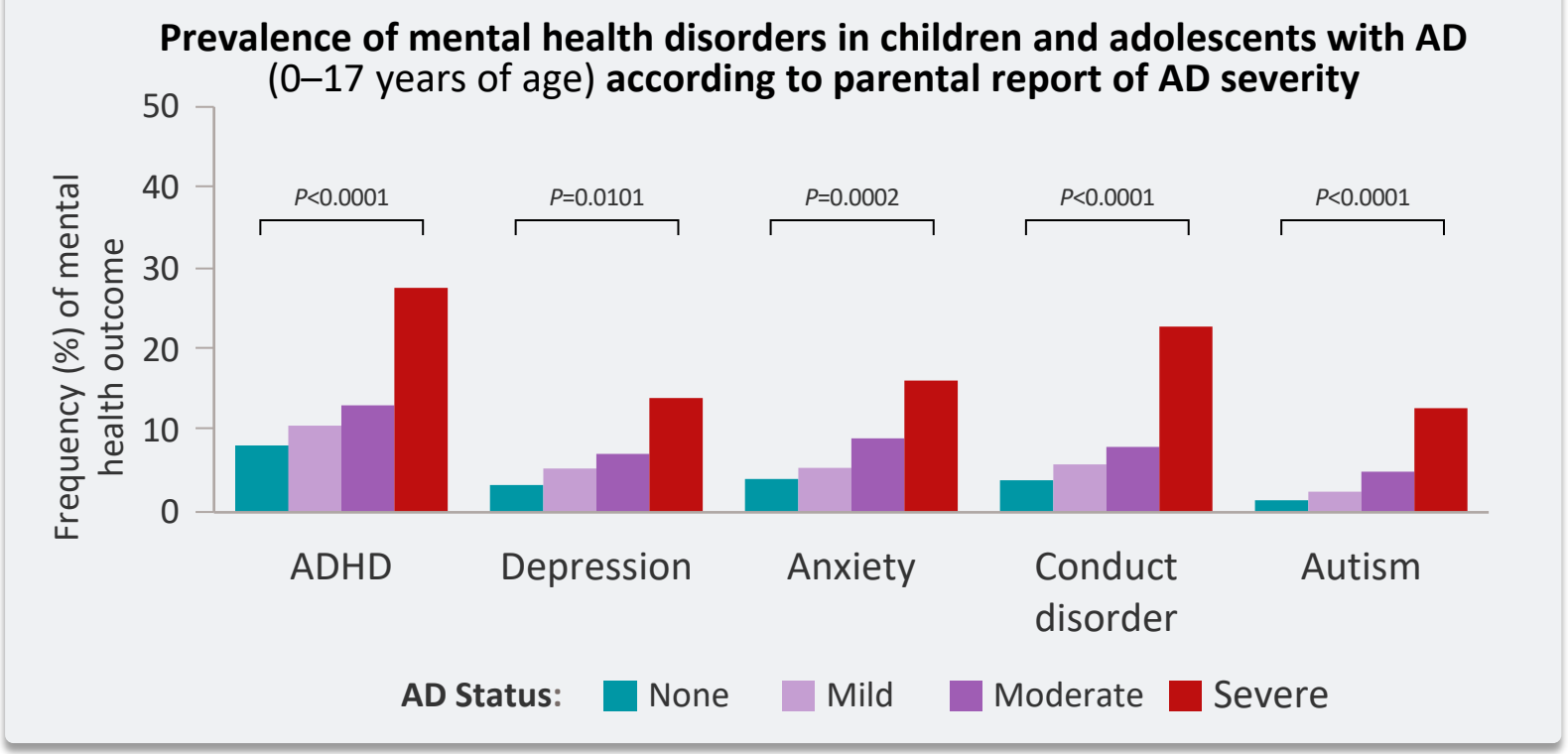
ADHD



Adapted with permission from Hou A, Silverberg JI. *Pediatr Dermatol*. 2021;38:606–612. Copyright 2021 John Wiley & Sons, Inc.
National Health Interview Survey: Cross-sectional data was analyzed from 228,898 children 2–17 years from the 1997–2018 National Health Interview Survey. Surveys were completed for a randomly selected child in the household by a caregiver.[1] Results presented were not analyzed by disease severity. Error bars represent 95% CI.
ADHD, attention deficit hyperactivity disorder.
Hou A, Silverberg JI. *Pediatr Dermatol.* 2021;38:606–612.

The Severity of AD Correlates With an Increased Risk of Mental Health Disorders

2007 National Survey of Children's Health (N=92,642)



The probability of having mental health disorders directly correlated with increasing AD severity in this US population

Cross-sectional study analyzing data from the 2007 National Survey of Children's Health, a survey reporting on the health status of 92,642 non-institutionalized children aged 0–17 years.
Yaghmaie P, et al. *J Allergy Clin Immunol.* 2013;131:428–433.

Children With AD are More Likely to Have Decreased Bone Mineral Density, Which May Impact Their Long-term Bone Health

Evidence suggests that AD is associated with:

Decreased bone mineral density[1,2,a]

Increased risk of fractures[3,a]

Potentially reversible growth impairment[4]

Factors that may contribute to poor bone health in patients with AD

- Earlier onset age of AD[3,5]
- Chronic poor sleep[3,4]
- Corticosteroid use[1,3]
- Effect of chronic inflammation on bone turnover[1,5]

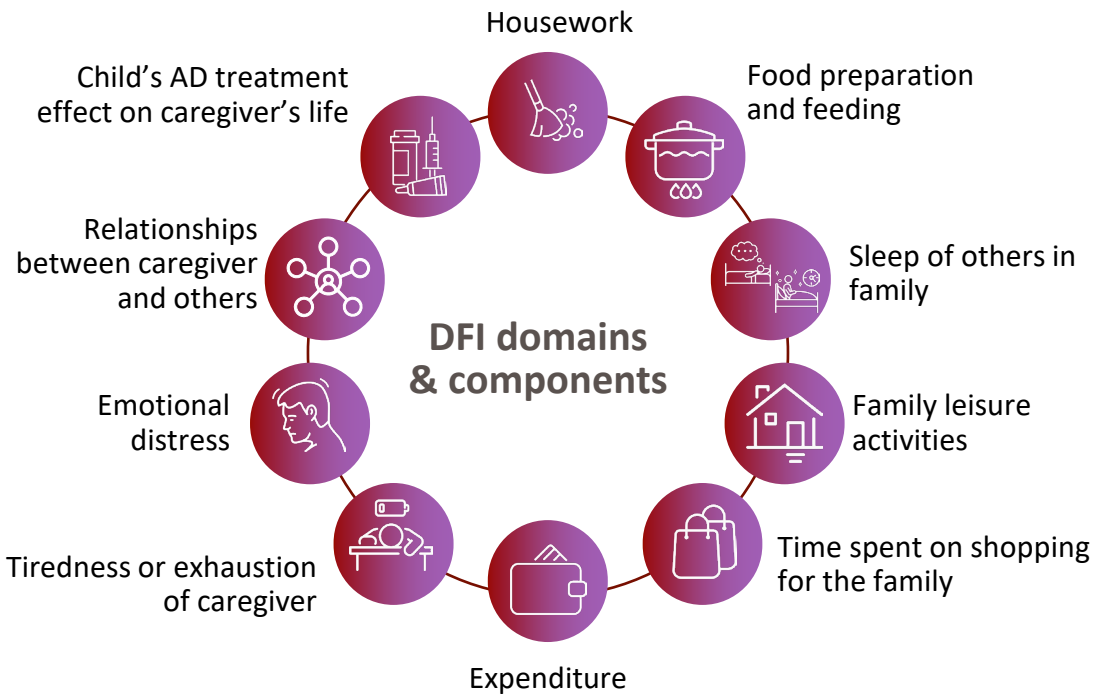
Studies investigating the link between inflammation in AD and bone health are ongoing

[a]In children and adolescents with AD vs healthy controls.[1–3]

1. Wu D, et al. *Ann Transl Med.* 2021;9:40. 2. Silverberg JI. *Pediatr Allergy Immunol.* 2015;26:54–61. 3. Lee AW, et al. *Allergy*. 2023;78:871–875. 4. Silverberg JI, et al. *JAMA Dermatology.* 2015;151:401–409. 5. Kim S, et al. *Sci Rep.* 2021;11:24228.

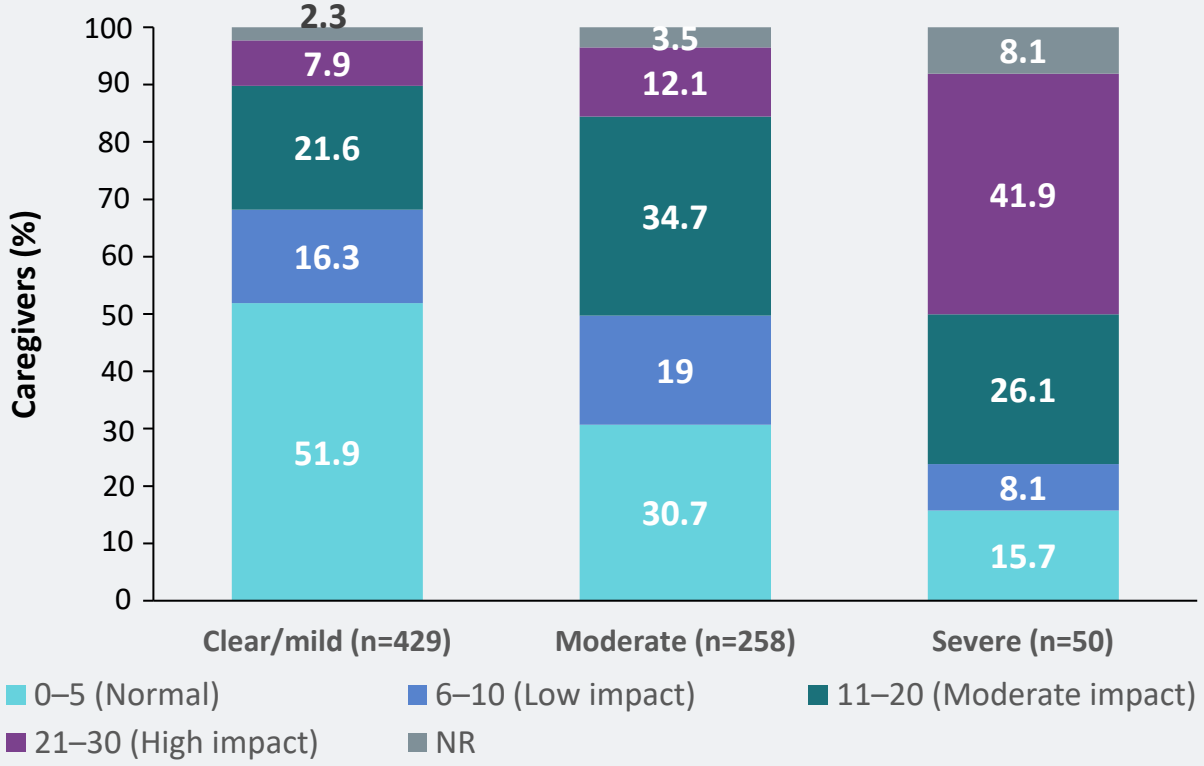
AD in Pediatric Patients Also Negatively Impacts Family Members and Caregivers

Pediatric AD negatively impacts the parents and caregivers of patients as measured by DFI[1,a]



EPI-CARE (N=740)[2]

DFI distribution by AD severity for caregivers of patients aged 6 months to <18 years



Graph Adapted with permission from Simpson E, et al. *RAD*. 2022. Poster 15.
P<0.05 vs mild; *P*<0.05 vs moderate.
[a]DFI asks how much effect a child's eczema has on 10 domains: housework, feeding, sleep of family, family leisure, shopping, expenditures, tiredness, emotional distress, relationships, and help with treatment.
DFI, Dermatitis Family Impact Questionnaire.
1. Barbarot S, et al. *J Pediatr*. 2022;246:220–226. 2. Simpson E, et al. *RAD*. 2022. Poster 15.

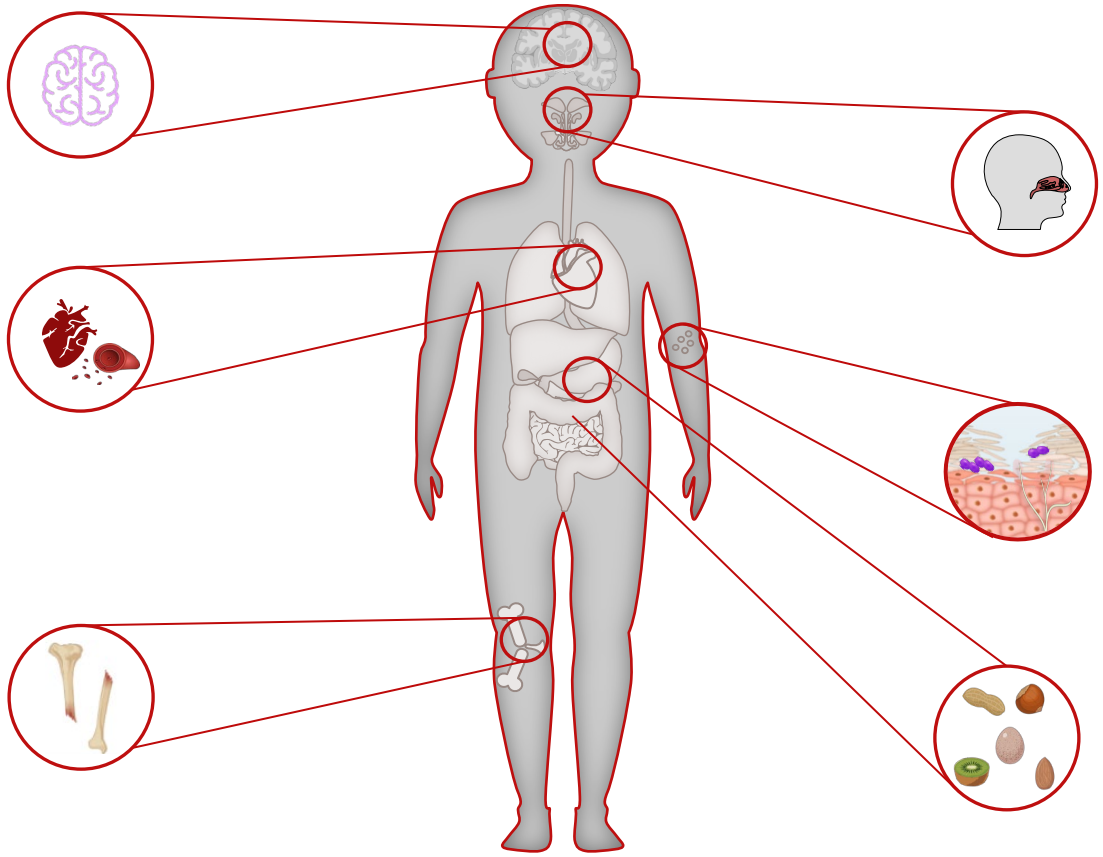
The Multidimensional Disease Burden of Moderate-to-Severe AD Has Potential Long-term Consequences

Pediatrics

Mental health disorders, sleep disturbances[1–4]

Cardiovascular and pulmonary health[5,a]

Skeletal growth impairment, fracture risk[6,7]



Allergic rhinitis, CRSwNP[8,a]

Skin barrier dysfunction, neuroimmune dysregulation, AD signs and symptoms, dysbiosis, and infection[9–11]

Food allergy[8]

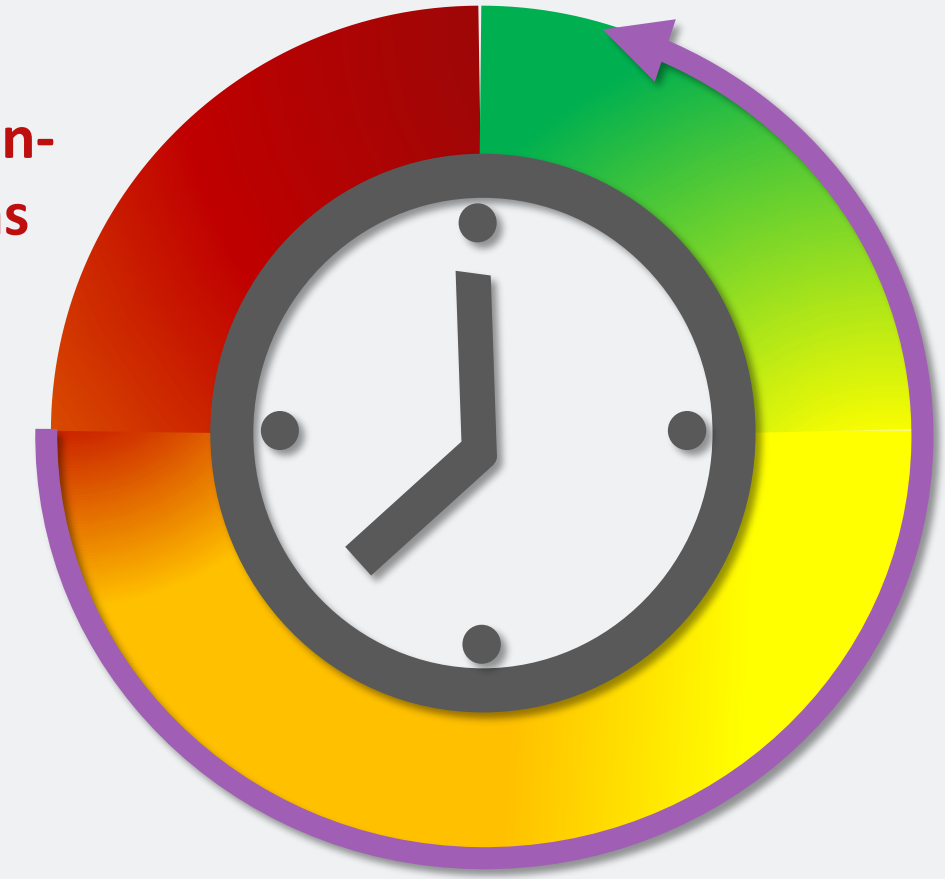
[a]Cardiovascular disease and CRSwNP are more typical in adulthood[5,8]

CRSwNP, chronic rhinosinusitis with nasal polyps.

1. Cameron S, et al. *Allergy*. 2023;00:1–11. 2. Hou A, Silverberg JI. *Pediatr Dermatol*. 2021;38:606–612. 3. Kern C, et al. *JAMA Dermatol*. 2021;157:1200–1208. 4. Bawany F, *J Allergy Clin Immunol Pract*. 2021;9:1488–500. 5. Wan J, et al. *J Allergy Clin Immunol Pract*. 2023;11:3123–3132. 6. Wu D, et al. *Ann Transl Med*. 2021;9:40. 7. Lee SW, et al. *Allergy*. 2023;78:871–875. 8. Geba GP, et al. *J Allergy Clin Immunol*. 2023;151:756–766. 9. Beck LA, et al. *JID Innov*. 2022;2:100131. 10. Haddad EB, et al. *Dermatol Ther (Heidelb)*. 2022;12:1501–1533. 11. Leung DYM, et al. *J Allergy Clin Immunol Pract*. 2023;11:1421–1428.

Early interventions focused on reducing systemic type 2 inflammation in the initial stages of AD may reduce the likelihood of future development of multimorbidities, reverse structural changes in the skin, and change disease course[1,2]

Atopic and non-atopic burdens



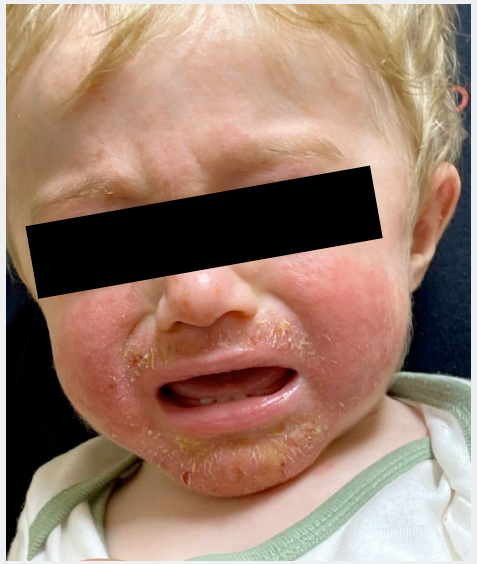
- AD often precedes atopic diseases at other body sites suggesting the skin may be an important site for allergen sensitization[3–5]
- Skin disruption can increase allergen exposure and skin sensitization, which may increase the risk of other atopic diseases[2,4,6]
- Non-atopic, systemic comorbidities may also develop, impacting mental, skeletal, and cardiovascular health[7–9]

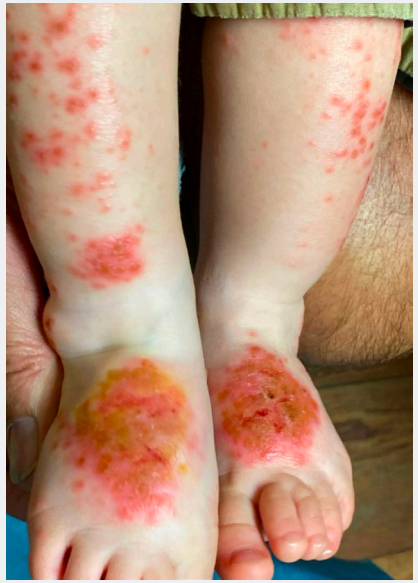
1. Paller AS, et al. *J Allergy Clin Immunol*. 2019;143:46–55. 2. Bieber T. *Nat Rev Drug Discov*. 2023;22:662–680. 3. Lack G, et al. *N Engl J Med*. 2003;348:977–985. 4. Ziegler SF. *Ann Allergy Asthma Immunol*. 2021;127:306–311.
5. Han H, et al. *Immunol Rev*. 2017;278:116–130. 6. Ghezzi M, et al. *Children.* 2021;8:1165. 7. Kern C, et al. *JAMA Dermatol*. 2021;157:1200–1208. 8. Wu D, et al. *Ann Transl Med*. 2021;9:40.
9. Wan J, et al. *J Allergy Clin Immunol Pract.* 2023;11:3123–3132.

More Than Skin Deep: Early Intervention May Help Address the Multidimensional Burden of AD

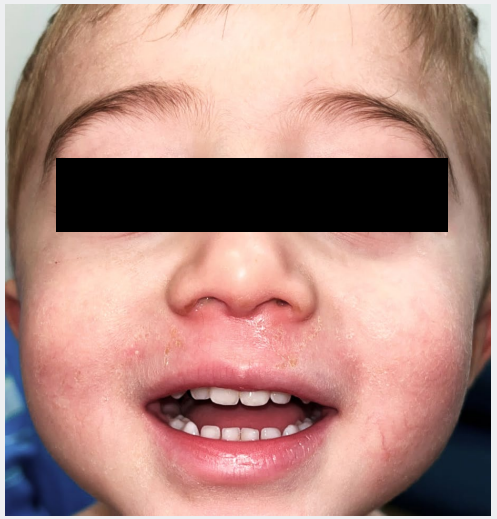
Matthew

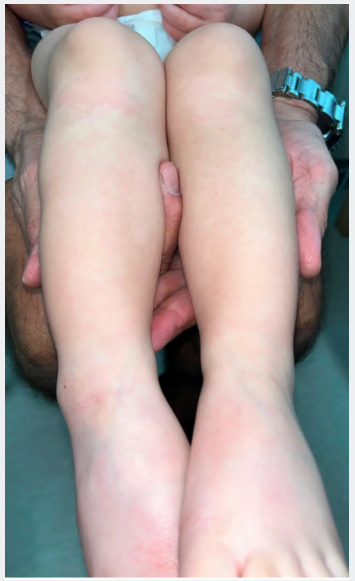
Pre-intervention





On treatment





Photos reprinted with permission from Eichenfield LF.

Summary

Children with AD experience a multidimensional disease burden, which may have long-term consequences later in life

The long-term effects of type 2 inflammatory processes have negative implications in the skin as well as other organ systems

Early intervention may modify disease and prevent the development or the progression of atopic and non-atopic comorbidities, improving patients' and caregivers' lives

Polling Question

Which of these statements about the of prevalence atopic comorbidities in pediatric patients with AD is correct?

Select one response

A. Approximately 1/3 of patients have ≥1 atopic comorbidity, this number increases with age and asthma is the most frequent comorbidity

B. Approximately 2/3 of patients have ≥1 atopic comorbidity, this number decreases with age, with asthma and allergic rhinitis being the most frequent

C. Over 75% of patients have ≥1 atopic comorbidity, this number increases with severity and age, with food allergy, allergic rhinitis, and asthma being the most frequent

www.adventdermatology.com

Polling Question

Which of these statements about the of prevalence atopic comorbidities in pediatric patients with AD is correct?

Select one response

A. Approximately 1/3 of patients have ≥1 atopic comorbidity, this number increases with age and asthma is the most frequent comorbidity

B. Approximately 2/3 of patients have ≥1 atopic comorbidity, this number decreases with age, with asthma and allergic rhinitis being the most frequent

C. **Over 75% of patients have ≥1 atopic comorbidity, this number increases with severity and age, with food allergy, allergic rhinitis, and asthma being the most frequent**

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Polling Question

Do you believe that by addressing dysregulated type 2 inflammation early in infants with severe AD we can impact the incidence or progression of the disease?

Select one response

A **Yes**

B **No**

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Panel Discussion 1

New Data on the Systemic Burden of AD in Children and the Need for Early Intervention

1. What are the barriers to early intervention?
2. What drives you to treat earlier?

Importance of Achieving Disease Control in Adults With Moderate-to-Severe AD

Eric Simpson, MD, MCR

Polling Question

How do you define disease control in your patients with AD?

Select one response

A Absence of flares (no disease worsening with need of treatment escalation) for at least 3 months

B Clear or almost clear skin, no or minimal itch, no impact in quality of life for at least 6 months

C Maintaining ADCT score <7 for 6 consecutive months

D Maintaining EASI<7 and itch <4 over at least 3 months

E Other

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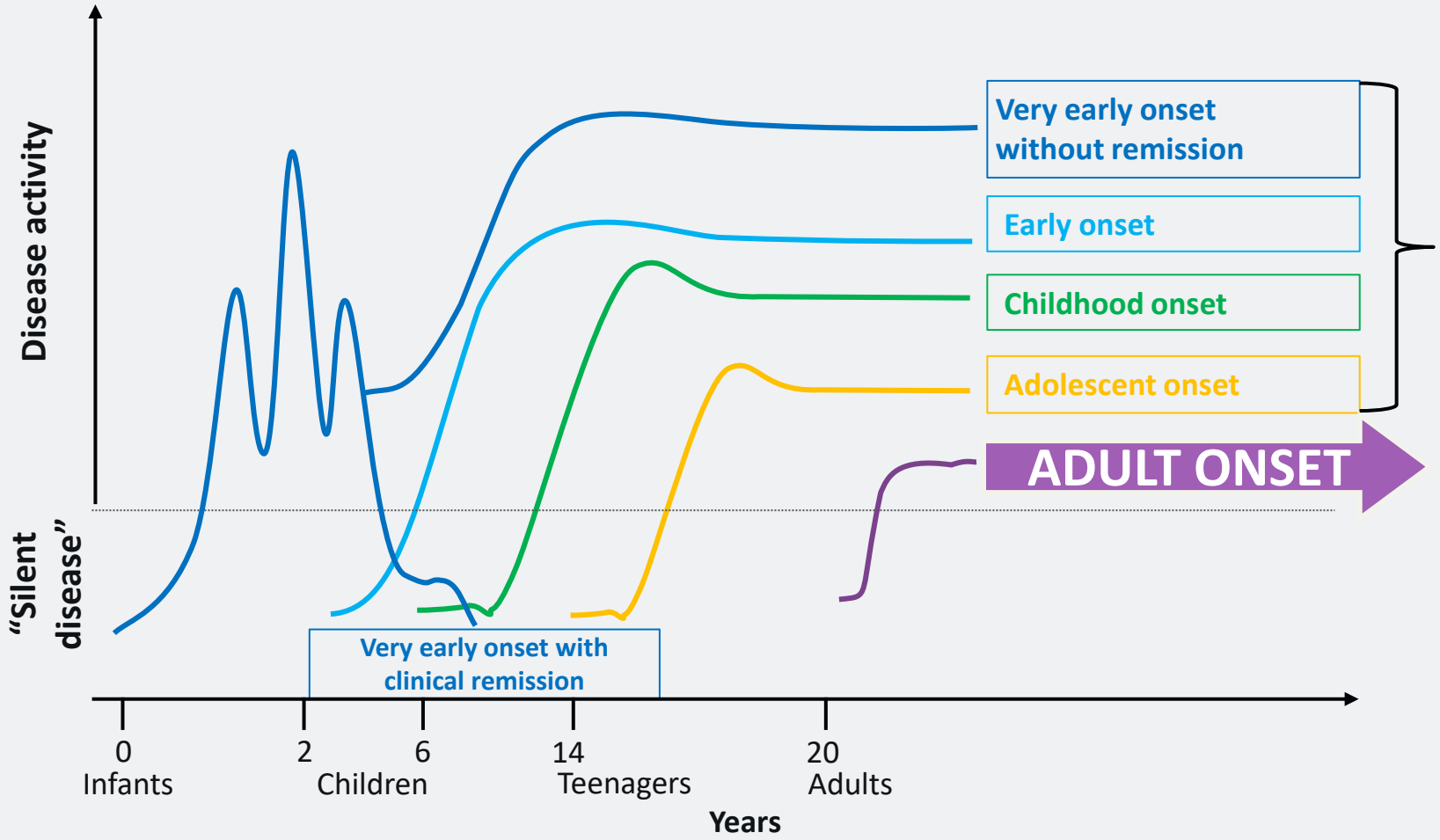
ADCT, Atopic Dermatitis Control Tool; EASI, Eczema Area and Severity Index.

Many Adults With AD Have Had the Disease Since Childhood, But It May Also Develop in Adulthood

Most patients with moderate-to-severe AD have persistent disease independent of the age of onset

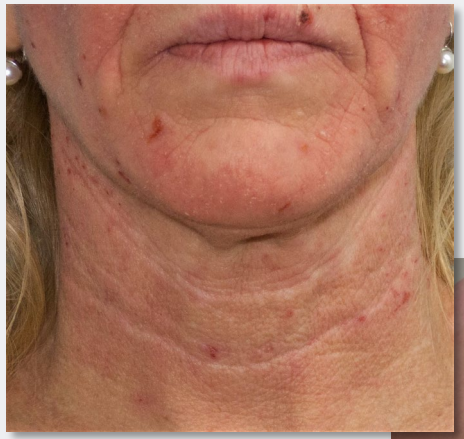


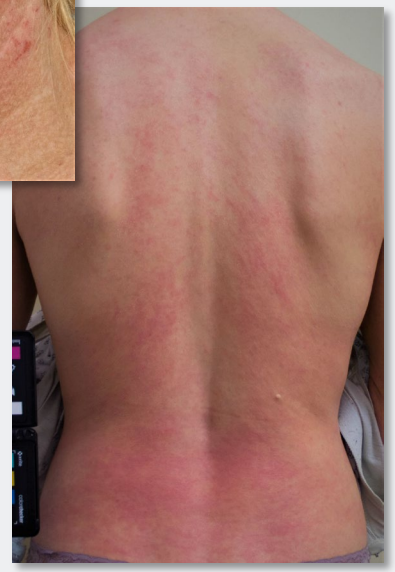
Adapted with permission from Bieber T, et al. *J Allergy Clin Immunol*. 2017;139:S58–S64. Copyright 2017 Elsevier.
Bieber T, et al. *J Allergy Clin Immunol*. 2017;139:S58–S64.

Case Study: AD in an Adult Patient

Maria

Female
38-year-old





Clinical history	• Diagnosed with AD in childhood • Experiences intense itch almost every day • AD often flares with eczematous lesions over trunk, back, and extremities including hands, and face • Also diagnosed with asthma and allergic rhinitis
Treatment history	• Mometasone furoate 0.1% cream • No ongoing or concomitant treatments
Burden	• Maria feels her skin is constantly itchy, cracking, weeping/oozing and bleeding • Her sleep is disturbed every night by her AD

Case study and photos adapted with permission from Sanofi and Regeneron.

Patient and Physician Goals in the Treatment of AD

Patients' most important desires
- No flares
- No impact on quality of life
- Minimal itch and no impact on sleep

Physicians' definition of disease control
- Clear or almost clear skin
- Minimal disease activity

Atopic Dermatitis Control Tool

ADCT helps facilitate meaningful patient–physician discussion on control of AD in everyday clinical practice. Six main areas are used to assess the multi-dimensional aspects of disease control over the course of a week:


Overall severity of AD symptoms


Days with intense itching episodes


Intensity of AD-related bother


Frequency of sleep impact


Impact of AD on daily activities

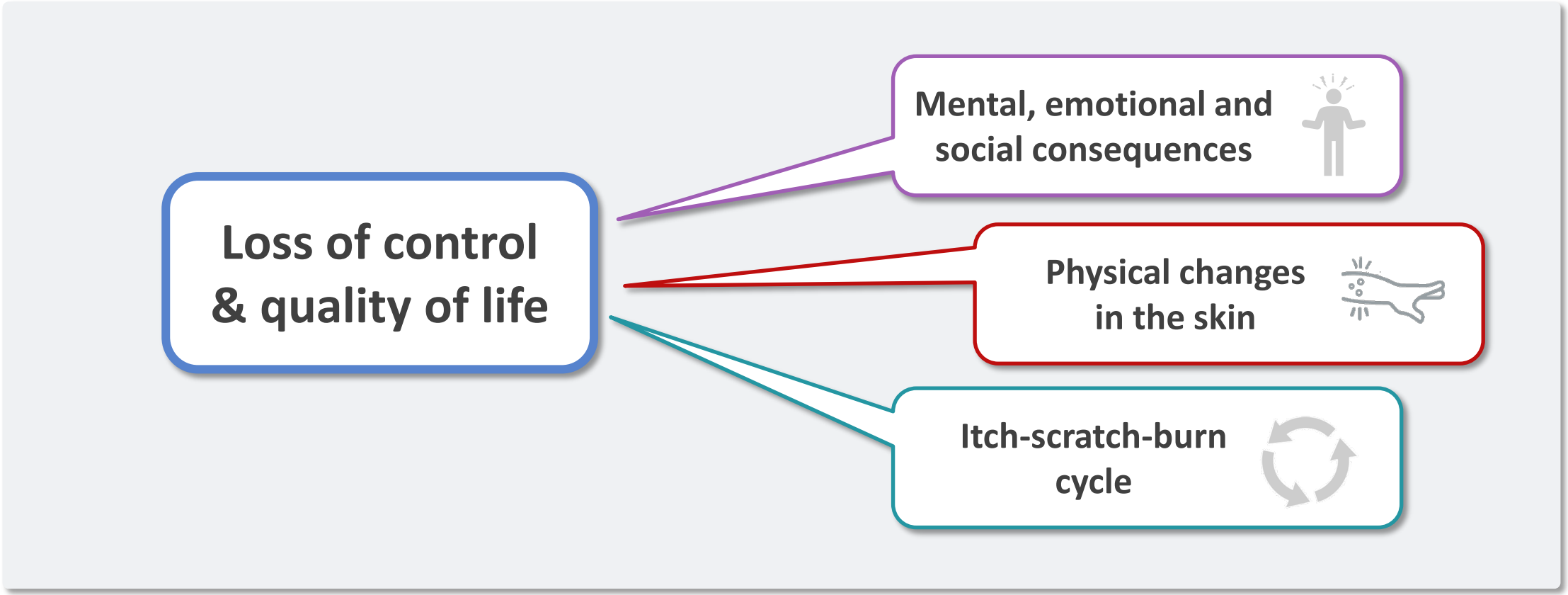

Impact of AD on mood or emotions

ADCT, Atopic Dermatitis Control Tool.

Simpson E, et al. *BMC Dermatol*. 2019;19:15. doi: 10.1186/s12895-019-0095-3.

Constructs That Define AD Flares From the Patient Perspective

In an NEA study, a focus groups of US adult patients with AD identified important aspects when describing an AD flare

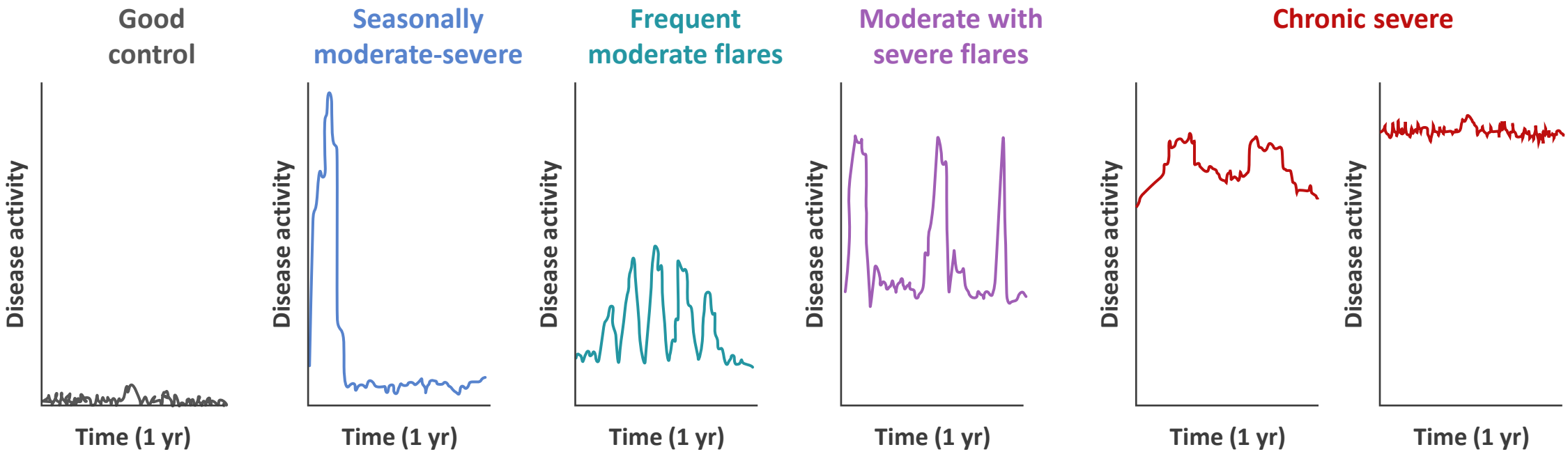


NEA, National Eczema Association.

Dainty KN, et al. *Br J Dermatol*. Published online January 30, 2024. doi:10.1093/bjd/ljae037.

The Prevention of Flares Is an Important Treatment Goal for Patients and Physicians

Several AD Disease Course Patterns:



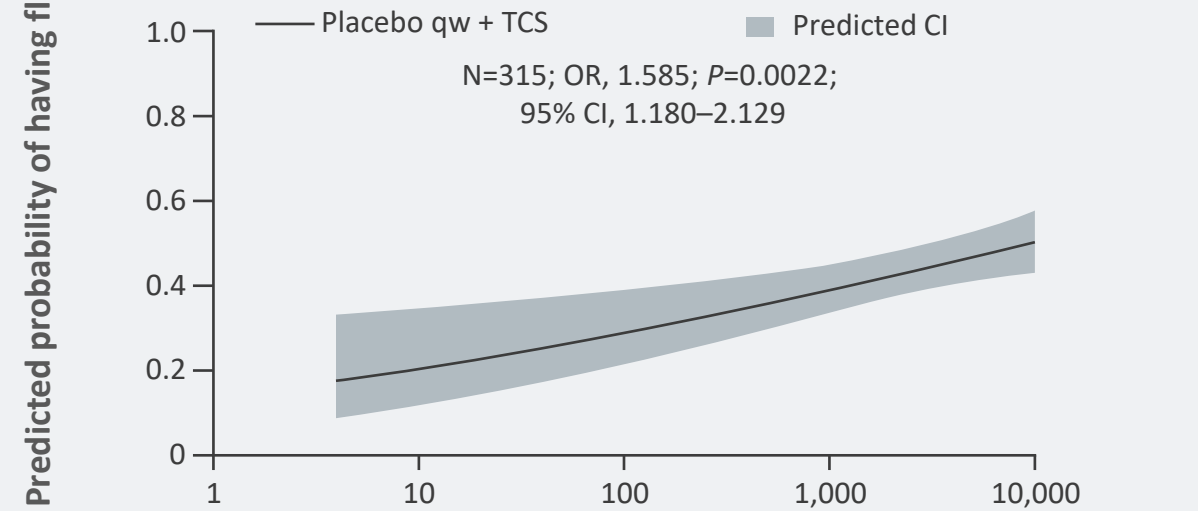
In real-world practice, most individuals with moderate-to-severe AD experience flares and fluctuating signs & symptoms over time

Reproduced with permission from Chovatiya R, Silverberg JI. *Am J Clin Dermatol*. 2022;23:459–468. Copyright 2022 Springer Nature.
Chovatiya R, Silverberg JI. *Am J Clin Dermatol*. 2022;23:459–468.

Total IgE Levels are Associated With Flares in AD

Most patients with moderate-to-severe AD have elevated IgE serum levels, which may be associated with probability of flares[1,2]

Frequency of flares is associated with high **levels of IgE** in adult patients[2,a]



Patients with total IgE by category, n (%)	<1	(1–10)	(10–100)	(100–1000)	(1000–10,000)	≥10,000
Placebo + TCS	0	1 (0.3)	28 (8.9)	67 (21.3)	82 (26.0)	134 (42.5)

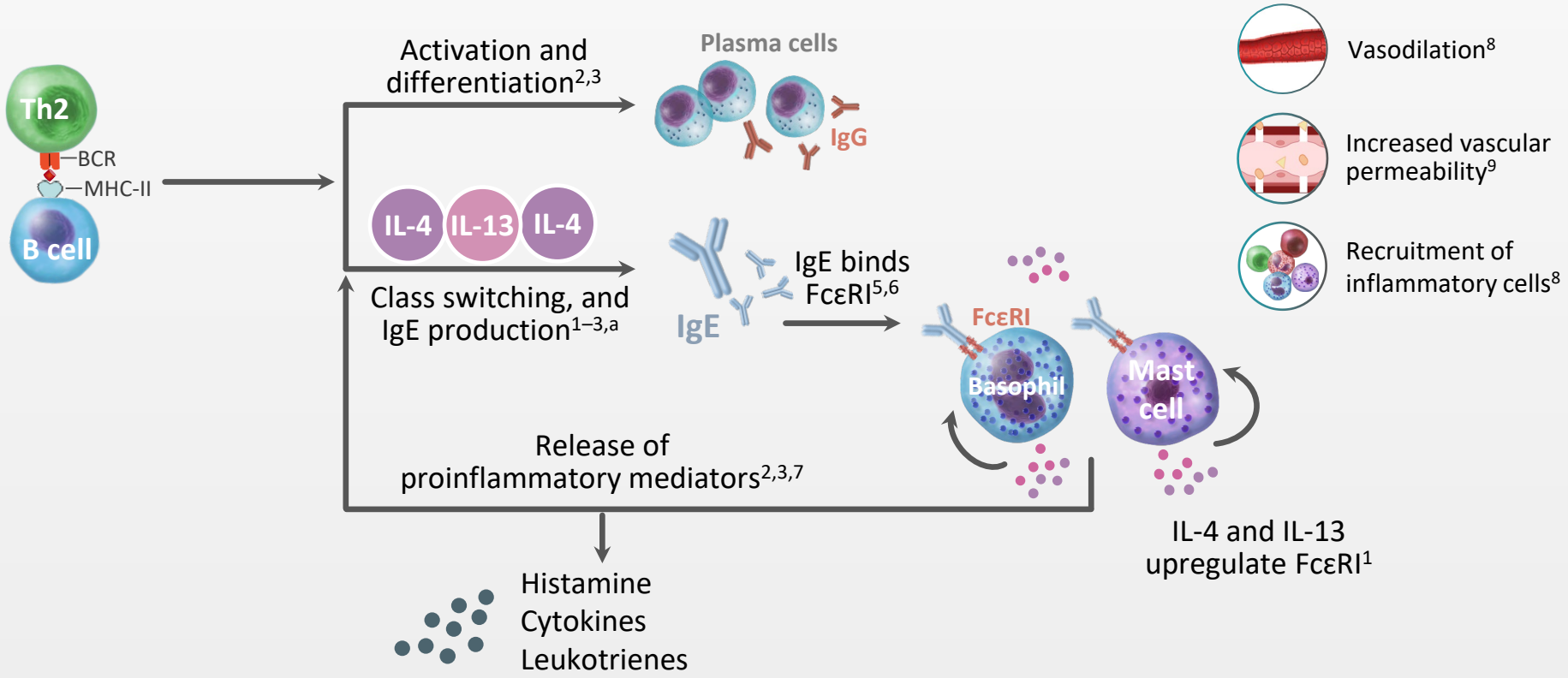
Figure adapted with permission from Kim B, et al. *WCI*. 2023. Poster.
[a]Missing values: 3 (1.0%). In patients with moderate-to-severe AD managed with TCS only, the probability of having flares increases with total IgE levels at baseline. The odds of having flares increases by 59% (1.59 times, *P*=0.002) with every 10-fold increase of IgE level at baseline.
EASI, Eczema Area and Severity Index; IgE, immunoglobulin E; qw, weekly; TCS, topical corticosteroid.
1. Hu Y, et al. *J Clin Lab Anal*. 2020;34:e23214. 2. Kim B, et al. *WCI*. Poster. 2023.

IgE and AD Pathophysiology

Clinical features

- Allergic symptoms
- Disease exacerbations

IL-4 and IL-13 feed into a cycle of B cell activation, IgE production, and granulocyte activation, leading to the repeated release of inflammatory mediators[1–3]



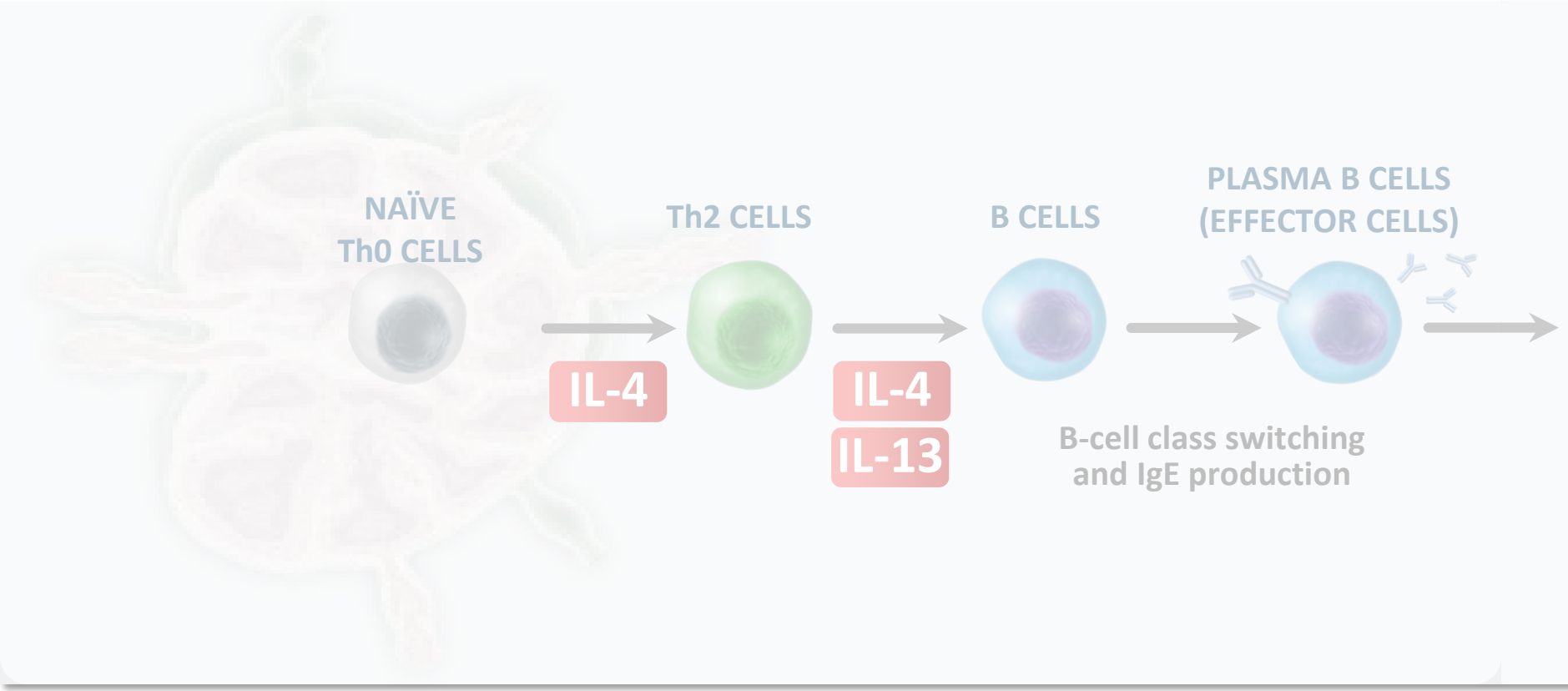
[a]IL-4 is generally more potent than IL-13 in inducing IgE synthesis[1,4].

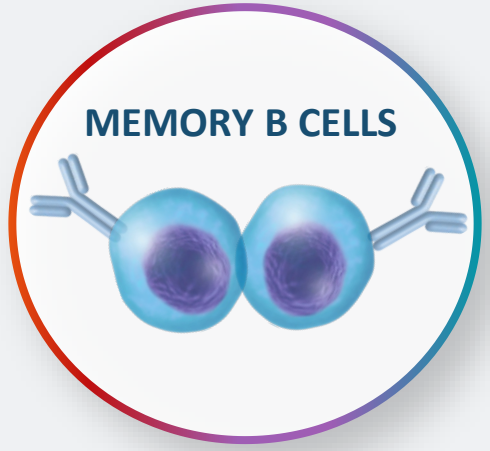
BCR, B-cell receptor; IgE, immunoglobulin E; FcεRI, high-affinity IgE Fc receptor; IL, interleukin; MHC, major histocompatibility complex; Th, T helper.

1. Gandhi NA, et al. *Nat Rev Drug Discov*. 2016;15:35–50. 2. Kolkhir P, et al. *Ann Allergy Asthma Immunol*. 2020;124:2–12. 3. Granato A, et al. *J Immunol*. 2014;192:5761–5775. 4. Wills-Karp M, Finkelman FD. *Sci Signal*. 2008;1:pe55. 5. Kaplan AP. *Allergy Asthma Immunol Res*. 2017;9:477–482. 6. Giménez-Arnau AM, et al. *J Allergy Clin Immunol Pract*. 2021;9:2195–2208. 7. Wang F, et al. *Cell*. 2021;184:422–440.e17. 8. Haddad EB, et al. *Dermatol Ther (Heidelb)*. 9. Leung DY, et al. *J Allergy Clin Immunol.* 2023;105:860–876.

IL-4 and IL-13 Promote the Activation of Memory B Cells Which Contribute to Chronic, Sustained Inflammation

IL-4 and IL-13 contribute to B cell class switching including the enhancement of memory B cell differentiation[1,2]



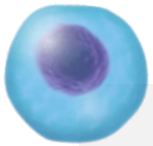


Memory B cells have a longer lifespan than plasma cells, enabling them to rapidly respond upon second exposure to the same antigen[3]

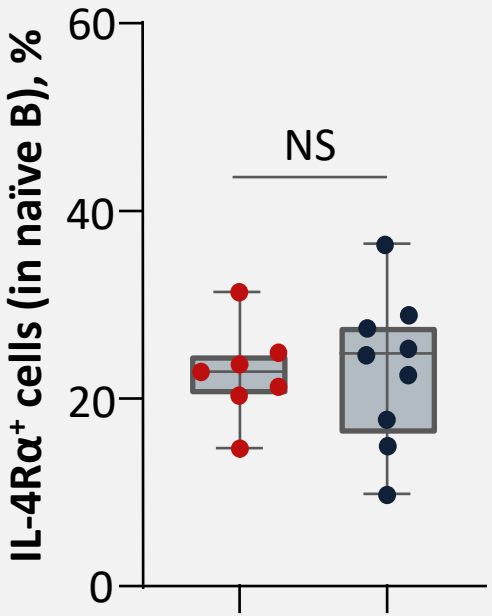
IgE, immunoglobulin E; IL, interleukin; Th, T helper.

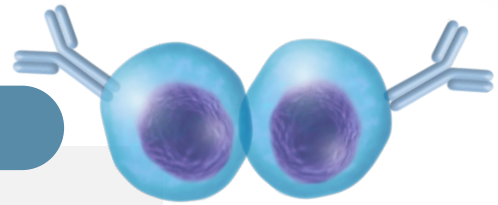
1. Duan L, et al. *Immunity.* 2021; 12;54:2256–2272. 2. Haddad EB, et al. *Dermatol Ther (Heidelb).* 2022;12:1501–1533. 3. Palm AK, Henry C. *Front Immunol.* 2019;10:1787.

New Data Suggest IL-4Rα is Upregulated on Memory B Cells of Adult Patients With AD Compared to Healthy Controls[a]

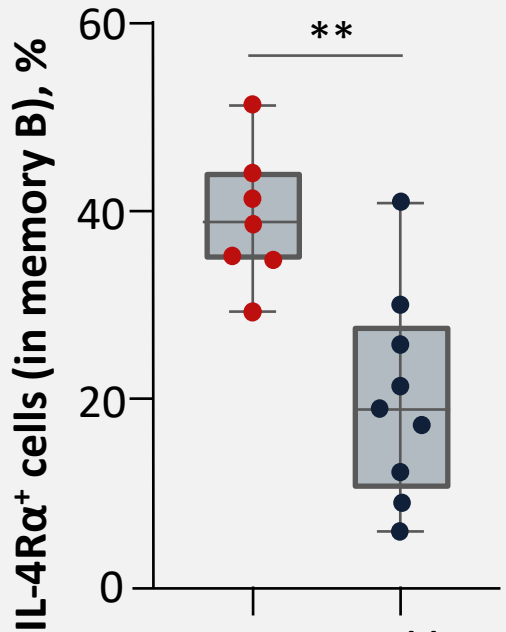


Naïve B Cells





Memory B Cells



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***P*<0.01.
[a]Sample (n=16) included patients with severe, early-onset allergic diseases, including AD (n=15).
IL4R, interleukin 4 receptor; NS, not significant; STAT, signal transducer and activator of transcription.
Data show expression of IL4Ra quantified as a percentage of positive cells in STAT6 patient cells (n=7) and healthy controls (n=9), as assessed by flow cytometry of peripheral blood mononuclear cells.
Sharma M, et al. *J Exper Med.* 2023;220:e20221755.

AD is Associated With Multiple Atopic and Non-atopic Comorbidities in Adults

Atopic comorbidities in adults

- Allergic rhinitis[1,2]
- Conjunctivitis[1,2]
- Asthma[1,2]
- Food allergies[1]

Other comorbidities in adults

- Anxiety or Depression[1,3]
- Infections (*S. aureus*)[4]
- Suicidality[3]
- Heart disease[1,5]

1.Calzavara-Pinton P, *et al. Adv Ther.* 2023;40:5366–5382. 2. Simpson EL, *et al. Dermatol Ther (Heidelb).* 2024;14:261–270. 3. Sandhu JK, et al. *JAMA Dermatol*. 2019;155:178–187 . 4. Simpson EL, et al. *J Allergy Clin Immunol Pract*. 2023;11:2504–2515. 5. Wan J*, et al. J Allergy Clin Immunol Pract.* 2023 Sep 20 [epub ahead of print].

Adults with AD Commonly Have Comorbid Atopic Diseases

Atopic comorbidities in adults

- Allergic rhinitis[1,2]
- Conjunctivitis[1,2]
- Asthma[1,2]
- Food allergies[1]

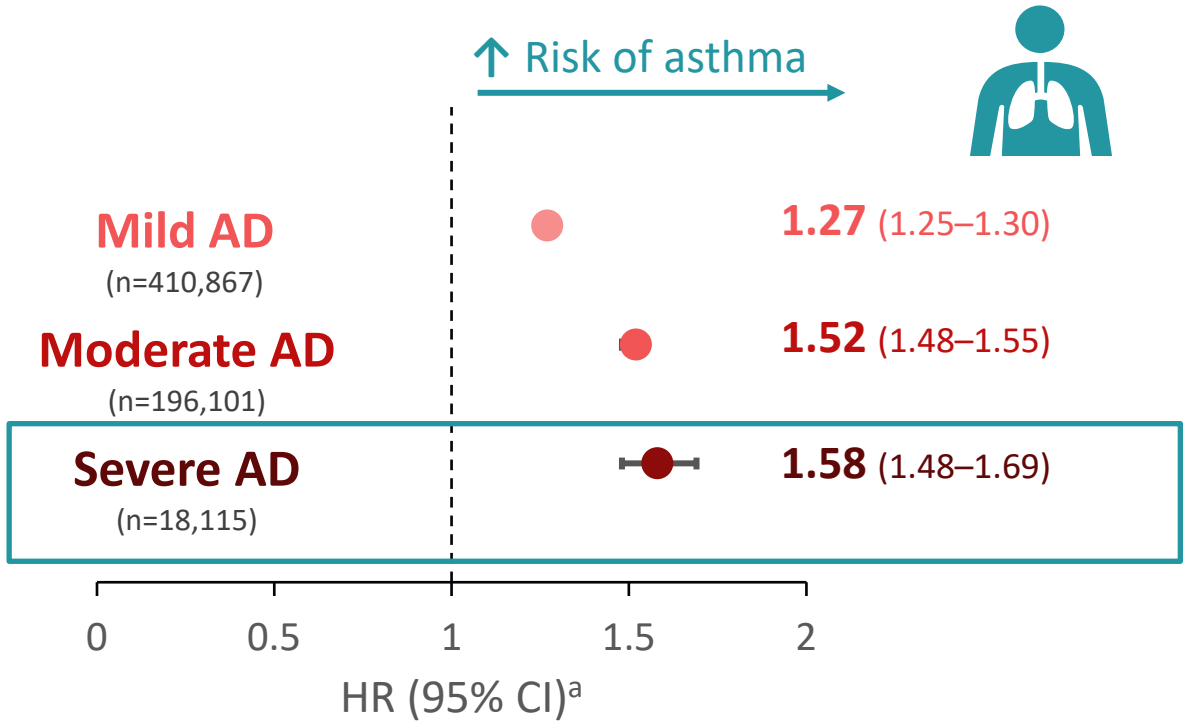
59–78% of patients with moderate-to-severe AD in real-world studies had ≥1 atopic comorbidity[1,2a]

[a]Includes adolescent and adult patients

1.Calzavara-Pinton P, et al. *Adv Ther.* 2023;40:5366–5382. 2. Simpson EL, et al. *Dermatol Ther (Heidelb).* 2024;14:261–270.

Risk of Asthma and Asthma-related Events Increases With AD Severity

Asthma was more likely among patients with AD vs without AD, and increased with AD severity

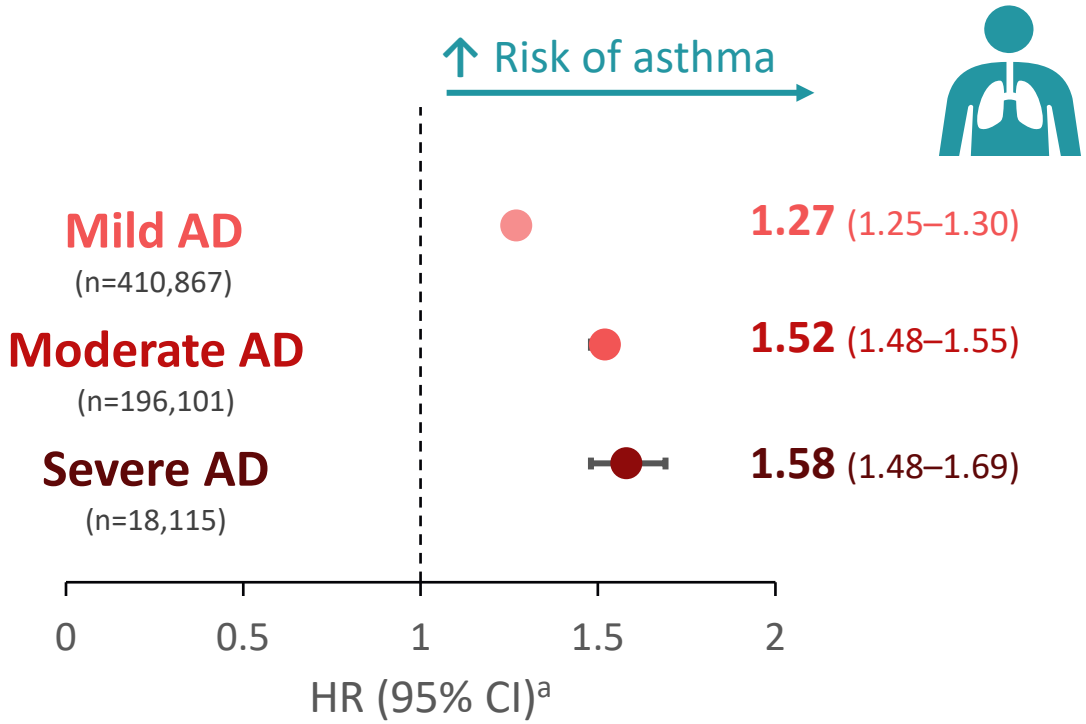


58% ↑ Asthma risk for severe AD vs no AD

[a]HR is for comparison vs patients without AD.
Cohort study using electronic medical records from The Health Improvement Network in the United Kingdom. Data were collected between 1994 and February 2015 were used.
HR, hazard ratio.
Wan J, *et al. J Allergy Clin Immunol Pract.* 2023:S2213-2198(23)01251-5.

Risk of Asthma and Asthma-related Events Increases With AD Severity

Asthma was more likely among patients with AD vs without AD, and increased with AD severity



Patients with AD and asthma were more likely to have asthma exacerbations and asthma-related hospitalizations

For patients with asthma and **severe AD vs no AD**:

37% ↑ Asthma **exacerbation** risk

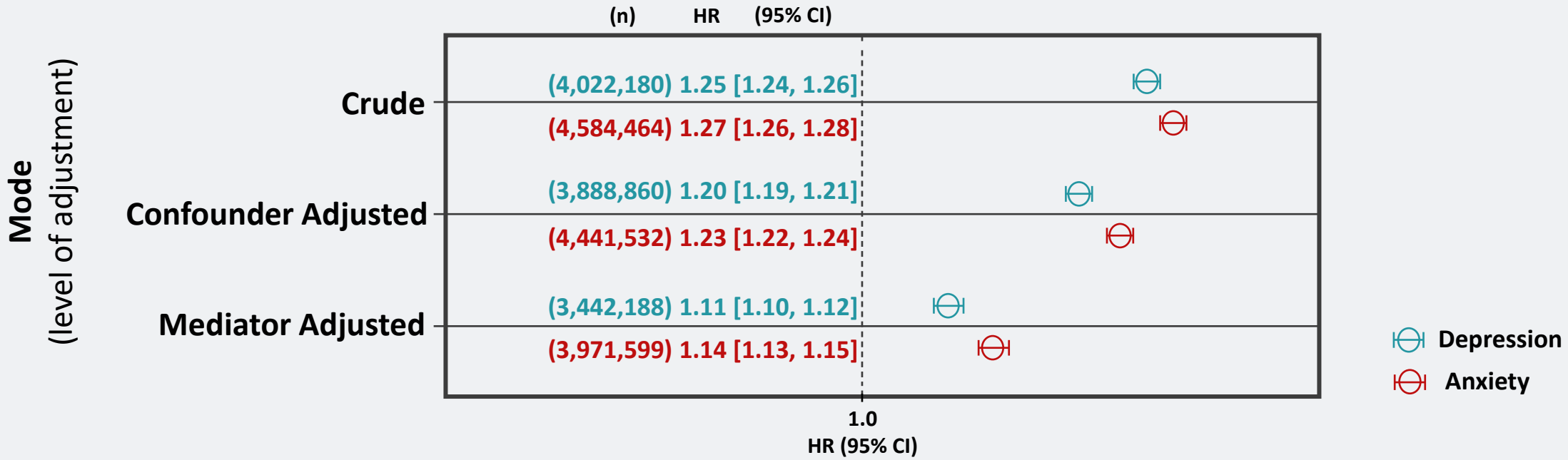
44% ↑ Asthma-related **hospitalization** risk

[a]HR is for comparison vs patients without AD.
Cohort study using electronic medical records from The Health Improvement Network in the United Kingdom. Data were collected between 1994 and February 2015 were used.
HR, hazard ratio.
Wan J, *et al. J Allergy Clin Immunol Pract.* 2023:S2213-2198(23)01251-5.

AD in Adults is Associated With Increased Incidence of Anxiety and Depression

UK Clinical Practice Research Datalink GOLD

HRs for the association between AD and anxiety or depression from stratified Cox models[1,a]



Risk factors that may contribute to increased anxiety and depression in adults with AD include sleep loss and systemic corticosteroid use[1–3]

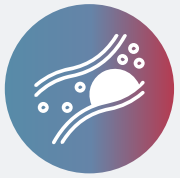
Figure adapted under the Creative Commons Attribution (CC-BY 4.0). Hedderson AD, et al. *BMC Med*. 2023;21:285.
[a]The crude model adjusted for matched set only (age, sex, practice). The confounder-adjusted model additionally adjusted for deprivation, calendar period, asthma, and Charlson comorbidity index. The mediator-adjusted model additionally adjusted for BMI, smoking status, harmful alcohol use, sleep problems, and immediate risk following a prescription of high-dose oral glucocorticoids.
Dots; estimated HR. Lines; 95% CI.
HR, hazard ratio.
1. Henderson AD, et al. *BMC Med*. 2023;21:285. 2. Cameron S, et al. *Allergy*. 2023;00:1–11. 3. Neri I, et al. *J Asthma Allergy*. 2023;16:383–396.

Disease Severity and Duration of AD in Adults Have Been Associated With Increased CV Risk Factors and CV Events[1–3]

UK THIN database cohort study, adult cohort (N=3,303,971)[1]

Pulmonary embolism
HR: 1.39
(1.21–1.60)

Myocardial infarction
HR: 1.27
(1.15–1.39)



Deep vein thrombosis
HR: 1.64
(1.49–1.82)

Stroke
HR: 1.21
(1.13–1.30)

Adult patients with AD are at risk for various CV events

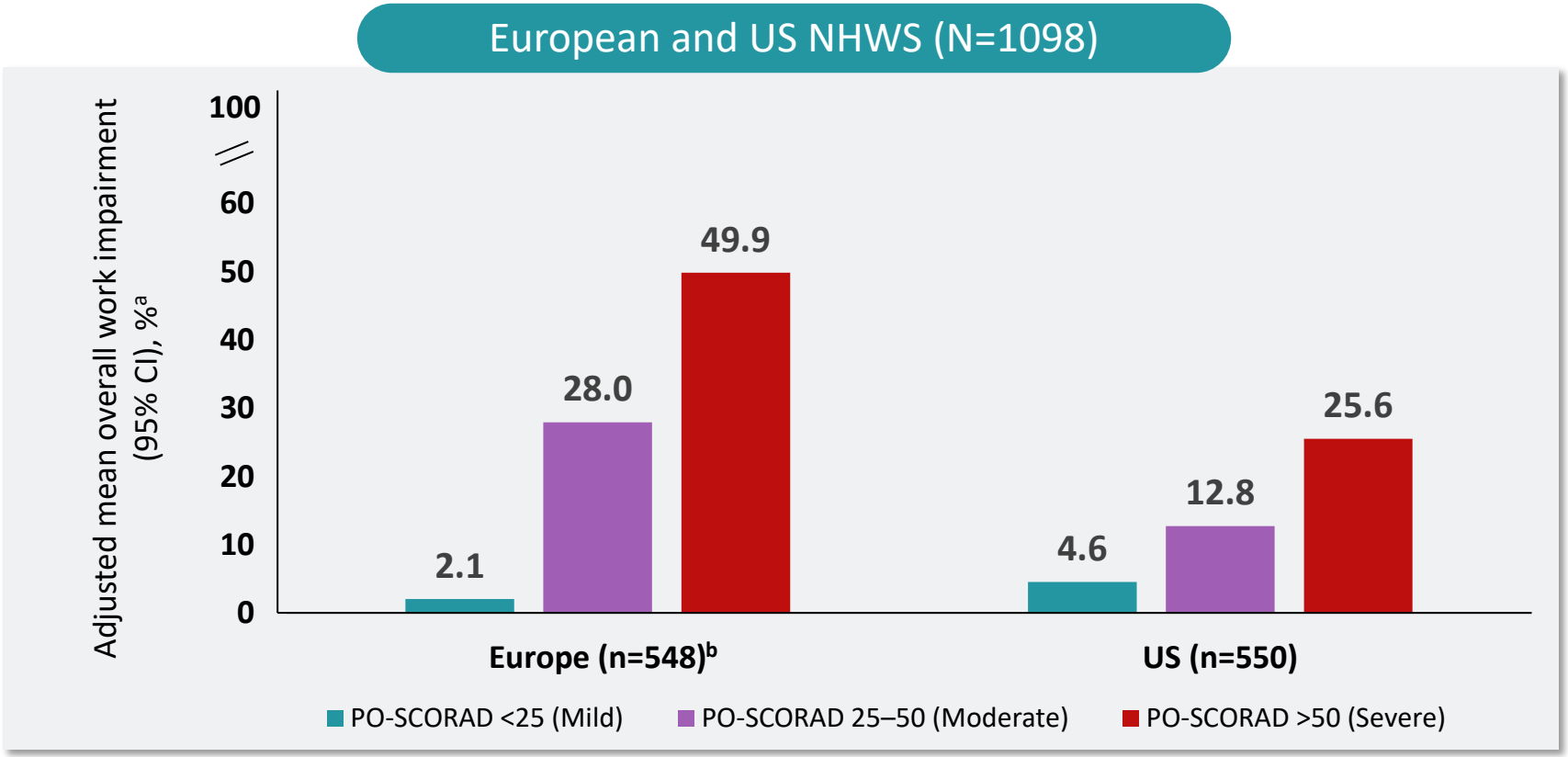
Cohort study using THIN, an electronic health record database of general practices in the UK that is broadly representative of the general population. Data were collected between 1994 and 2015, with the aim to analyze background risk of cardiovascular disease in children and adults with AD in the absence of biologic and other targeted immunomodulatory therapies, which may separately modify the effect of AD on cardiovascular disease. All patients in THIN with a diagnosis of AD were included. Each AD patient was matched to up to 5 non-AD patients based on age (±3 years), same practice and encounter date. Outcomes were MI, CVA (stroke), diabetes, hypertension, dyslipidemia, DVT, PE. Cox regression analysis was used to compare outcomes in patients with AD vs those without AD patients. 95% CI are shown in parentheses below HR.

[a]Of the 625,083 adult patients with AD, 2.9% of patients had severe disease. AD severity was estimated using treatments and referrals as proxies.

CV, cardiovascular; THIN, The Health Improvement Network.

1. Lee SW, et al. *Allergy Asthma Immunol Res*. 2023;15(2):231. 2. Lundin S, et al. *J Eur Acad Dermatol*. 3. Wan J, et al. *J Allergy Clin Immunol Pract*. 2023;11:3123–3132.

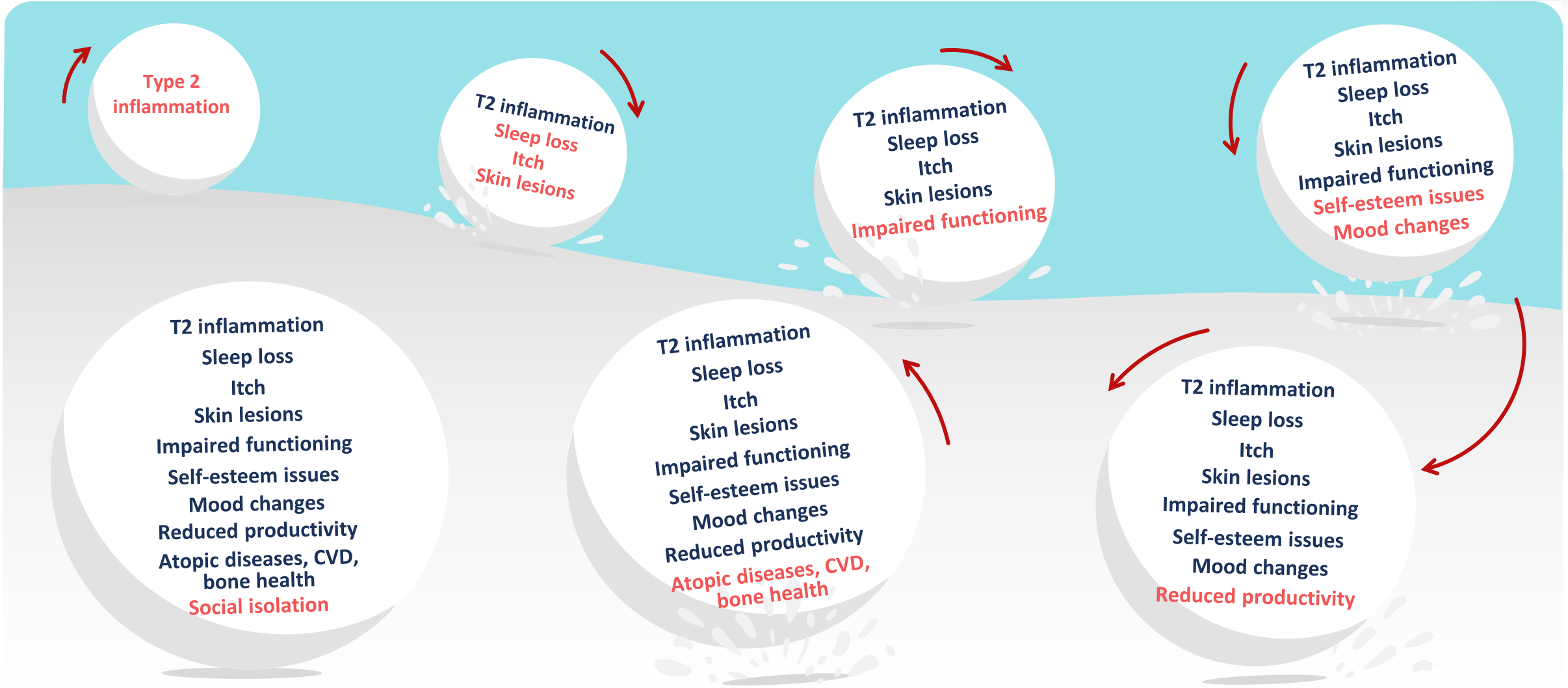
AD Negatively Impacts Career Performance and Productivity in Adults



An average **9.6 hours** of work productivity per week are lost among adults with **moderate AD** and an average of **19 hours** per week are lost among adults with **severe AD**

Adapted with permission from Andersen L, et al. *Br J Dermatol*. 2020;182:1007–1016. Copyright 2020 Oxford University Press.
[a]As determined by the WPAI-SHP questionnaire as an aggregate of percentage of time missed from work and impairment while at work due to health in the past 7 days; [b]Includes Germany, France, and the UK.
NHWS, National Health and Wellness Survey; PO-SCORAD, Patient-Oriented Scoring Atopic Dermatitis; WPAI-SHP, Work Productivity and Activity Impairment – Specific Health Problem.
Andersen L, et al. *Br J Dermatol*. 2020;182:1007–1016.

The Cumulative Effects of AD Contribute to the Burden of Disease, Emphasizing the Importance of Early Intervention



CVD; cardiovascular disease; T2, type 2.

1. Haddad EB, et al. *Dermatol Ther (Heidelb).* 2022;12:1501–1533. 2. Beck LA, et al. *JID Innov*. 2022;2:100131 3. Paller AS, et al. *Dermatol Ther*. 2023;13:961–980. 4. Neri I, et al. *J Asthma Allergy*. 2023;16:383–396. 5. Ramirez FD, et al. *Jama Pediatr.* 2019:173:e190025. 6. Wan J, et al. *J Allergy Clin Immunol Pract*. 2023;11:3123–3132. 7. Wan J, *et al. J Allergy Clin Immunol Pract.* 2023:S2213–2198(23)01251-5. 8. Andersen L, et al. *Br J Dermatol*. 2020;182:1007–1016.
9. Henderson AD, et al. *BMC Med*. 2023;21:285. 10. Lowe KE, et al. *J Allergy Clin Immunol*.

Summary

Achieving disease control is an important treatment goal for both patients and physicians, minimizing the impact of disease

IL-4 and IL-13 play key roles in the signs and symptoms of AD and contribute to the cumulative burdens that develop over time when the disease is uncontrolled

Future studies should address the benefit of early intervention on reducing systemic type 2 inflammation, thereby reducing atopic and non-atopic comorbidities associated with moderate-to-severe AD

IL, interleukin.

Polling Question

How do you define disease control in your patients with AD?

Select one response

A **Absence of flares (no disease worsening with need of treatment escalation) for at least 3 months**

B **Clear or almost clear skin, no or minimal itch, no impact in quality of life for at least 6 months**

C **Maintaining ADCT score <7 for 6 consecutive months**

D **Maintaining EASI<7 and itch <4 over at least 3 months**

E **Other**

ADCT, Atopic Dermatitis Control Tool; EASI, Eczema Area and Severity Index.

Panel Discussion

Importance of Achieving Disease Control in Adults with Moderate-to-Severe AD

1. What are the cumulative impacts of uncontrolled AD in adults?
2. Do you observe any differences in the clinic regarding the burden between adults with early-onset vs adult-onset AD?
3. What barriers do you see to early intervention in adults?

Practical Considerations in Older Patients With AD

Katrina Abuabara, MD, MA, MSCE

Polling Question

Late onset AD needs to be appropriately diagnosed, making sure to exclude all of the following diseases that might present similarly, except

Select one response

A Cutaneous lymphoma

B Food allergy

C Paraneoplastic dermatomyositis

D Toxicoderma

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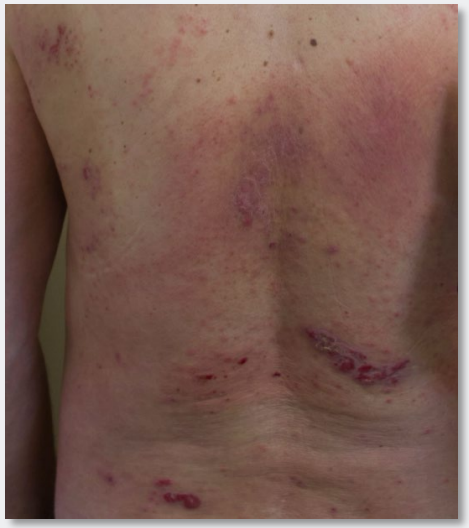
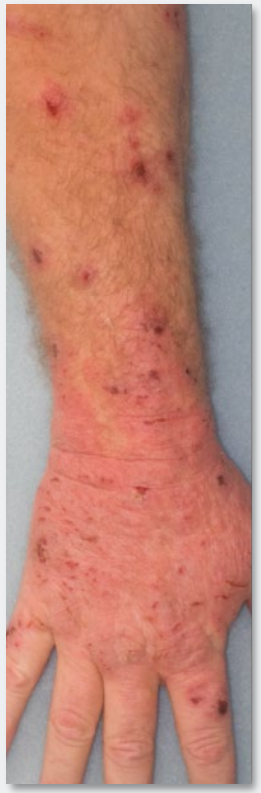
Case Study: Atopic Dermatitis in an Older Adult Patient

Thomas

Male
64-years-old





Clinical history

- Diagnosed at 45 years of age
- Xerosis and erythematous plaques on back and extremities
- Has experienced 2 episodes of skin infections in the last year

Treatment history

- Tacrolimus 0.1% ointment and betamethasone 0.1% ointment
- Stopped cyclosporine after 6 weeks due to increased cholesterol
- Sitagliptin phosphate 100 mg qd, metformin 1 g qd, and gliclazide 12 mg qd for diabetes mellitus
- Ezetimibe 10 mg qd for hypercholesterolemia
- Bupropion hydrochloride 150 mg qd for depression/anxiety

Burden

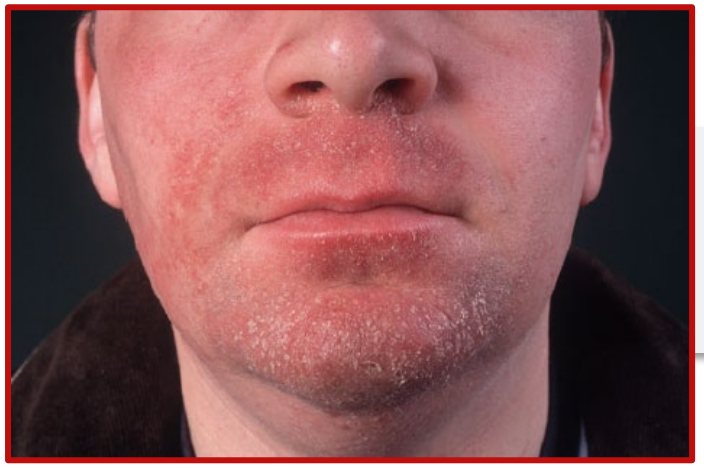
- Thomas reports severe pain/discomfort, his skin is continuously itchy, sore, painful and stinging, and he feels very embarrassed and self-conscious
- He also suffers from anxiety and depression according to the HADS scale

Fictional case study and photos adapted with permission from Sanofi and Regeneron.
HADS, Hospital Anxiety and Depression Scale; qd, once per day.

Considering Differential Diagnoses in Late-onset AD Is Important

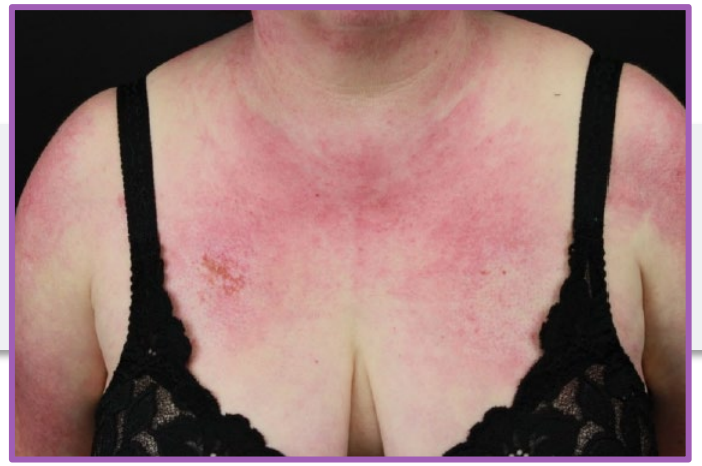
Familiarity with cutaneous diseases that can mimic, coexist with, or complicate AD is critical for correct and timely diagnosis and optimal treatment[1,2]

Cutaneous lymphoma[2]



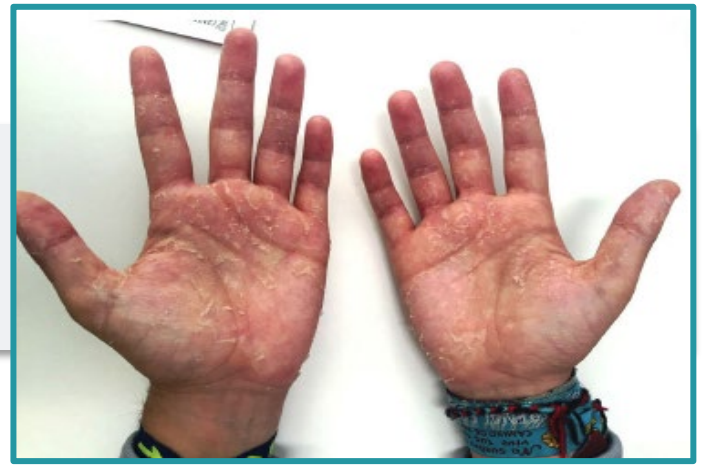
- May present as scaly patches/plaques or generalized erythema
- Lesions may respond favorably to TCS, delaying diagnosis
- Adult onset, lack of atopy, and weight loss/malaise are key to differential diagnosis

Paraneoplastic dermatomyositis[3]



- Manifests as pruritic, erythematous rash and edema on the trunk and eyelids
- Lesions precede diagnostic muscle weakness by months or years in 50% of patients, complicating diagnosis

Toxicoderma[4]



- Drug-induced erythroderma and edematous or vesicular lesions may be indecipherable from AD
- Diagnosis may be complicated by polypharmacy and drug interactions

Left photo reproduced with permission from Nashan D, et al. *Br J Dermatol*. 2007;156:1–10. Copyright 2007 from John Wiley & Sons.; center photo reproduced under the Creative Commons Attribution (CC-BY 4.0). Didona D, et al. *Int J Molec Sci*. 2020;21:2178.; right photo reproduced with permission from Vizcaino Castillo B, et al. *Nefrología*. 2019;39:211–213. Left photo: Mycosis fungoides, the most common cutaneous T-cell lymphoma[5]; center photo: erythematous maculopapular rash of the upper chest[3]; right photo: pruritic, erythematous-desquamative lesions on the palms following 3 weeks of PD.[6]

AR, adverse reactions; PD, peritoneal dialysis; TCS, topical corticosteroids

1. Tétart F, Joly P. *Eur J Dermatol*. 2020;30:663–667. 2. Siegfried EC, Hebert AA. *J Clin Med*. 2015;4:884–917. 3. Didona D, et al. *Int J Molec Sci*. 2020;21:2178. 4. Madrid MJ, et al. *Int J Med Sci Clin Res*. 2022;2:1447–1451. 5. Nashan D, et al. *Br J Dermatol*. 2007;156:1–10. 6. Vizcaino Castillo B, et al. *Nefrología*. 2019;39:211–213.

AD is a Chronic, Inflammatory Disease That Can Present at Any Age

PEDIATRIC AD

- **Early onset** of disease is typical in AD[1–3]
- **Early-onset severe AD** may be a risk factor for disease persistence and the development of comorbidities[4]
- **The proportion of children** whose AD symptoms persist into adulthood varies among studies[5,6]

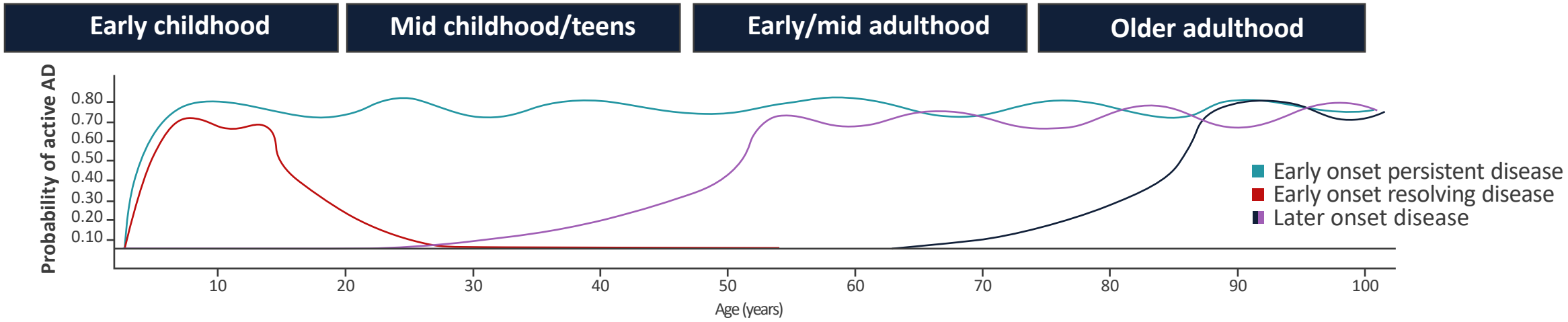
ADULT AD

- **Later onset** after early childhood is also common, however[3,7]
- **AD in older adults** (n=118,430) was active for a greater proportion of follow-up time compared to children (n=255,622) and adults (n=520,402) in a longitudinal study[8]
- **~7.0–9.3%** of the older adult population is estimated to be affected by AD[8]

1. Bieber T, et al. *J Allergy Clin Immunol.* 2017;139:S58. 2. Weidinger S, et al. *Lancet*. 2016;387:1109. 3. Abuabara K, et al. *J Allergy Clin Immunol*. 2019;144:710–719. 4. Irvine AD, Mina-Osorio P. *Br J Dermatol*. 2019;181:895–906. 5. Kim JP, et al. *J Am Acad Dermatol*. 2016;75:681. 6. Abuabara K, et al. *JAMA Dermatol*. 2021;157(10):1191–1199. 7. Lee HH, et al. *J Am Acad Dermatol.* 2019;80(6):1526–1532. 8. Chan LN, et al. *PloS one*. 2021;16:e0258219.

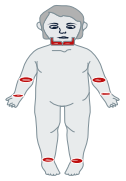
Clinical Disease Onset May Occur at Any Age, and the Most Common Phenotypic Patterns Can Vary at Different Ages

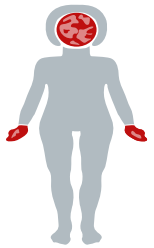
Disease course

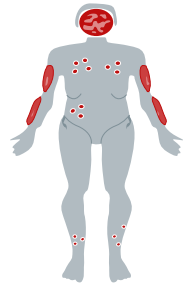


Phenotype

- Heterogeneous but differential distributions by age
- Most severe in early childhood and older adulthood
- More common in male infants and older adults



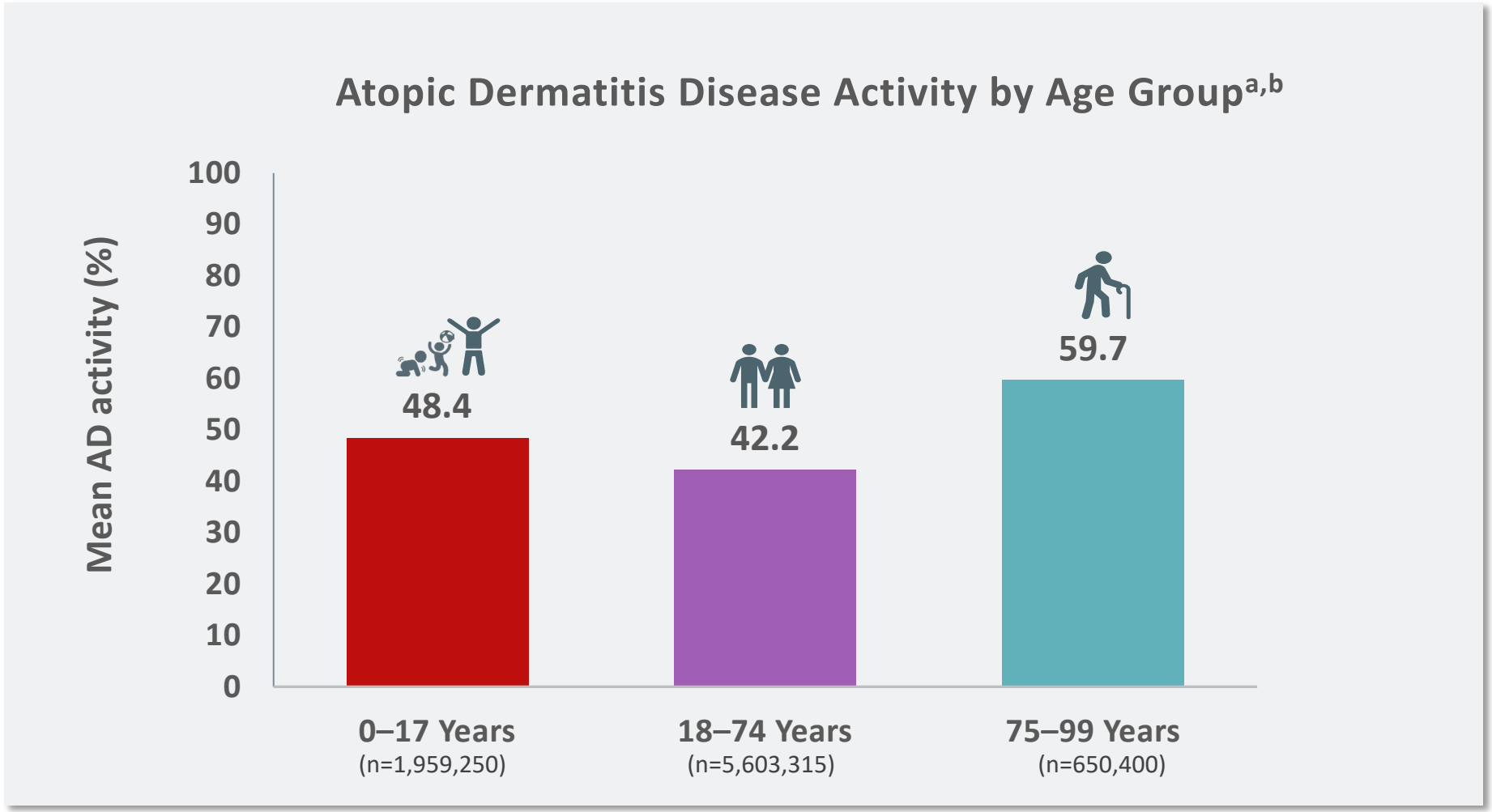




AD is a heterogenous condition with respect to its highly variable disease course and its age-associated phenotype/clinical presentation

Graph and figure adapted with permission from Abuabara K, Langan SM. *Br J Dermatol*. 2023;188:709–717. Copyright 2023 Oxford University Press.
Data are based on cross-sectional evaluations of clinic populations and did not examine changes among individuals over time.
Abuabara K, Langan SM. *Br J Dermatol*. 2023;188(6):709–717.

AD in Older Adults Is More Active Than in Children and Adults



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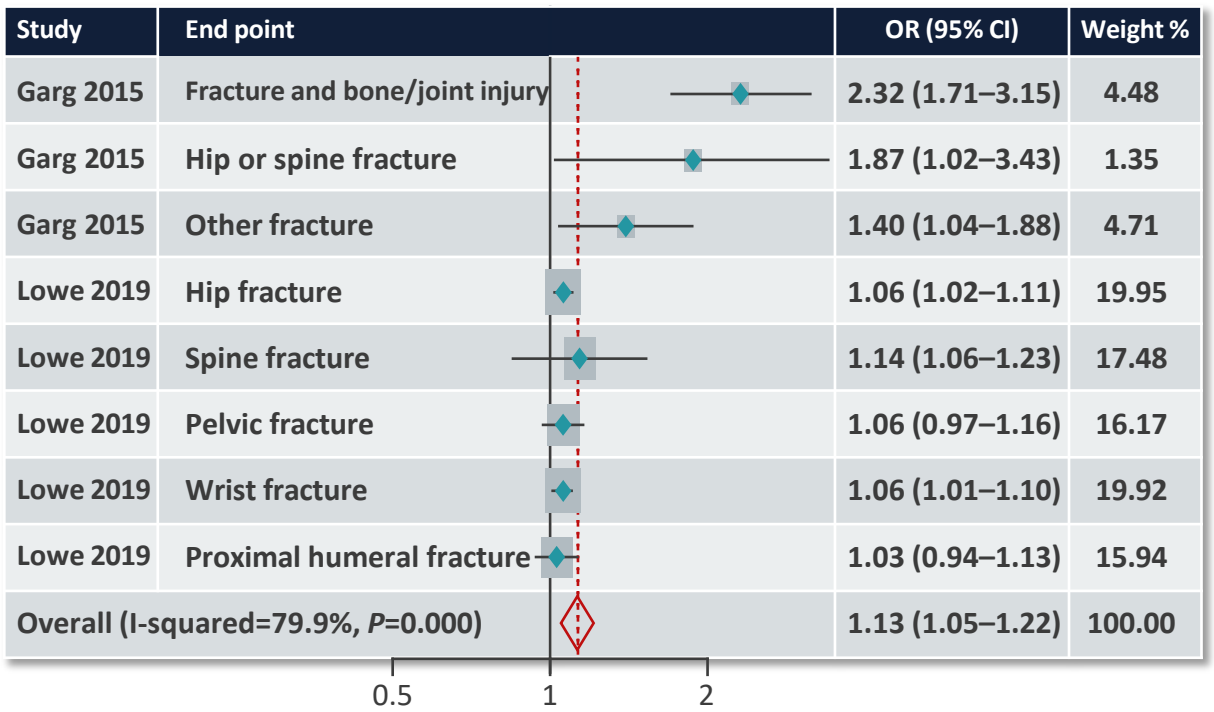
[a]Disease activity was determined by dividing the number of years in which an individual had an additional diagnosis or treatment code for AD by the total number of years of follow-up for that individual. [b]Mean proportion of years with prevalent AD as a percent of total years of follow-up 95% CI by age category.

Chan LN, et al. *PloS one*. 2021;16:e0258219.

Moderate-to-Severe AD is Associated With an Increased Risk of Fractures, Osteoporosis, Osteopenia, and Decreased Bone Mineral Density[1,2]

Risk of fracture is higher among adult patients with AD compared to those without[2]

Study	End point	OR (95% CI)	Weight %
Garg 2015	Fracture and bone/joint injury	2.32 (1.71–3.15)	4.48
Garg 2015	Hip or spine fracture	1.87 (1.02–3.43)	1.35
Garg 2015	Other fracture	1.40 (1.04–1.88)	4.71
Lowe 2019	Hip fracture	1.06 (1.02–1.11)	19.95
Lowe 2019	Spine fracture	1.14 (1.06–1.23)	17.48
Lowe 2019	Pelvic fracture	1.06 (0.97–1.16)	16.17
Lowe 2019	Wrist fracture	1.06 (1.01–1.10)	19.92
Lowe 2019	Proximal humeral fracture	1.03 (0.94–1.13)	15.94
Overall (I-squared=79.9%, *P*=0.000)		1.13 (1.05–1.22)	100.00



Forest plot showing fracture risk in patients with AD.
Weights are from random effects analysis.

Patients with severe AD are at greater risk of vertebral, pelvic, and hip fractures[2–4]

~10% ↑ fracture risk

in people **with atopic eczema** compared to people without[3]

18% ↑ **spine** fractures[3]

10% ↑ **pelvis** fractures[3]

7% ↑ **wrist** fractures[3]

10% ↑ **hip** fractures[3]

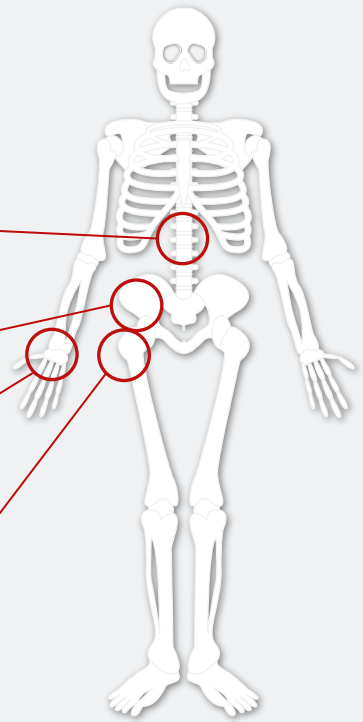


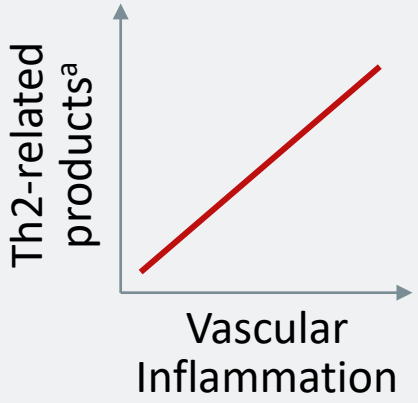
Table adapted with permission from Wu D, et al. *Ann Transl Med.* 2021; 9:40.; figure adapted under the Creative Commons Attribution (CC-BY 4.0). Lowe KE, et al. *J Allergy Clin Immunol.* 2020;145:563–571.
OR, odds ratio.

1. Shaheen MS, Silverberg JI. *J Am Acad Dermatol.* 2019;80:550–551. 2. Wu D, et al. *Ann Transl Med.* 2021; 9:40. 3. Arkwright PD, Mughal MZ. *J Allergy Clin Immunol.* 2020;145:487–488.
4. Lowe KE, et al. *J Allergy Clin Immunol.* 2020;145:563–571.

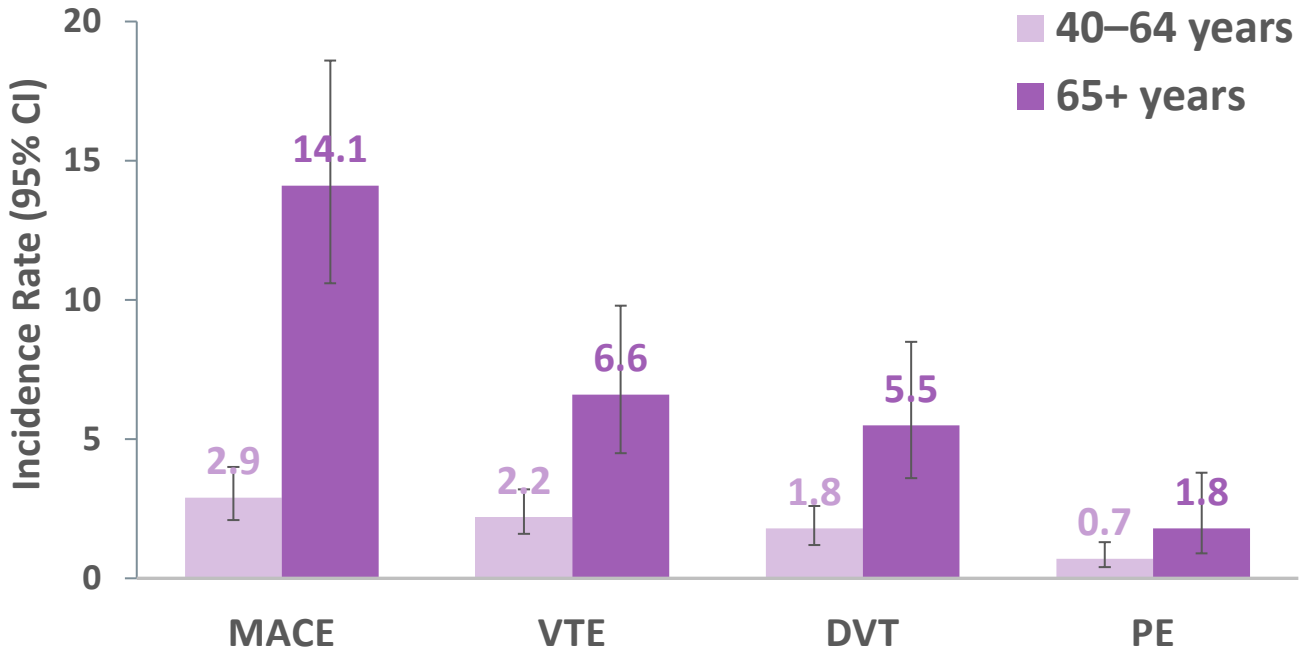
Older Adults With Moderate-to-Severe AD Are at High Risk of CVEs

Adults with AD had significantly **greater vascular inflammation**, as indicated by increased endothelial-derived microparticles compared with non-AD controls[1]

Vascular inflammation correlated with Th2-related products in patients with AD[1]

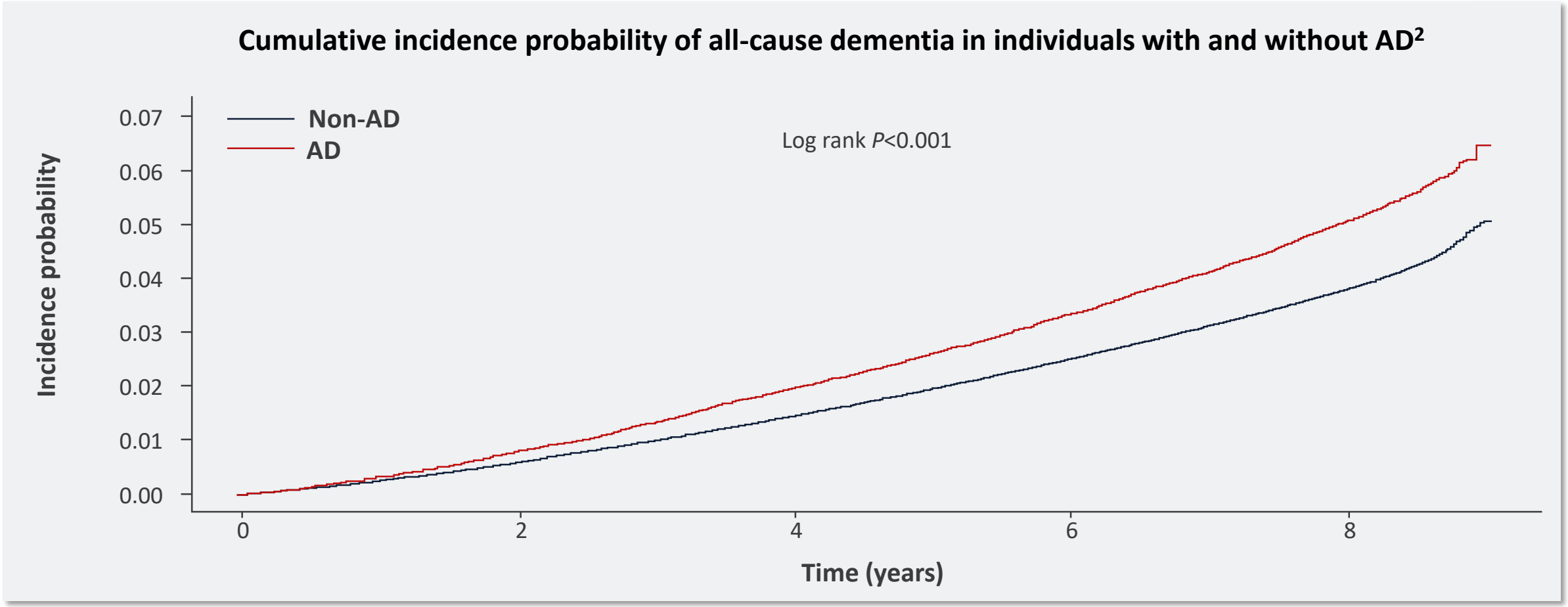


Incidence rates of MACE, VTE, DVT, and PE are higher in older than younger patients with moderate-to-severe AD[2,b]



Graph adapted under the Creative Commons Attribution (CC-BY 4.0). Hedderson MM, et al. *PLoS One*. 2022;17:e0277469.
[a]IL-4R, IL-13, CCL13, CCL17, CCL18. [b]Incidence rates of cardiovascular events per 1000 person-years by age group in patients with moderate-to-severe AD.
CCL, C-C motif chemokine ligand; CVE, cardiovascular event; DVT, deep vein thrombosis; IL, interleukin; MACE, major adverse cardiovascular events; PE, pulmonary embolism; Th, T helper; VTE, venous thrombotic event;
1. Villani AP, et al. *Allergy*. 2021:76:3107–3121. 2. Hedderson MM, et al. *PLoS One*. 2022;17:e0277469.

AD Is Associated With an Increased Risk of Dementia and Alzheimer's Disease in Middle-aged and Older Adults[1,2]



The possible mechanisms underlying this association may include chronic inflammation, oxidative stress, sleep disturbance, psychological distress, and reduced quality of life[1]

Graph adapted with permissions from Woo YR, et al. *Acta Derm*. 2023;103.

1. Zhou Q, Yang D, Xiong C, Li X. *Plos one*. 2023;18:e0292987. 2. Woo YR, et al. *Acta Derm*. 2023;103.

Sleep Disturbances Impact Older Adult Patients With AD to a Greater Extent Than Younger Adult Patients

Adults with AD were significantly **more likely to report sleep disturbances** than adults without AD[1,2,a,b]

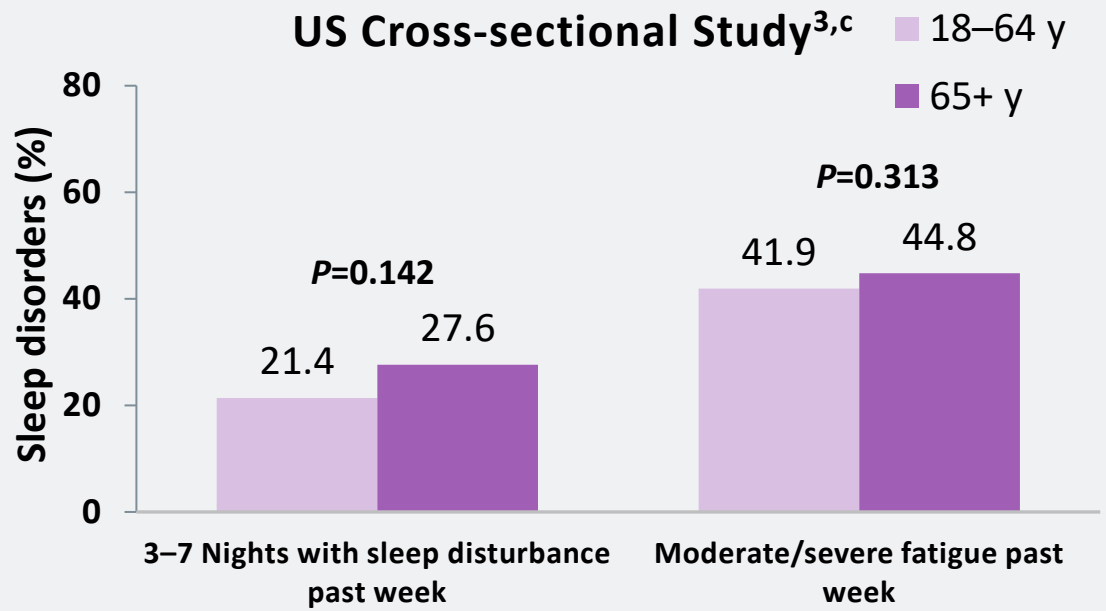
AD sleep disturbance

22–33%

Non-AD sleep disturbance

13–19%

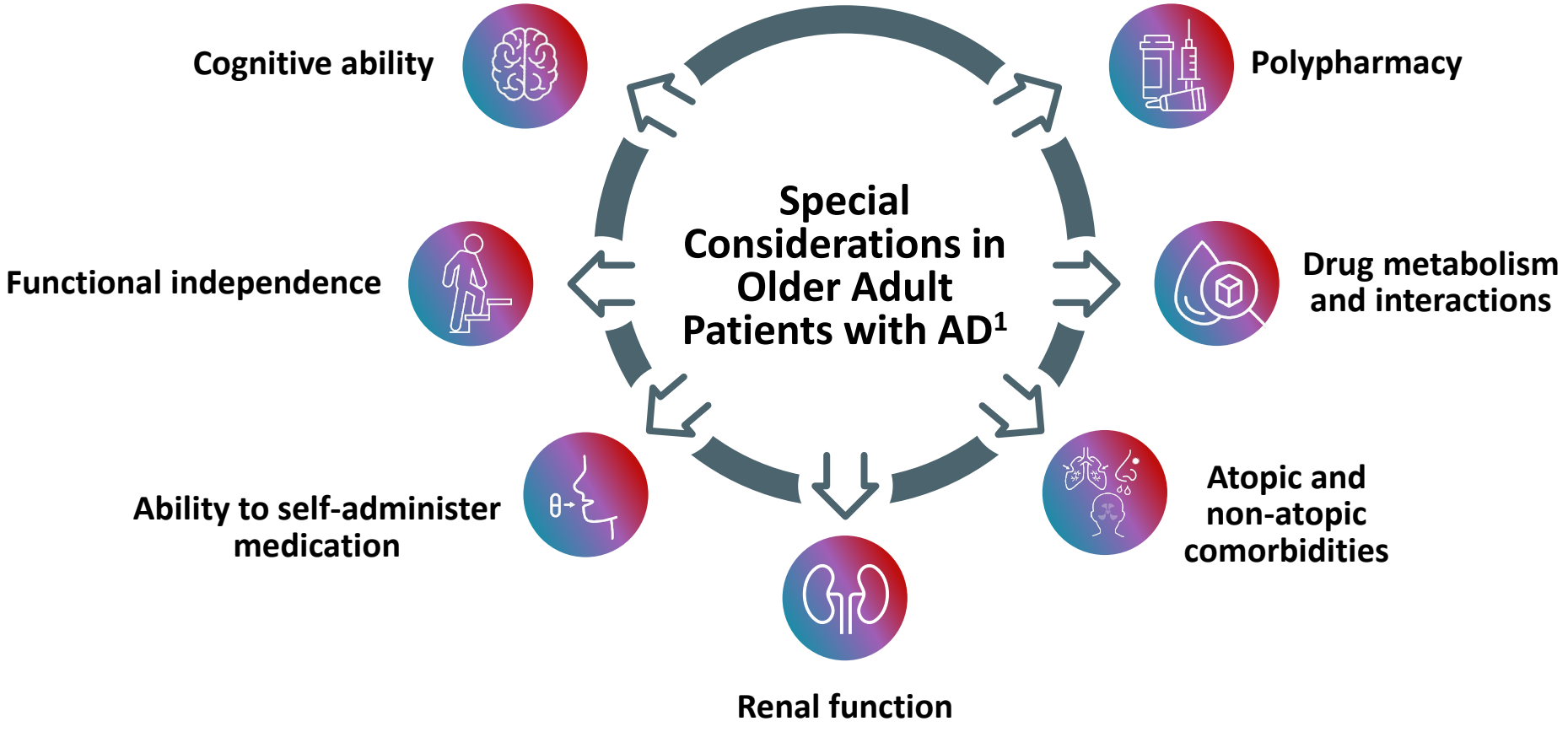
Older adult patients with AD had more profound sleep disturbance than younger adult patients[3]



[a]Survey of US adults; analyses included 349 adults with AD matched to 698 adults without AD. [b]Survey of European adults; analyses included 1860 adults with a self-reported diagnosis of AD who were propensity score matched to 1860 adults without AD. [c]A cross-sectional study of adults (≥18 years) with AD diagnosed based on the Hanifin-Rajka criteria completed self-administered electronic questionnaires on their sleeping habits.
Older adult AD is associated with increased number of nights with sleep disturbance due to eczema as well as delays in falling asleep and night-time awakenings due to itching.

1. Eckert L, et al. *J Am Acad Dermatol*. 2017;77:274–279. 2. Eckert L, et al. *J Am Acad Dermatol.* 2019 Jul;81:187–195. 3. Manjunath J, Silverberg JI. *J Am Acad Dermatol*. 2022;87:206–208. MAT-GLB-2305896 V4 03/2024

Special Considerations Are Warranted Prior to Making Management Decisions in Older Adult Patients With AD[1]



Although older adults exhibit a distinct presentation of AD and important comorbidities, many investigations and AD guidelines do not differentiate them as a separate group from younger adults[2,3]

1. Adam DN, et al. *J Eur Acad Dermatol Venereol*. 2023;37:1135–1148. 2. Williamson S, et al. *Br J Dermatol.* 2020;182:47–54. 3. Lam M, et al. *JAMA Dermatol.* 2020;156:1240–1245.

Polypharmacy and Its Associated Risks Can Act as a Burden in Older Patients With AD

Polypharmacy (ie, the regular use of numerous treatments for ≥1 condition) is associated with medication-related AEs, inappropriate medication use, medication non-adherence, and, especially among older adults, increased frailty, falls, and mortality[1]

Individuals on multiple medications had more **severe AD** (severe: 46.0%), **poorer disease control** (minimally controlled: 37.1%), **increased days of flare** in the past month (≥11: 37.5%), and **increased HCP visits for AD** in the past year (≥5: 61.9%) (all *P*<0.001)[1]

Topical treatment regimens for AD are time-consuming, difficult to apply, can lead to stinging, burning and other AEs, stain clothing and linens, cause overheating and inhibit sweating, increase OOP costs, and provoke anxiety[1]

In a general population of older adults, **mortality risk** was increased in individuals consuming **≥6 medications** (HR=1.83, 95% CI: 1.51-2.21, *P*<0.001) compared to a nonmedicated reference group[2,a]

[a]Controlled for baseline age, sex, comorbidity index, Parkinson's disease, current smoker, and current drinker.
AE, adverse event; HCP, healthcare professional; HR, hazard ratio; OOP, out of pocket.
1. Chovatiya R, et al. *J Drug Dermatol*. 2023;22:154. 2. Gómez C, et al. *Gerontology*. 2014;61:301–309.

Summary

Late onset dermatitis should be appropriately diagnosed, excluding potential cutaneous lymphoma, paraneoplastic dermatoses, and toxicoderma

Older adult populations are especially vulnerable to AD-related, systemic comorbidities which add to the combined burden of the disease and must be considered when managing AD

The treatment of older adult patients with AD is complicated by several age-dependent factors, adherence challenges, and clinical considerations such as polypharmacy and its associated risks

Polling Question

Late onset AD needs to be appropriately diagnosed, making sure to exclude all of the following diseases that might present similarly, except

Select one response

A Cutaneous lymphoma

B **Food allergy**

C Paraneoplastic dermatomyositis

D Toxicoderma

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Panel Discussion 3

Practical Considerations in Older Patients With AD

1. What are some key disease burdens your older adult patients have faced?
2. Have you observed any differences in comorbidities between younger and older patients?

Perspectives on the Management of Patients With Moderate-to-Severe AD Across Age Groups

Eric Simpson, MD, MCR

Management Perspectives on Therapeutic Classes in AD[1,2]

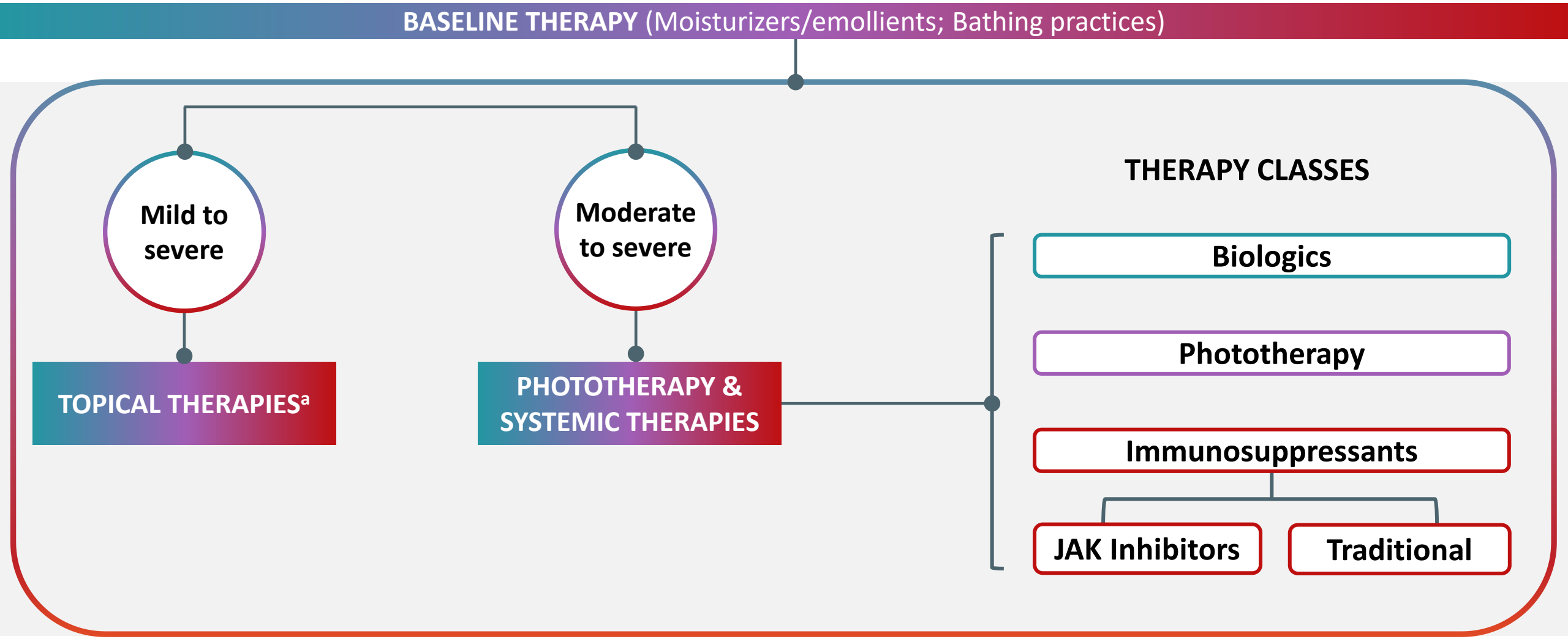


Figure adapted with permission from Davis DMR, et al. *J Am Acad Dermatol*. 2024;90:e43-e56.

[a]Topical agents can be used concurrently with phototherapy or systemic agents for maintenance of response, rescue, or treatment of flares.

1. Davis DMR, et al. *J Am Acad Dermatol*. 2024;90:e43-e56. 2. Chu DK, et al. *Ann Allergy Asthma Immunol*. 2023.

Symposium Summary and Conclusions

Eric Simpson, MD, MCR

Understanding the Cumulative Impact of AD Highlights the Potential Benefit of Early Intervention[1,2]

Even when an individual is performing well according to individual component measures, they may still have **significant life course impairment** due to the **cumulative impact of past events**[a]

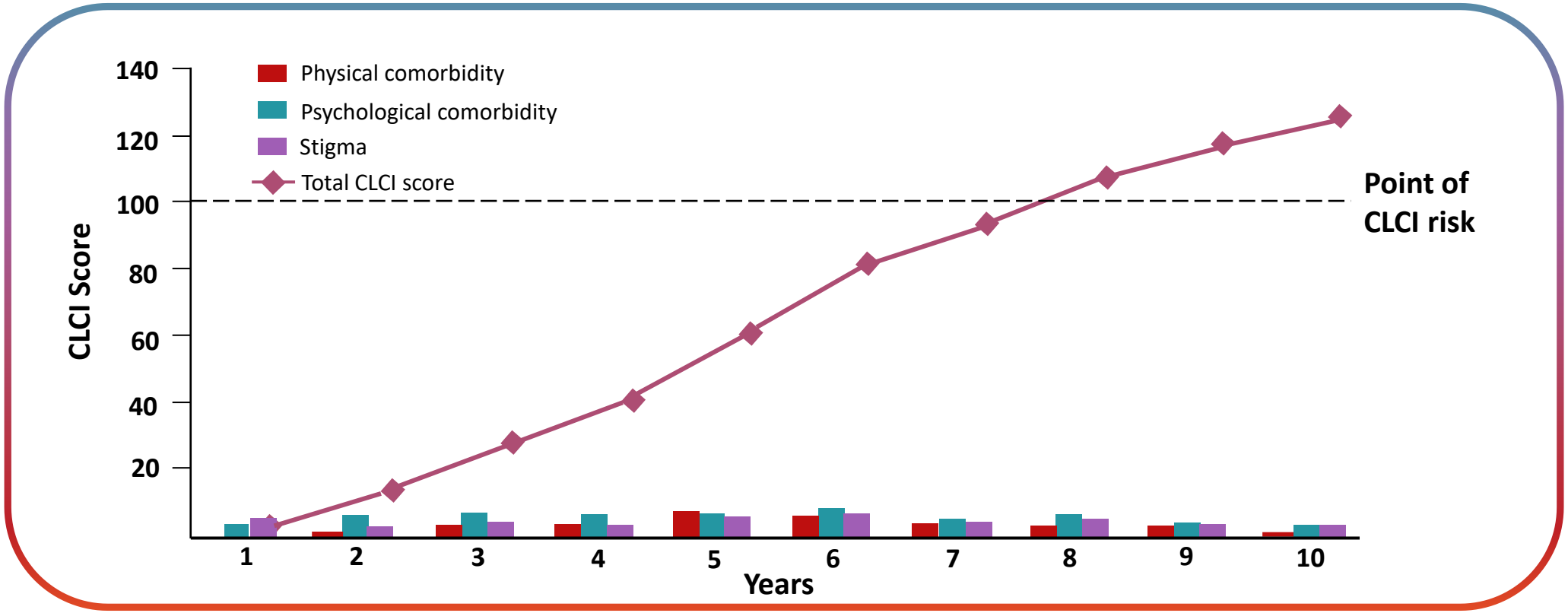


Figure adapted with permission from Kimball AB, et al. *J Eur Acad Dermatol Venereol.* 2010;24:989–1004. Copyright 2010 John Wiley & Sons, Inc.
[a]As seen with another chronic inflammatory skin disease with both physical and psychological comorbidities, and stigma, even when an individual is performing well on individual component measures, they may still have significant CLCI.
CLCI, cumulative life course impairment.
1. Kimball AB, et al. *J Eur Acad Dermatol Venereol.* 2010;24:989–1004. 2. von Stülpnagel CC, et al. *J Eur Acad Dermatol Venereol.* 2021;35:2166–84.

Conclusions

Atopic dermatitis is a chronic, systemic, disease in which type 2 inflammation impacts both the **skin** and an array of **other organ systems** over an individual's **life course**

Atopic dermatitis presents unique and overlapping burdens in **pediatric, adult, and older adult populations**, complicated by age-dependent factors and associated **cumulative life impacts** that may compound over time

The **cumulative impact** of systemic inflammation emphasizes the **importance of early intervention**, regardless of age group, to stop or limit the progression of AD **and reduce these burdens**

Concepts to Consider When Discussing the Potential for Disease Modification

Impact on disease itself

*"Any intervention that endurably impacts the **pathomechanisms** and the **natural course of the disease** leading to a **sustained remission** after cessation of treatment"*

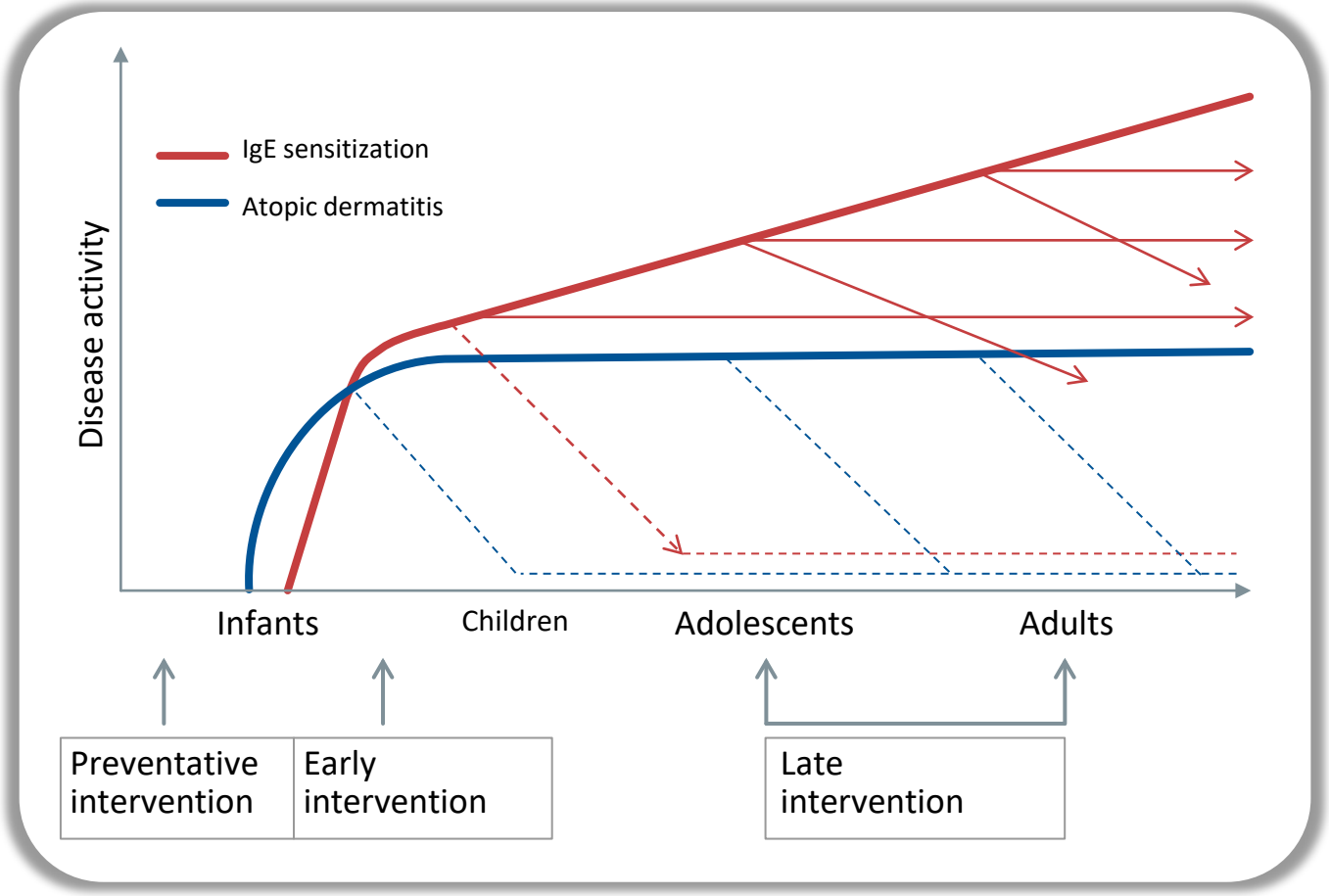
Impact on associated comorbidities

*"An intervention successfully **preventing the development or the progression of atopic comorbidities** (food allergy, allergic asthma and/or allergic rhinitis, before or during their development)"*

There is currently **no agreed definition for disease modification**

Bieber T. *Nat Rev Drug Discov*. 2023;22:662–680.

AD Can Follow Multiple Trajectories From Childhood Through to Adulthood



During infancy and childhood[1]

- Could early intervention in infancy and childhood stop the progression of AD and the development of atopic comorbidities?
- The natural course of allergic sensitization starts early after AD onset and increases during the persistency of the disease

Adolescents and adults[1]

- At a later stage in adolescents and adults, a complete therapy-free remission could be reached for AD
- Comorbidities could potentially be stabilized or even partially reversed[a]

Limiting exposure to allergens through the skin and controlling type 2 inflammation at an early age may help to modify disease course in AD[2]

Figure adapted with permission from Bieber T. *Nat Rev Drug Discov*. 2023;22:662–680. Copyright 2023 Springer Nature.

[a]These are only indicative scenarios that may not represent all possible trajectories in this complex phenotype. Solid blue line illustrates the persistent trajectory of AD without disease-modifying intervention, whereas the dotted line shows the full and endurable remission on successful disease modification. The solid red line illustrates the natural course of allergic sensitization as a surrogate for atopic comorbidities, which starts early after AD and increases during the persistency of the disease.

1. Bieber T. *Nat Rev Drug Discov*. 2023;22:662–680. 2. Paller AS, et al. *J Allergy Clin Immunol*. 2019;143:46–55.

Panel Discussion 4

Potential for Disease Modification in AD

1. Do you agree with the proposed definitions for disease modification in AD?
2. How could real world evidence be leveraged to evaluate whether disease modification is occurring?

Evaluation form

Please remember to complete the evaluation form

Thank you!

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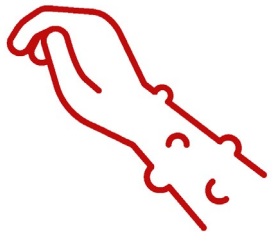

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